Review of exposure-response relationships for diesel exhaust particulate and lung cancer

A summary for public release

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## CONTENTS

**BACKGROUND**  
4

**SUMMARY**  
4

1 INTRODUCTION  
6

2 THE EXPOSURE ASSESSMENTS IN THE THREE KEY STUDIES  
8

2.1 The US mining study  
8

2.2 The two Trucker studies  
9

2.3 Overall conclusions from the exposure studies  
11

3 EXPOSURE-RESPONSE ANALYSIS  
12

3.1 The US mining study  
12

3.2 A published pooled analysis  
13

3.3 An Alternative Pooled analysis  
14

4 CONCLUSIONS AND DISCUSSION  
15

5 REFERENCES  
16
BACKGROUND

BHP Billiton commissioned IOM to assess all the relevant and related literature and advise whether there is sufficient data available to develop exposure-response curve(s) to enable BHP Billiton to review its health-based occupational exposure limit for diesel exhaust.

This document provides a summary of the critical analysis that was performed to develop the most appropriate exposure-response curve, the key assumptions that underpin it, potential sources of bias and their impact, limitations and the margins of error around the risk estimates.

BHP Billiton and IOM have agreed to make this document publicly available to interested parties, particularly industry associations and professional societies, to support informed discussion, debate and decision-making by all key stakeholders about management of diesel exhaust emissions.

SUMMARY

This review examines three key epidemiological studies where workers were exposed to diesel engine exhaust emissions: a cohort of US miners and two studies in truckers. These studies were all well conducted epidemiological studies that used the same general approach to reconstruct past exposures. The methods used to estimate exposure to diesel exhaust particulate (DEP) are generally accepted by the scientific community and are widely applied in studies that are used to inform the development of exposure-response relationships. Each study used different proxy measures of DEP to adjust recent measures of personal occupational exposure to elemental carbon (EC) as a marker of DEP.

We concluded from a detailed review of the exposure assessment for the miner study that exposures are likely to have been over-estimated giving rise to a probable under-estimate of risk. This over-estimation arises from the approach used to model exposure and also a failure to take account of the use of respiratory protection, which would have been widely used to protect against dust exposure. The over-estimation of exposure is believed to apply to the whole range of exposures and is therefore unlikely to have impacted on the shape of the exposure response relationship. The exposure assessment for one of the two trucker studies (reported by Steenland and colleagues) was judged much less reliable than for the other study, and very likely to be strongly positively biased. This study was not considered suitable to define an exposure-response relationship.

The mechanisms by which DEP causes lung cancer are not sufficiently understood to inform the shape of an appropriate exposure-response relationship. Comparison with exposure-response information for other agents such as smoking and particulate matter in ambient air, which may have similar mechanisms and hence exposure response curves was also
uninformative. We therefore consider that the shape of the exposure response relationship should be guided by the statistical analysis alone.

Various curves were fitted to the data available from the three epidemiological studies resulting in similar relative risk (RR) at lower exposures but vastly different estimates at higher exposures. The lack of data at very high exposures levels, and lack of evidence supporting a particular shape for the exposure-response curve implies that the choice of the best exposure-response function should be based on statistical significance.

The derived exposure-response relationships suggest that exposure to DEP is associated with a marked elevation in lung cancer risk even at relatively low levels of exposure. There are practical difficulties in lowering exposures to a level associated with a predicted lifetime cancer risk of less than 0.1% or even 1%. It may therefore be impractical to set a meaningful health-based limit on occupational exposure to DEP. However, the evidence is, in our opinion, strong enough to recommend controlling exposures to DEP to the lowest level that is technically achievable. In the absence of a threshold for lung cancer, any reduction in exposure to DEP will be beneficial. In using the exposure-response relationships to decide the level at which to set a limit, it would be appropriate to review existing levels of occupational exposure and the opportunities for exposure reduction. The limit value should be set low enough to drive an overall reduction in exposure to DEP and to lead to a meaningful reduction in cumulative exposure in the working population. Ideally a long-term programme of planned reductions in exposure should be in place to ensure ongoing improvement in exposure control and an associated reduction in the risk of lung cancer in the workforce.
1 INTRODUCTION

