

WORKING GROUP ON ACTION TO CONTROL CHEMICALS

WATCH/MIN/2007/3

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WORKING GROUP ON ACTION TO CONTROL CHEMICALS

Minutes of the 11th meeting of the Working Group on Action to Control Chemicals held from 7th – 8th November 2007 at the Crowne Plaza Hotel, NEC, Birmingham.

Members present

Steve Fairhurst (Chair)
 Steve Bailey
 Robin Chapman (Day 2 only)
 Rosemarie Hutchinson
 Len Levy
 Steve Williams
 Martie van Tongeren (Day 2 only)
 Ching Aw
 Alastair Hay
 Tony Fletcher
 David Farrar (Day 2 only)
 Robin Howie (ad hoc member)
 Julian Peto (ad hoc member)
 Brian Miller (ad hoc member)

Observers

Francis Pollitt (Day 1)
 Ian Martin (Day 1)

Apologies

David Farrar (Day 1)
 Steve Binks (Days 1 and 2)

HSE staff present

Nicola Gregg (Secretariat)
 Hayley Keating (Secretariat)
 Anna Rowbotham (Secretariat)
 Helen Ferguson (Secretariat)
 Andrew Darnton
 John Hodgson (Item 4)
 Kevin Walkin
 Martin Gibson
 Gary Burdett (Item 4)
 Mike Wright
 Ian Gardner (Day 2)
 Dil Sen (Day 1)
 John MacAllinden
 Simon Edwards (Day 2)
 Patrick McDonald (Item 10)
 Peter Ellwood (Item10)

Day 1 : 7th November

1 Introductions and apologies

1.1 The Chairman welcomed everybody to the 11th meeting of the committee. He introduced the expert *ad hoc* members who had been invited to join the committee for the item on asbestos: Professor Julian Peto (Cancer Research UK Chair of Epidemiology, London School of Hygiene and Tropical Medicine), Robin Howie (Industrial Hygienist, Robin Howie Associates) and Dr. Brian Miller (Consultant Epidemiologist, Institute for Occupational Medicine). He welcomed Dr. Francis Pollitt from the Health Protection Agency and Secretary to the Committee on Carcinogenicity and Ian Martin from the Environment Agency who were attending as observers.

1.2 Apologies were received from David Farrar (day 1) and Steve Binks (days 1 and 2).

2	Administrative issues
2.1	The Chairman asked for any declarations of interest related to the items on the agenda. Steve Williams declared an interest in asbestos and metal working fluids. Len Levy expressed an interest in carbon black in relation to the item on low toxicity dusts.
2.2	WATCH secretary Dr Nicola Gregg reminded WATCH members to send in their 07/08 declarations of interest.
2.3	Adoption of agenda WATCH members agreed to adopt the proposed agenda (WATCH/Agenda/2007/3).
3	Minutes of 10th meeting
3.1	Members had been invited to comment by correspondence on the draft minutes of the 10 th meeting. No comments had been received. No further changes to the draft now presented were proposed. Members agreed the version presented here as being the finalised minutes of the June 07 meeting (WATCH/Min/2007/2).
3.2	Matters arising/Secretary's report The Secretary summarised the actions that arose at the 10 th meeting of June 2007 and provided an update on the progress that had been made. No comments were made.
4	Assessing the Risks Arising from Low Level Exposure to Asbestos
4.1	<p>The Chairman opened the item by reminding members that this had been deemed to be a priority "new and emerging issue" by WATCH at its meeting in November 2006. The aim now was for WATCH to consider the information provided in the package of papers, in conjunction with presentations from HSE and probably from ad hoc expert members and then through debate to seek to establish scientifically robust positions on the dose-response relationships (particularly at relatively low exposure levels) for lung cancer and mesothelioma causes by different asbestos fibre types - crocidolite, amosite and chrysotile. He thanked HSE for the work that had gone into preparing the package of papers and planning the session, a collective effort led by Garry Burdett. He advised members that the session would start with two presentations from HSE staff. He then envisaged a general discussion that would allow members to take stock and suggest the best approach for structuring the afternoon session. He invited any of the ad hoc expert members to give their presentations at whatever point in the debate they considered was most appropriate to the discussion at that time.</p> <p>The Chairman emphasised that this item was one of the most important issues that WATCH had addressed. In view of the importance and the complexity of the issues, he asked all members to ensure that they maintained a full understanding of all aspects of the debate and requested clarification whenever needed.</p>
4.2	HSE presentation [1] - available data from occupational cohort studies : key issues The Chairman introduced the line of thinking that one approach to trying to understand the levels of risk posed by low level exposures to different asbestos fibre types could involve using evidence from the existing body of occupational epidemiological data, such as the cohort studies reviewed by Hodgson and Darnton (Annex 1) and Berman and Crump (Annex 2) to construct dose-response relationships that might then be extrapolated to lower exposure levels. If such an approach were to be followed, then it was important that WATCH, in the first instance, appreciated what is known from the available occupational epidemiological studies