Epidemiology is the scientific study of links between exposures and health, where an exposure can be anything from tobacco smoke and air pollution to diet or physical activity. Occupational epidemiology focuses on the health effects associated with work-related exposures, such as inhaling asbestos or crystalline silica. It is important when investigating links between exposures and disease to gather reliable quantitative information on the relevant exposures, the health effects of interest and other factors that may have an impact on those health outcomes. An important concern is to avoid sources of bias that may lead to misinterpretation of the data.

Sometimes associations between exposures and disease may occur by chance or may result from biases in the epidemiological study. To show causality it is necessary to have multiple sources of information from epidemiological studies, along with toxicological and other scientific investigations that provide a weight of evidence to support the conclusion. An important indicator of a causal relationship is an epidemiological association where the risk increases with increasing exposure, after accounting for other potential risk factors. The resulting relationship, often described as an exposure-response or dose-response relationship, can then be used to identify “safe” limits on workplace exposure or make recommendations for public health interventions. Often it is assumed that the cumulative exposure to an agent over a whole working life is most closely associated with the risk. Cumulative exposures are calculated by multiplying the level or intensity of exposure by the duration of exposure, for example if the exposure level is expressed as mg/m$^3$ then the cumulative exposure can be expressed in ‘mg/m$^3$.years’.

In order to ensure that any exposure-response relationship is suitable to be used for risk assessment various aspects of the relevant studies should be evaluated, for example the quality of the information regarding the health effects of interest, the methods used to estimate the exposures and the statistical methods used in both the design and analysis of the study.

Occupational epidemiology typically investigates a defined group of workers (cohort) within which the level of exposure is likely to vary. Often the health effect of interest is death from specific causes or incidence (diagnosis) of specific diseases. This information is usually recorded by the state of health authorities and retrievable, with appropriate ethical safeguards, from national records agencies. Many studies of occupational cancers and other chronic diseases are carried out retrospectively, i.e. we define a cohort of workers from historic company records and then identify who is alive and dead today.

Exposure information is often more difficult to access as there are no national recording systems. Ideally, measurements of the actual exposure experienced by every member in the cohort would be available. This is almost never the case, particularly when carrying out retrospective studies where exposures may have occurred many decades prior to death or
disease. In such circumstances, it is necessary to reconstruct past exposure levels to produce estimates of cumulative exposure, for each person in the cohort. Researchers have developed a number of strategies to estimates past exposure, for example by extrapolating recent estimates of exposure (eg based on measurements) back in time using one or more proxy indicators to predict past exposure levels. In order for the exposure-response relationships to be judged reliable it is important that the exposure assessment methodology is robust and that bias is minimised.

Recruitment bias in retrospective cohort studies needs to be minimised to ensure that the individuals recruited into the study are representative of the population of interest and that individuals are generally recruited to the study without knowledge of whether they have the health effect of interest. The analysis of the study should be appropriate, generally using logistic regression where the shape of the exposure-response curve should be chosen based on a combination of statistical fit and, where available, toxicological evidence. In order to have confidence that any relationships identified between exposure and response is sound the analysis should take account of other factors that may have an effect on the response (e.g. smoking status in the case of lung cancer). Furthermore, the analysis should also take into account the possibility that exposures do not instantaneously result in disease and may in fact take a number of years to have an effect. This is done by employing a lag period in the analysis, which essentially excludes exposures in the years immediately before disease/death (i.e. excludes 5 years before for a 5-year lag).

Diesel engine exhaust (DEE) emissions arise from the combustion of diesel fuel in compression ignition engines. It comprises a complex mixture of gasses and particulates, including water vapour, nitrogen, oxygen, carbon dioxide, carbon monoxide, sulphur oxides, nitrogen oxides, volatile hydrocarbons, aldehydes, and elemental carbon particles.

Based on the published epidemiological and toxicological evidence, DEE has been classified by the International Agency for Research on Cancer (IARC) as a cause of lung and bladder cancer. The risk appears to be related to exposure to the diesel exhaust particulate (DEP), generally measured as the concentration of elemental carbon in the air inhaled by workers. However, to date the available research evidence has generally not been considered appropriate to be used for setting risk based quantitative exposure standards.

Recently a number of epidemiological studies have been undertaken to investigate associations between DEE and lung cancer, and these were relied upon by IARC in identifying DEE as carcinogenic. These studies provide a basis for setting limits for exposure to DEE and various national and international organisations are currently evaluating these possibilities. There are three epidemiological studies that form the main evidence base: a study of underground miners in the USA (by Silverman and colleagues), and two studies of truckers (Garshick and others and Steenland and colleagues). These studies all carried out quantitative retrospective
exposure assessments based on combinations of measurement data and modelling techniques using various proxy measures of exposure with the aim of identifying exposure-response relationships that could be used for quantitative risk assessment.

We begin by evaluating the exposure assessment methods used in the three epidemiological studies and then move on to consider how these data have been used to identify exposure-response curves, and the possibility to combine the data to provide a single curve.

2 THE EXPOSURE ASSESSMENTS IN THE THREE KEY STUDIES

2.1 THE US MINING STUDY

The methods used to derive exposure estimates for the members of the cohort in the Silverman miner study were described in a series of scientific papers. The main metric selected a priori by the researchers to characterise diesel particulate emissions was respirable elemental carbon (REC). This is widely accepted as a specific marker of DEP in mines and there is good toxicological evidence to support that the main risk for cancer is associated with the particulate rather than the gaseous emissions from diesel engines.

A comprehensive exposure measurement survey was carried out by the research team in 7 of the 8 mines under study between 1998 and 2001 (the 8th mine had closed by the time of the surveys). Unfortunately, there was no good information on REC exposure levels prior to these surveys. Instead, the researchers estimated relative trends in exposure based on carbon monoxide (CO) measurement data plus information on historic changes in diesel equipment power and mine ventilation, and used these historical trends together with the recent measurements of REC to obtain retrospective estimates of REC exposure levels back over 20 years. These estimates were made for a range of specific job titles.

The researchers assumed that differences in exposure between the job titles were maintained throughout the time period. This approach will have introduced a small amount of misclassification of worker exposures, although this was probably as often to overestimate as to underestimate exposure. While the relative exposure between jobs may have changed over time, the main between-job differences, e.g. between someone working at the face and someone working in an underground workshop, would have been broadly maintained.

There was no account taken of respirator use by the workers, and the researchers justify this by arguing that usage was optional and that there was no certification (by the US National Institute for Occupational Safety and Health) for the respirators that were used. In our opinion, not
accounting for respiratory protection will have resulted in an overestimation of exposure, although the extent of this bias is unclear. Workers are likely to have used respirators primarily as protection for mine dust rather than DEP, so the failure to account for respirator use may have led to over-estimation of exposure across the full range of DEP exposures rather than simply the high DEP exposure groups.

Despite these reservations, we consider that the general pattern of the modelled exposure changes is appropriate. The temporal change shows a rise in REC exposure after the introduction of diesel equipment in the mines reaching a maximum sometime in the 1970s to 1980s. The REC levels then decrease due to improved ventilation and the introduction of more modern and cleaner diesel equipment. However, we are inclined to believe there is a positive bias in the model estimates.

The authors extrapolated backwards from the measurements made in 1998-2001 assuming that the relationship between CO and REC was linear. However, in their statistical analysis they found that REC was better related to CO in a power relationship that meant that at higher CO levels REC was less than predicted by a linear relationship. If the researchers had used the relationship they identified in their own mine data to extrapolate REC levels the exposure estimates would have probably been less biased. We consider that this bias may have affected the whole range of cumulative exposures and not just those people who were most highly exposed.