	<p>and consider the quality and reliability of the data provided by these studies. He referred members to Annex 5 that set out the extent, types and quality of the exposure data associated with occupationally exposed asbestos worker cohorts and invited Dr. Garry Burdett (HSE, HSL) to provide an overview of the key issues reflected in Annex 5.</p>
4.3	<p>Garry Burdett re-emphasised to WATCH that the purpose of the session was to explore the scope for extrapolating from risk estimates derived for occupational scenarios encountered and studied in the past, to lower level exposure scenarios. He gave a brief presentation covering a number of key issues:</p> <p>(1) Ranges of airborne PCM fibre concentrations & cumulative exposures</p> <p>By way of introduction to the concept of exposure, Garry Burdett highlighted that measures of airborne PCM fibre concentrations and estimates of cumulative exposure were indirect measures or indices for the dose of asbestos fibres. Also he pointed out that the industry cohorts had good information on the duration of the exposure from payroll records and his presentation would focus on the airbourne levels.</p> <p>He informed WATCH that in the various asbestos industries of the past, the airborne concentration of asbestos varied across several orders of magnitude for different exposure scenarios. Levels between 100-1000 f/ml may have been prevalent in factories from the 1930s-50s. Historical averages from the 1930s - 60s were likely to be in the range 10-100 f/ml. Much lower levels of around 1 f/ml were reported for the manufacturing sectors in the 1970s and 80s. The first asbestos control limit, based on the phase contrast microscopy (PCM) counting method, was set at 10 f/ml.</p> <p>The current asbestos control limit is 0.1 f/ml. Obviously this is considerably lower than the historical levels of exposure referred to above. He described the EU approach to regulatory standards for asbestos control as having been to seek successive reductions in the limit value, without necessarily having a full understanding of the level of risk associated with any proposed new value. Garry Burdett pointed out to members that it was important to recognise that the airborne levels and exposure scenarios encountered by workers in more recent times (from the 1970's and 80s onwards) were much different than those that were typical of workplaces associated with the cohort studies in asbestos industries.</p> <p>As examples of the kinds of exposure levels in which there is now interest and about which questions arise, a so-called "clearance limit" of 0.01 f/ml is often used to assess the appropriateness of clean-up operations following asbestos removal work in buildings. Typical levels of contamination of indoor air in an occupied building where asbestos-containing materials are present and subject to disturbance are around 0.0005 f/ml. These are the levels of exposure for which WATCH may wish to consider whether or not estimations of the associated level of risk can be made .</p> <p>Garry Burdett highlighted that estimates of cumulative exposures (the product of airborne asbestos fibre concentration in f/ml and exposure duration, in years) provided the best estimate of the dose received by an individual. The cumulative exposure values that have formed the basis of the dose-response relationships established thus far for asbestos incorporate measures or estimates of the asbestos air levels involved. To illustrate to WATCH the range of cumulative exposure estimates that it might be necessary to address, Garry Burdett indicated that, based on PCM measurement, average cumulative exposures of 13-750 fibre.years/ml were derived for the asbestos worker cohorts featured in the Hodgson & Darnton analysis, whereas a cumulative exposure of 1 fibre.years/ml is entailed for lifetime exposures at the current asbestos control limit and 0.01 fibre.years/ml for exposure to asbestos in buildings or to "high" urban background levels. He pointed out that the asbestos</p>

	<p>worker cohorts would also have received additional exposure due to elevated environmental levels around the factories. He contrasted the exposure scenarios experienced by these workers – relatively high levels of asbestos inhaled over relatively short periods - with the very different situation of continuous exposure to much lower levels, possibly over a lifetime.</p> <p>(2) Asbestos cohort studies: considering uncertainties</p> <p>Garry Burdett referred to Annex A of the Berman and Crump analysis. He pointed out that in comparison to the Hodgson and Darnton analysis, Berman and Crump had considered additional cohort studies and had analysed the uncertainties associated with the data sets. This was done by assigning each of the 23 cohort studies they considered with uncertainty coefficients, ranging from 0.5 to 4 for five separate influencing factors. These factors were: (F1) estimating exposure; (F2) converting exposure estimates based on other methodology to values that would be produced using the current PCM method and (F3) assigning job histories; and two additional factors (F4 and F5 for lung cancer and mesothelioma respectively) to account for uncertainties in the mortality data (e.g. associated with diagnosis of mesothelioma or the use of approximations or assumptions when data were not presented in the form needed for fitting the exposure-response models). Garry Burdett pointed out to WATCH that of these 5 factors, the greatest uncertainty across the studies was associated with the exposure estimates, particularly with regards to estimating airborne asbestos fibre concentrations. In addition, a high degree of uncertainty was associated with the conversion of early PCM-based exposure estimates in to estimates which were comparable with those derived using more recent PCM methods. He then discussed these in more detail in terms of the available data.</p> <p>(3) Methods used to measure airborne concentrations and the associated issues</p> <p>Garry Burdett informed WATCH that a range of sampling devices and counting techniques based on optical microscopy (with x200-x2000 magnification) were used from 1927 to the 1960s to determine airborne concentrations of asbestos. The efficiencies of the methods employed were variable and influenced by a number of factors that included: the sampling method, the length, width and aspect ratio of the counted particles and the microscopical method employed. A midget impinger sampling technique was commonly used in the US asbestos worker cohort studies, but was not reliable for a number of reasons. The main problems with this method were the poor collection efficiencies for fibres < 1 µm in width and the tendency of the technique to cause dispersion of larger intact asbestos bundles into individual fibres.</p> <p>Garry Burdett also pointed out that determination of very high airbourne concentrations was challenging. Consequently many of the cohorts did not have any measurements for processes that produced very high airbourne concentrations of asbestos.</p> <p>The choice of microscopy method also had an important impact on asbestos fibre counts. These factors will have had important implications for the reliability of historical measurements. However, he considered that it was also important to recognise that even using modern PCM methods, a large proportion of the total numbers of asbestos fibres in a given sample would be missed.</p> <p>In summary, Garry Burdett emphasised that the available asbestos exposure data associated with the worker cohorts studied was subject to a number of systematic errors arising from the sampling and counting methods employed.</p>
4.4	Initial discussion following presentation [1] - quality and reliability of asbestos measurements

	<p>The Chairman thanked Garry Burdett for the presentation explaining important issues concerning exposure assessment within the available epidemiological studies on asbestos worker cohorts. He opened the item for general discussion.</p> <p>A WATCH member added his concerns that in many of the workforces studied, asbestos exposure in most of particularly dirty areas of the workplaces involved was not measured. He pointed out the apparent anomaly that some cohorts who had been exposed to very high levels of asbestos had much lower incidences of mesothelioma than would be expected, based on observations of elevated risk in other cohorts. The basis of this was not clear, but this observation added to the uncertainty surrounding whether or not we had adequate knowledge of exposure, expressed in the appropriate metric.</p>
4.5	<p>A WATCH member asked how the performance of the microscopy methods used was influenced by the use of oil immersion? Garry Burdett replied that a range of methods had been used over time. Oil immersion had been used in some studies in the UK (e.g. using x2000 oil immersion microscopy and a thermal precipitator) and had successfully provided counts of fibres of diameters as low as 0.1µm. However several US cohort studies, had used the midget impinger method. This technique was based on a sedimentation cell and was not very effective for accurately counting fibres on the basis of size. The WATCH member referred to the North Carolina textiles industry cohort that appeared to be an outlier study with respect to the particularly high lung cancer risks reported. He asked whether or not this could stem from the measurement methods used? Garry Burdett commented that the historical assessment of exposure carried out in the North Carolina cohort study may have underestimated the true airborne levels. Another WATCH member commented that the apparently anomalous nature of the North Carolina data might be illustrative of our lack of appreciation of the most important features of the exposures that resulted in the health consequences observed.</p> <p>Dil Sen (HSE, Senior Medical Advisor) asked whether the fragility of fibres was a key issue affecting the reliability of measurements – could the analytical technique itself produce separation and/or breakage of fibres? Garry Burdett replied that asbestos fibres were generally quite tough. However, in his experience the distribution of fibre lengths could vary between different samples from the same site and in some cases it was possible that the number of shorter fibres in a sample could increase because of breakage of longer fibres.</p> <p>A WATCH member commented that, given the issues over reliability of measuring asbestos fibre levels in air, it may be more realistic to consider exposures in terms of approximate, general categories expressed as “high”, “medium” and “low” concentrations.</p>
4.6	<p>A WATCH member asked if any information about urban environmental air levels of asbestos were available for the time periods associated with the cohort studies? Garry Burdett replied that environmental air levels of asbestos in the vicinity of asbestos factories were assumed to be relatively high, certainly in comparison with the present, but he couldn't recall any actual values that have been reported. However, he also commented that he would have expected the background levels of asbestos in environmental air in the UK 80 years ago to be less than they were 40 years ago, when asbestos was imported into the UK in large quantities. Garry Burdett added that there was some information on environmental air levels in more recent times, for example due to the use of chrysotile in vehicle brake-linings, but a comprehensive, fully representative set of accurate estimates was not available.</p>
4.7	<p>A WATCH member commented that in his view, based on the discussions so far, there was a clear indication that much of the asbestos worker cohort data was unreliable in respect of exposure assessment. He asked whether it was possible to</p>