The authors carried out some limited validation of their modelled CO concentrations by comparing model estimates with CO measurement data from 1976-77, which was not included in the model building. In five of the six mines for which the data were available the model overestimated the measured CO concentrations (average relative difference was +29%, range -25% to +49%). In our opinion, this further confirms the view that estimated REC concentrations in the 1970s, which are based on the CO models, might on average be about 25% higher than the actual concentrations. The most likely reason for this is the linear CO – REC model utilised by the researchers.

Overall, we consider the exposure assessment for the Silverman et al studies is suitable for estimating an exposure-response relationship for DEP.

2.2 THE TWO TRUCKER STUDIES

Both trucker studies chose to estimate exposure as submicron EC rather than REC. Submicron EC is likely to be slightly lower than REC, because it comprises particles with a diameter below 1 micrometer rather than particles less than around 7 µm, as for REC. According to limited data from a Canadian research study carried out around railroad diesel engines, the submicron EC was about 25% lower than REC.

Steenland and colleagues developed quantitative exposure estimates for an epidemiological study of members of the Teamsters Union in the USA.
Workers were categorised into five job categories: short-haul drivers, long-haul drivers, mechanics, dockworkers and other jobs. The authors relied on a related earlier survey undertaken to measure submicron EC exposure levels in the trucking industry. Steenland and colleagues estimated historical exposure levels by modifying exposure estimates from this exposure study based on historical changes in the vehicle miles travelled and the estimated diesel engine emissions (g/mile). Further adjustments were made to account for background levels and for leaks into long-haul trucks (exposure levels multiplied by 1.5, i.e. a 50% increase). Estimates of exposure for each person in the cohort were derived for the period from 1949 through to the end of the study (1983), and these were combined to produce cumulative exposure estimates. Steenland and his colleagues carried out some sensitivity analyses to investigate the reliability of their results, but they did not attempt any validation of their estimated exposure levels.

The pattern of change is the same in each job category with peak levels predicted between 1970 and 1980. Levels increase steadily from the 1950s up to the peak during the 1970s and then declined between 1980 and 1990. The highest estimated exposure levels were for mechanics (around 120 μg/m³) and for drivers the peak levels were around 20 to 40 μg/m³. These levels are much higher than has been reported in the scientific literature for truck drivers, and for example, the highest arithmetic mean exposure for mechanics was reportedly around 40 μg/m³ and for drivers around 20 μg/m³. It is in our opinion likely that Steenland and colleagues have considerably overestimated past exposure to EC from diesel trucking operations, although the general temporal form of their exposure estimates is probably correct.

Another group of scientists carried out a revision of the exposure estimates used by Steenland and colleagues, following on from a critical appraisal from the US Health Effects Institute (HEI). This work was supported by industrial bodies, who all “provided comments and input on this work”. The authors used the same basic model format as Steenland and colleagues, with the exception that for mechanics they removed the term for vehicle miles travelled and replaced it by a term adjusting for the proportion of trucks “for-hire” that were powered by diesel. The critique resulted in radically different set of exposure estimates with much lower maximum exposure levels that occurred around 1990. The temporal trends for the different job classifications were mostly monotonically increasing with time. We consider that this analysis supports our view about the unreliability of the analysis in the Steenland et al paper.

For the above reasons we do consider the epidemiological analysis by Steeland and colleagues to be unsuitable to derive an exposure-response relationship for DEP.

Garshick and colleagues studied a cohort of workers from a number of trucking companies in the USA. They also had the advantage of a parallel exposure monitoring exercise carried out in 2000 to measure submicron EC
levels, which was described in a series of scientific papers. In addition, they used historic (1971 to 2000) data on environmental air pollution levels (the “coefficient of haze”, CoH, which the researchers reported as being strongly correlated with EC, $r^2=0.94$) to adjust the exposure levels for 2000 to estimate past exposure levels. They carried out a careful statistical analysis of the measurement data and derived exposure estimates for different job groups, including both drivers and terminal and other workers, taking into account terminal characteristics, ventilation, job location in the terminal, and background environmental exposures. The authors compared their data with the measurements made by the researchers associated with the Steenland et al study to derive a series of “historical multipliers”, allowing for changes in background levels, to adjust exposure levels for changes in job characteristics.