	<p>determine some sort of uncertainty range for the data as a whole, or to distinguish the better data sets from those meriting greater concern about the unreliability of the exposure data cited. Garry Burdett thought that this idea could be developed. He commented that the quality and conditions under which measurements were made in the different studies was quite varied and that in some of the cohort studies, no exposure measurements were taken at all. In acknowledging limitations in the quality of the exposure data Hodgson and Darnton, and Berman and Crump, had each tried to apply what the authors considered to be the best approach in the circumstances. Hodgson and Darnton had used an average air concentration of asbestos as a representative level for each cohort studied. Berman and Crump had tried a systematic approach to looking at issues of variability and uncertainty within the available data. He said that the following presentation from Andy Darnton (HSE) would bring out these points.</p>
4.8	<p>HSE presentation [2] – overview of Hodgson & Darton and Berman & Crump analyses</p> <p>The Chairman invited Dr. Andrew Darnton (HSE, Statistics Branch) to give a presentation on the key aspects of these two analyses, highlighting the strengths and weaknesses of the approaches that had been used.</p> <p>(1) Comparison of approaches and outcomes</p> <p>To give WATCH members a clearer picture of findings across the available asbestos worker cohort studies, Andy Darnton used figure 3 from the Hodgson and Darnton paper that showed exposure-specific excess lung cancer mortality by fibre type and cohort. He emphasised that the risk of lung cancer in each cohort had been related to average cumulative exposure and hence the position of a cohorts on the chart would change if a different level of exposure for that cohort was assumed. Figure 2 showed in a similar manner the profile of mesothelioma risks for the different cohorts.</p> <p>To provide a comparison with figure 3 of the Hodgson and Darnton paper, Andy Darnton showed WATCH members a slide of “K_L” values (a potency indicator in relation to the induction of lung cancer) for each of cohorts included in the Berman and Crump analysis, with the associated uncertainty intervals. He explained that, unlike the Hodgson and Darnton analysis, Berman and Crump had fitted a model to the dose-response relationships derived from within individual cohorts and had used this approach to determine the K_L, together with the associated uncertainty intervals. He pointed out that for many of the cohorts, the uncertainty around the estimate of K_L was large. For example, in the case of one mixed-fibre cohort (MP8), the uncertainty around the K_L value spanned the range of K_L values for the entire dataset assessed by Berman and Crump. A similar analysis had been performed for mesothelioma (to derive values denoted as K_M).</p> <p>(2) Berman and Crump adjustments for fibre length</p> <p>Andy Darnton informed WATCH that Berman and Crump had considered the problem posed by the distribution of fibre size between the cohorts and had adopted an approach to adjusting for this using weighting factors. The justification for the approach stemmed from three hypotheses considered by the authors to explain the striking difference observed in the excess risk of lung cancer between the Quebec mines [remarkably low] and North Carolina textile [remarkably high] cohorts, both exposed predominantly to chrysotile: (1) the exposure estimates were unreliable; (2) there were differences in the distribution of fibre size between industries; and (3) potential co-exposure to another carcinogen may have occurred (e.g. use of mineral oil spray to suppress dust) in the North Carolina cohort. Based on the analysis of lung fibre burden data, in combination with data on the proportion of amphibole fibres used, Berman and Crump considered the exposure estimates in the cohorts to be</p>

4.9	<p>fairly reliable and therefore discounted hypothesis (1). In relation to hypothesis (2), analysis of fibres in lung tissue samples indicated that the Carolina cohort had been exposed to higher proportions of longer fibres than the Quebec cohort. Berman and Crump dismissed the third hypothesis, based on the findings of a nested case-control study by Dement and Brown that showed no change in the exposure-response relationship after adjusting for mineral oil exposure. Berman and Crump concluded that these observations indicated the potential for fibre length to influence cancer risk and therefore that an adjustment approach was warranted.</p> <p>(3) Adjustments for fibre length and implications for fibre potency</p> <p>Andy Darnton summarised the model-fitting methods used by Berman and Crump to account for uncertainties associated with fibre size (e.g. adjusting for fibres of diameter <0.4 µm and length >40 µm) and discussed the outcomes in terms of the predicted potency of amphiboles (K_A) and chrysotile (K_C) to induce lung cancer and mesothelioma. Although Berman and Crump had selected a fibre length metric of 40 µm as being a key factor influencing carcinogenicity, the size distributions of fibres for a range of occupational settings studied was only available in terms of fibres >10 µm in length. The data available on fibre length was used to apply “fibre length” adjustment factors for each of the cohorts. Additional adjustments were also made for asbestos fibre type.</p> <p>Although Berman and Crump had suggested that the length of asbestos fibres was an important factor that influenced their potency, Andy Darnton informed WATCH that in his opinion this was not clearly apparent from the data presented by Berman and Crump and the effects on their analysis of adjusting for fibre length were subtle. This is indicated by the following.</p> <p>In terms of lung cancer:</p> <ul style="list-style-type: none"> - When the relative potency of fibres < 10 um was assumed to be 0.003 (e.g. a weighting of 99.7% was given to fibres >10 um) the potency of amphiboles was estimated to be four times that of chrysotile. - When the relative potency of fibres was assumed to vary, the potency of amphiboles was also four times that of chrysotile - When no adjustments were made for fibre size, the potency of chrysotile was half that of amphiboles <p>In terms of mesothelioma:</p> <ul style="list-style-type: none"> - When the relative potency of fibres < 10 um was assumed to be 0.003 (e.g. a weighting of 99.7% was given to fibres >10 um) the potency of amphiboles was estimated to be 800 times that of chrysotile. - When the relative potency of fibres was assumed to vary, the potency of amphiboles was also 800 times that of chrysotile. - When no adjustments were made for fibre size, the potency of amphiboles was 300 times that of chrysotile. <p>Andy Darnton concluded that, when the weighting for fibre length was applied, there was little improvement in the ‘certainty’ associated with the risk estimates. This probably related, in part, to the large variability in the quality of the underlying data. Adjusting for both the length and type of fibre had more of an influence, but substantial inconsistency in the data was still apparent. Furthermore, any substantial reduction in variability was restricted to the “pure amphibole” cohorts; the variability among “pure chrysotile” cohorts was no different after weighting.</p> <p>Discussion of the quality and reliability of the asbestos worker cohort studies</p>
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	<p>The Chairman thanked Andy Darnton for the presentation. He then asked WATCH to consider the quality and reliability of the 20 or so cohort studies that had been included in the Hodgson & Darnton and the Berman & Crump analyses; before moving on to considering what scope there was for using this data as the basis for extrapolating to estimations of risk at substantially lower levels of exposure. He opened this issue for general discussion.</p>
4.10	<p>A WATCH member raised questions on the North Carolina textiles and Quebec miners chrysotile-exposed cohorts. He asked whether it was possible that the North Carolina findings were atypical because of the way that the airborne asbestos fibres had been measured? Andy Darnton was not sure of the reason, but emphasised that this dataset was unusual because the cumulative exposure estimates for that particular cohort were relatively low. When these cumulative exposure estimates were combined with the health outcomes for the cohort, relatively high estimates of lung cancer risk were obtained. In contrast, the average exposures for the Quebec miners cohort were quite high, but associated with substantially lower risk estimates. The WATCH member commented on two anomalies – one was these differences in lung cancer risks for the North Carolina and Quebec cohorts and the other was the fact that both cohorts showed a similar level of risk for mesothelioma. Andy Darnton commented that this issue had been the subject of much debate but, as yet, no clear explanations were available. Another WATCH member returned to the more general point that measurements of airborne asbestos levels were only made in some of the cohort studies. Other cohort studies may not have had any measured exposure data, particularly for the tasks where exposures to asbestos had been very high, and assumptions were therefore made about what the associated airborne fibre levels may have been. There was even less knowledge about parameters such as fibre length distribution in the exposures received by many of the cohorts.</p>
4.11	<p>A member asked for clarification about the aims of this WATCH assessment. He commented that there are many workers currently involved in asbestos-related tasks who are in situations in which there is adherence to the current asbestos control limits and guidelines on appropriate practices are followed. If there were doubts about the robustness of the underlying models that have been used to estimate the level of risk involved in such situations, he asked what this could imply for such workers? The Chairman acknowledged that there was an important societal context for issues relating to asbestos exposure. Nevertheless, he emphasised that the purpose of this item was to allow WATCH, as the scientific advisory committee of HSE/ACTS, to examine the available body of evidence that informs on estimating the risks of lung cancer and mesothelioma associated with low level exposure to asbestos.</p> <p>John Hodgson (HSE, Statistics Branch) added that there is currently no direct observational evidence that the available risk estimates for relatively low level exposures to asbestos are inaccurate.</p>
4.12	<p>A WATCH member commented that the discussions so far seemed reminiscent of debates on asbestos held some 20 years ago. He felt that the data were too limited to pursue theoretical considerations about the relationship between fibre length and cancer risk, for any particular fibre type. He also suggested that most of the currently observed cases of mesothelioma in the UK were most likely to be linked to amosite exposure, as the use of crocidolite in the UK had ceased in 1965. He considered that the exclusive focus of attention at the time on crocidolite had prevented the crucial realisation that amosite, another amphibole asbestos, was also a very significant potential cause of cancer.</p> <p>Another WATCH member referred to the estimate that thousands of further cases of mesothelioma were predicted to occur in the UK by 2050, due to past exposures and practices. He stressed the importance of thoroughly examining the available evidence</p>