Exposures occurring before 1971 were assigned the relevant 1971 exposure level. The authors state that 8% of the total person-years in their study were for people employed before this time. However, this still represents a large proportion of the total cumulative EC exposure because in all cases the estimated exposure level in 1971 was the highest estimate; for some job categories the difference was around a factor of ten higher than in 2000. In addition, around a third of the cohort members were hired before 1970. In our opinion, Garshick and colleagues will probably have overestimated exposure levels prior to 1971 because of the gradual increase in the use of diesel trucks from the 1950s to date, and this will have affected a relatively large proportion of the cohort. The likelihood of someone driving a petrol rather than a diesel truck will have introduced some exposure misclassification, although much of an individual’s exposure to DEP will come from the general road traffic so this is unlikely, in our opinion, to be an important source of misclassification in the epidemiological analysis.

We consider the Garshick et al estimates are more credible than those made in the Steenland et al study and we consider this study is suitable to estimate an exposure-response relationship for DEP.

### 2.3 OVERALL CONCLUSIONS FROM THE EXPOSURE STUDIES

We consider the analysis reported by Steenland et al to be biased and unreliable, and in our opinion, it is unsuitable for developing an exposure-response relationship. The other two studies considered here, Silverman et al and Garshick et al are both based on well-conducted retrospective exposure assessments that have used measurements of recent exposure along with available data to extrapolate earlier exposure levels. In principle, both studies could be a suitable basis to define risk of lung cancer for workers exposed to EC from diesel engine exhaust. However, like most studies of this type there are likely errors, both random errors and systematic biases. The important question is whether the errors are such as to invalidate the study conclusions.
It is always possible that retrospective exposure estimates may be biased, and bias is often more difficult to identify in epidemiological studies. The presence of bias in an exposure estimate may not affect the ability to identify statistically significant exposure-response relationships, but rather it may just affect the slope of the relationship. Positive exposure bias may result in an underestimate in the risk per unit exposure with negative bias having the converse effect. After reviewing the methodologies we consider that there may be a modest positive bias in both sets of exposure estimates, but more particularly in the Silverman et al study.

3 EXPOSURE-RESPONSE ANALYSIS

3.1 THE US MINING STUDY

Silverman and colleagues undertook a specific analysis of lung cancer experience within their study of eight cohorts of mineworkers (technically a nested case-control study) to investigate any potential exposure-response relationship between DEP exposure and lung cancer.

The authors investigated a number of alternative exposure-response models using complex statistical analyses (i.e. conditional logistic regression, with various exposure metrics such as average REC, cumulative REC, different lag periods (0, 3, 5, 7, ..., 23, 25 years) and a number of potential confounders, including smoking status, smoking intensity, and location of work).

The authors determined that the best model was that which included a 15-year lag and used cumulative exposure to REC as the exposure metric. A variety of lines were fitted to the data, resulting in very similar risk estimates at the lower end of the range of exposures, but quite different predictions at the upper end. This was mainly driven by the inclusion or exclusion of two estimates of risk at the upper end of the exposure range which, when included, suggested that the risk flattened off, or even decreased, with very high exposures.

The suggestion of a flattening off of the exposure-response relationship at high levels of cumulative exposure may be an artefact arising from errors in the exposure estimation. However, it is also possible that it reflects a bias because of the necessity to be healthy to remain in work, which might arise if the risk of lung cancer is correlated with increased risks of other work-related illness, e.g. chronic bronchitis or other respiratory disease, or cardiovascular illness.