	<p>and acting accordingly now, to prevent the issue of asbestos carcinogenicity being revisited by future generations, still facing the same problems.</p>
4.13	<p>The Chairman brought WATCH members back to the issue of the quality and reliability of the epidemiological data and the associated exposure measurements.</p> <p>A WATCH member commented that the exposure data were, in the most part, unreliable. He considered that the epidemiological studies relating to past exposure situations in asbestos industries were of limited value when considering cancer risks linked to current occupations and/or entailing substantially lower level exposures because the two sets of exposure scenarios are so very different. In his opinion a more worthwhile approach would involve attempting to study directly the risks posed to specific asbestos-exposed groups of contemporary interest.</p> <p>The Chairman asked WATCH if it agreed with this perspective? Several members concurred. Garry Burdett offered the opinion that the historical data might still be of some value and suggested that there was scope for looking more closely at the individual occupational epidemiological studies included in the Hodgson and Darnton (and Berman and Crump) reviews, with a view to distinguishing those which are of better quality (and hence contain more reliable information) from those which have identifiable serious deficiencies in respect of exposure data quality.</p> <p>Professor Peto suggested that this was a good point to introduce the findings of a recent study from his research group.</p>
4.14	<p>Mesothelioma and lung cancer study – Peto et al (awaiting publication)</p> <p>To inform the debate further, Professor Julian Peto gave a presentation on a British case-control study of mesothelioma and lung cancer patients born in or after 1940; the study is currently awaiting publication. The aim of the study was to identify the occupations and work practices that conferred the highest risks of mesothelioma and involved interviews with 622 mesothelioma patients, 425 lung cancer patients and 1114 population controls.</p> <p>Professor Peto began his presentation by outlining the distribution of the mesothelioma cases and controls in the study by year of birth and sex and emphasised the fact that, of the subjects born before 1960, many more men than women were exposed to asbestos. Data from male subjects demonstrated that exposure to asbestos for 10 years or more before the age of 30 years greatly increased the risk of developing mesothelioma, compared to controls, with an odds ratio (OR) of 6.5 (95% confidence interval 3.3-12.8), rising to 12.7 (8.6-18.6) following an additional 10 years or more exposure to asbestos after the age of 30. Professor Peto went on to show data demonstrating that of those subjects exposed to asbestos before age 30, carpenters had the highest risk of developing mesothelioma with an odds ratio of 23.1 and a lifetime risk for ≥10 years in job category of 5.9% compared to the general population. In addition, one-fifth of all the mesothelioma cases in the study were carpenters. The study also revealed that domestic “para-occupational” exposure before age 30 doubled the risk of developing mesothelioma. Professor Peto concluded his discussion of mesothelioma cases by acknowledging the difficulties in predicting the number of future cases of mesothelioma particularly because of the differences in exposure patterns across generations but by using an age/birth analysis model to analyse data after exposure stopped Professor Peto indicated that it is possible that the total number of mesothelioma cases by 2050 will be much higher than those predicted by HSE in 2005.</p> <p>In terms of lung cancer, Professor Peto stated that in the cohorts studied in the Hodgson & Darnton and Berman & Crump analyses, particularly those with only short follow up periods, the number of cases of lung cancer were always higher than the number of mesothelioma cases but this trend diminishes with increased follow up</p>

	<p>times. The lung cancer:mesothelioma ratio is a lot lower with longer follow up periods and also reduces as subjects give up smoking. Professor Peto stated that it is unclear what will be the ratio of lung cancer to mesothelioma cases in the future. He highlighted work by Andrew Darnton in which British occupational Proportional Mortality Ratios (PMRs) for lung cancer and mesothelioma (adjusted for smoking) predicts 0.7 – 1.0 excess lung cancers per mesothelioma. The ratio was higher in Professor Peto’s study. Professor Peto also pointed out that for lung cancer the high risk jobs were different to those found to be high risk jobs for mesothelioma, for example with construction workers showing high risks for lung cancer and carpenters showing high risks for mesothelioma. At present there is not a clear explanation for these differences but Professor Peto pointed out that good smoking data were not available for these groups, which confounds interpretation of the lung cancer data. He also pointed out that a possible explanation for the difference in the PMR data of Andy Darnton and this cohort may be because PMR data is based on the job the subject did when they died, whereas the Peto et al study shows that the job performed before age 30-35 is most important in terms of the risk of developing mesothelioma and lung cancer. Professor Peto then drew other WATCH members attention to the falling rates of lung cancer in the UK and said that he believed the implication of this is that the ability of asbestos to produce lung cancer is of substantially less importance than the risk of mesothelioma. In hindsight, he suggested that the high level of concern surrounding lung cancer and asbestos in the past was misplaced and that, in contrast, mesothelioma had been somewhat neglected at that time. He offered some important reference points: the UK has the highest number of cases of mesothelioma in the world, but the specific job-related causes are unclear; and the highest asbestos exposures, those that occurred in the manufacturing industries, appear to be responsible for only about 1% of all the known cases of mesothelioma, with very many more cases being associated with the end-use of asbestos. In addition to occupational causes, environmental exposure may be important, as the lifetime risk in people seemingly not exposed to asbestos at work has increased to 1 in 1000. This cannot be entirely explained by better diagnosis of mesothelioma than in the past. Professor Peto concluded his presentation by stating his belief that the most important issue relating to asbestos risk is to determine if some people are still receiving significant occupational exposure and, if so, where.</p>
4.15	<p>The Chairman thanked Professor Peto for the presentation and opened the item up for general discussion.</p> <p>Discussion of cancers “non-attributable” to asbestos and environmental exposures to asbestos</p> <p>A WATCH member asked what was known about the exposure of women to asbestos? Garry Burdett replied that the term ‘para-occupational exposure’ was used to refer to women and family members of workers who had received secondary exposure to asbestos from a male worker’s contaminated clothing. Another WATCH member added that the airborne levels of asbestos in the houses of workers and analysis of fibre burden from tissues taken from deceased cancer cases in such “family member” situations would provide insights in to the extent of exposure in these cases. He also pointed out that he knew of studies planned to look at the fibre burden of the lungs of building workers, which would help to clarify the position regarding construction workers.</p>
4.16	<p>Another WATCH member asked if there were data available that allowed one to compare the cancer risks associated with “ambient” exposures to asbestos, compared to those associated with occupational scenarios? One example brought out was that in the UK the risk of carpenters developing mesothelioma was 40 times the risk in the general population. It was reiterated that the lifetime risk of mesothelioma in people seemingly not exposed to asbestos at work is now 0.12%</p>