There is insufficient understanding of the mechanisms by which DEP causes lung cancer to inform discussion of the likely shape of the exposure-response function. There is also no consensus as to the form of the exposure-response function linking lung cancer to smoking/tobacco smoke or outdoor particulate air pollution, which might be considered analogous exposures. Published exposure response functions for these agents show
either a steepening or a flattening off of risk at high exposures\textsuperscript{21}, although there is marginally more evidence to support a flattening off rather than a steepening of the risk function.

Without clear evidence of the shape of the relationship between DEP exposure and lung cancer it is difficult to advocate one line over the other based on anything other than the outcome of the statistical analysis. However, the two best fit lines found for the full data range and for cumulative exposures <1,000 $\mu$g m\textsuperscript{-3}.years give very similar risk estimates at lower exposures, despite having very different estimates at higher levels of exposure.

The exposure-estimation process will have had a critical impact on apparent exposure-response relationships reported in this study. Random misclassification will have simply weakened the power of the study to detect an effect but not necessarily resulted in bias in the exposure-response relationship. Systematic under or over estimation of exposure will have led to over or under estimation of risk, respectively, and modified the steepness of the exposure-response function. As discussed above, there are some uncertainties in the exposure assessment including random misclassification. In our opinion it is likely that exposures have been generally over-estimated giving rise to a potential under-estimate in risk. However, we consider it is unlikely that the bias in exposure estimation would substantially affect the shape of the apparent exposure-response relationship.

To ensure consistency in the exposure-response relationship at lower exposure levels it would be sensible to base any OEL decisions on the exposure-response relationship that excluded the two exposure groups at the higher end of the exposure range. This would imply an increase in the relative risk of lung cancer of about 0.4% per $\mu$g m\textsuperscript{-3}.year increment in cumulative exposure.

### 3.2 A PUBLISHED POOLED ANALYSIS

Vermeulen and colleagues\textsuperscript{22} combined the results from the exposure-response analysis of the three studies discussed previously (Silverman, Steenland and Garshick). Each of the studies had reported on the estimated risks for four categories of exposure. Using all of this data Vermeulen et al fitted exposure-response curves, while accounting for the variation in the original relative risk (RR) estimates by weighting the points by their variance. They also account for variation between and within studies.

They also fit lines to each of the individual studies included in the pooled analysis. All lines reported by Vermeulen were log-linear, not necessarily the same as the best-fit lines used in the original analysis. The exposure-response function based on the Silverman study shows a higher level of risk at exposure levels of $<1000$ $\mu$g m\textsuperscript{-3}.years than the data from the 2 trucker studies. The confidence intervals on the curves for each of the individual studies, however, are wide such that the exposure-response functions
cannot be considered to be significantly different. This implies that at the upper end of exposure the uncertainty is such that any of the fitted lines could be considered reasonable. At the lower end the estimated risks are very similar within each individual study, as well as within the pooled analysis.

### 3.3 AN ALTERNATIVE POOLED ANALYSIS

We carried out an evaluation of the exposure-response relationship using the same data as Vermeulen. A number of different curves were fitted to the data used by Vermeulen et al (RR for mid-point of exposure quartiles). As was evident from the discussion of the Vermeulen and Silverman analyses the line chosen can result in quite different estimates of risk at the upper end of the exposure scale, with the estimated risks being similar at the lower end. The log-linear model was the best fit to the data and as there is no biological evidence to support any other type of relationship between DEE exposure and lung cancer risk this was the model that was chosen.

Our evaluation of the exposure estimation methods used by the various papers led us to believe that the methodology used by Steenland et al was not as sound as the other two papers and also that the exposure estimates used by Silverman et al may have resulted in exposure estimates being up to 25% higher than expected. As a result we investigated the exposure-response relationship using only the Garshick data and the Silverman data (reduced by 25%).