	<p>(about 1 in 1000).</p> <p>A WATCH member made a further point about the lung cancer risk from asbestos exposure in the general population. He drew on experience with cigarette smoking, informing WATCH that lung cancer mortality increases as a function of smoking duration, but when someone stops smoking, the risk of developing lung cancer remains constant for that individual for the rest of their life and does not decline with time. He expected this to also apply to asbestos exposure. Ambient exposure to asbestos starts from birth and continues throughout an individual's lifetime. One would therefore predict that the length of asbestos exposure will be a crucial determinant of asbestos-induced lung cancer risk.</p>
4.17	<p>A WATCH member asked how the models used to predict risks of mesothelioma took into account the duration of time over which an individual was exposed? It was explained that risk models for mesothelioma contain an exponential function in which the duration of exposure is raised to the power three. He also asked Professor Peto specifically whether there were any particular known factors which would account for higher risks of mesothelioma in carpenters? Professor Peto commented that little was known about this occupational group other than their exposures to asbestos most likely arose from sawing and working with amosite insulation board.</p>
4.18	<p>In response to further questions about his presentation, Professor Peto clarified that the term 'spontaneous', used for some cases of mesothelioma referred to instances that could not readily be attributed to any occupational exposure to asbestos; he considered that the most likely cause was ambient exposure from environmental air. A WATCH member asked if there was any indication of a bias towards an urban setting for these cases? Prof Peto replied that this had not been determined.</p>
4.19	<p>With age since first exposure to asbestos being an important determinant of cancer risks, Garry Burdett wondered if increased longevity of life in recent times could be contributing to the increased "spontaneous" mesothelioma figures? Professor Peto replied that this was not the case, as the data were age-adjusted. Several WATCH members asked Professor Peto if he had any ideas for what the increase in "spontaneous" cases of mesothelioma could be due to? Given that amosite had been used extensively in place of crocidolite in the 1960's, Professor Peto proposed that widespread environmental contamination with amosite may have occurred which, in turn, may have given rise to higher ambient levels. The spontaneous cases of mesothelioma may therefore be due to past exposures of the general population to ambient levels of amosite that were higher than nowadays. He added that there were differences with respect to rates of mesothelioma for men and women and this could provide insights into the source of their respective exposures.</p>
4.20	<p>A WATCH member suggested that further exploration of this issue could examine the links between "spontaneous" mesothelioma cases and possible sources of asbestos exposure, for example domestic renovation and decorating tasks. Martin Gibson (HSE) commented that there was anecdotal evidence that in the past a significant number of people may have been exposed to asbestos without having been aware of it and this may have given rise to higher numbers of mesothelioma cases not attributable to recognised occupational exposures. John Hodgson added that it was feasible that people could have been inadvertently exposed to asbestos fibres in the 1960s and 70s from walking past building sites. A WATCH member commented that he did not see a clear case for intervening in current environmental exposures to chrysotile. He based this on reassuring evidence that cohorts of workers in chrysotile mines, many of whom had worked there for over 20 years, did not show increased risks of lung cancer.</p>
4.21	<p>A WATCH member referred back to the Hodgson and Darnton paper. He asked what might be the implications of errors in the exposure assessments in terms of the risk</p>