Table 1 illustrates the relative risks associated with a range of exposures, assuming this exposure for working life of 45 years, and the confidence interval (95% CI). The relative risk is consistently above 1, indicating an excess risk associated with this exposure, although this is not significant for the lower exposure levels considered. With no statistically significant RR estimate there is a chance that the risk estimate is not different from 1, i.e. the risk may be the same as for an unexposed group. As the exposure level increases the associated confidence intervals also increase. The confidence interval for exposure of 100µg/m$^3$ per year is very wide, which reflects the level of uncertainty in the relative risks at higher exposures as well as the fact that the prediction is being made outside of the range of data used for the fitting of the line. The initial model (including Steenland data and with no adjustment to Silverman data) results in slightly lower relative risks as the slope of the fitted line is not as steep.
Table 1: Our estimated Relative Risks using the full data set (Initial model) and that excluding the data from the Steenland study and decreasing the Silverman data by 25% (Recommended model) for specific exposure levels per year, assuming 45 years of exposure. The 95% confidence interval is also given.

<table>
<thead>
<tr>
<th>Exposure level (µg/m³)</th>
<th>Recommended Model</th>
<th>Initial Model</th>
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<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td>0.1</td>
<td>1.2</td>
<td>0.98</td>
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<tr>
<td>0.3</td>
<td>1.2</td>
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<td>3.78</td>
</tr>
<tr>
<td>100</td>
<td>221.3</td>
<td>49.05</td>
</tr>
</tbody>
</table>

Although the RRs are relatively similar at lower exposure levels the estimated risks at higher exposure levels differ considerably, despite the same log-linear relationship being used. There does seem to be evidence of an increasing trend in risk associated with DEP exposure, although the nature of the relationship, particularly for higher exposures, is still unclear resulting in uncertainty about which exposure-response function is the most appropriate to use to describe risks associated with DEP exposure, particularly at higher levels. Given the level of uncertainty at levels of 100 µg/m³ it does not make sense to make any predictions of risk at this level.

4 CONCLUSIONS AND DISCUSSION

For both the Silverman and Garshick studies the methods used for the exposure assessment are likely to have resulted in some bias, and in our opinion the exposures are likely to have been overestimated (in the case of Silverman this could be by up to 25%), which in turn will have led to an underestimation of risk. Regardless of this, these two studies are of a high quality and are good examples of how to carry out an historical exposure assessment. The Steenland study, however, was felt to have considerably over-estimated exposure and we did not consider it suitable to derive an exposure-response relationship.

Both the analysis carried out by Silverman and colleagues and the pooled analysis of the three studies by Vermeulen (Silverman, Garshick and Steenland) were felt to be statistically sound and identified exposure-response relationships. Both groups of researchers based their best fit line on statistical considerations, and with the lack of biological evidence to support one curve over another, as well as the limited amount of data at the higher end of the exposure range, there is no reason to disagree with their methodologies.
However, based on our evaluation of the exposure assessment we replicated the analysis excluding the data from the Steenland study (as it was not felt to be appropriate) and reducing the data from the Silverman study by 25% (as the exposures were felt to have been overestimated). The uncertainty of the relative risk of lung cancer was very high at higher levels of exposure because of the limited number of people exposed to these levels. However, at the lower end of the exposure range, which is considered more relevant to risk management decisions, the various fitted lines resulted in very similar relative risks.

There are practical difficulties in lowering exposures to a level associated with a predicted lifetime cancer risk of less than 0.1% or even 1%. It may therefore be impractical to set a meaningful risk-based limit for workplace exposure. However, the evidence is, in our opinion, strong enough to support recommending controlling exposures to DEP to the lowest level that is technically achievable. In the absence of a threshold for lung cancer, any reduction in exposure to DEP will be beneficial. In using the exposure-response relationships to decide the level at which to set a limit, it would be appropriate to review existing levels of occupational exposure and the opportunities for exposure reduction. The limit value should be set low enough to drive an overall reduction in exposure to DEP and to lead to a meaningful reduction in cumulative exposure (measured as EC in mgm⁻³. years) across the exposed population. Ideally, a long-term programme of planned reductions in exposure should be in place to ensure ongoing improvement in exposure control and an associated reduction in the risk of lung cancer in the workforce.

5 REFERENCES