	<p>estimates? He also commented that vast amounts of amosite were imported into the UK in the past, with only about 25% having been used in buildings. He agreed that this burst of amosite utilisation had a feasible role in the mesothelioma figures now being observed. Another WATCH member added that importation of crocidolite into the UK ended in 1965 whereas imports of amosite continued until 1976.</p>
4.22	<p>A WATCH member pointed out that talcum powder had, in the past, contained some asbestos fibres. He wondered if there was a possible connection between the spontaneous cases of mesothelioma observed in women and past use of talcum powder? He also wondered if there were any indications of mesothelioma in epidemiology studies of talc workers? It was not possible to address these issues during the meeting.</p>
4.23	<p>A WATCH member asked if it was possible that exploration of the more detailed information collected from people with mesothelioma might shed more light on potential sources of their asbestos exposure? Another member replied that this was unlikely - in addition to the emotional reactions following diagnosis, many mesothelioma cases involved legal actions and the people involved were unwilling to disclose information.</p>
4.24	<p>Asbestos exposure and age</p> <p>A WATCH member asked Professor Peto for further insights into the relationship between age, asbestos exposure and cancer risk. Professor Peto commented that first exposures to asbestos before the age of 30 were much more critical in terms of cancer risk than first exposures that occurred after 30. If first exposures occurred after the age of 40, the risks of developing cancer were relatively low. However, limited insights could be gained from age alone; time since first exposure was a more critical determinant of risk than the actual age at which exposures took place. This implied that exposure to asbestos in childhood would be an important factor in determining the appearance of cancer in later adult life.</p>
4.25	<p>Options for WATCH to take low level exposure to asbestos further forward</p> <p>The Chairman summarised the discussions so far by highlighting that a number of concerns had emerged over the reliability of existing asbestos worker cohort studies and hence their suitability for providing helpful insights into estimating the risks of low level exposure to asbestos. Nevertheless, the task WATCH had been set was to try to develop a position and/or to identify further work that the WATCH Secretariat could develop, in order to enable this issue to be progressed at future WATCH meetings. With this in mind, he asked WATCH to consider what the options were for taking this item further forward. He opened this issue for general discussion.</p>
4.26	<p>Option (1): Direct observations from low-level ambient exposure scenarios</p> <p>The Chairman noted that a WATCH member had proposed earlier that, instead of trying to extrapolating from high exposure scenarios, an alternative approach to addressing the risks of low-level exposure to asbestos could involve directly exploring exposures and risks in workers exposed to low levels, and/or in the general population receiving ambient exposures. In such an approach, the complex issues posed by the asbestos worker cohort data would not need to be addressed.</p> <p>Garry Burdett suggested that focussing on levels of exposure around the current asbestos control limit would be useful, in that it would help identify the level of risk to which we are regulating. However, a WATCH member considered that this might not be relevant if occupational exposures in recent times occurred in occupational settings entailing a lack of awareness and control of asbestos.</p>
4.27	<p>Another WATCH member stressed the importance of providing accurate information to people who have lived in buildings containing damaged asbestos for many years;</p>

	<p>such people deserved to know of the potential risks this may have posed to their health. In these circumstances, medical doctors and other health professionals would be expected to give advice to the public and would need to base this on valid risk estimates that are appropriate to such low-level exposure scenarios. There was a potential for the media to give a high profile to some of these cases – a scientifically robust position would help put the risks into context.</p> <p>Another WATCH member considered that the risks of asbestos-induced cancer from living in buildings containing damaged asbestos were very low. He referred to data he had showing the predicted eventual causes of death of 3000 ex-residents of a block of flats in London, within which there had been with airborne asbestos levels of around 0.001 f/ml. Using existing risk models, the estimated extra risks of dying from mesothelioma or lung cancer were very low.</p>
4.28	<p>A WATCH member raised a number of points. Firstly, he referred to “Asbestos Essentials”, the aim of which is to provide practical guidance on how to control asbestos to low levels of exposure. A difficulty remains when it comes to determining if the level of control achieved using the guidance (exposure levels of 0.01-0.1 f/ml) is adequate to protect health. He then commented that the inadequacies of the exposure data in the asbestos worker cohort epidemiological studies and the differences in exposure scenarios means that it seems to be still not possible to identify with confidence a “safe” level of exposure. However, it might be possible to use the exposure assessments made as indicative, which would facilitate relative ranking of risks in different situations. He pointed out that daily 8-hour exposure to airborne asbestos fibres at the control limit of 0.1 f/ml for 40 years would give a cumulative exposure that might still entail a significant risk estimate. Finally, he expressed difficulty in reconciling the calculated mesothelioma risks posed to carpenters with the apparently substantially lower risks posed to workers in crocidolite factories, given that sawing amosite board did not generate airborne levels of asbestos anything like as high as had been encountered in crocidolite factories.</p> <p>In response, another member commented that the actual levels of carcinogenic fibres generated in the factories were unknown. John Hodgson also pointed out that there are many more carpenters than there were asbestos manufacturing workers, and hence the former category represents a much larger population at risk of contracting mesothelioma.</p>
4.29	<p>A member commented that if one were to try to assess the risk of lung cancer at low levels of asbestos exposure from direct observations made on populations experiencing such low exposures, the only option available would be to calculate lung cancer incidence from the mesothelioma incidence, using the ratio of lung cancer to mesothelioma observed in higher exposure situations. An alternative means of addressing lung cancer for the “low-level” situation would be if it were possible to identify from the available dose-response data a threshold dose, below which lung cancer would not occur. He felt that this was probably not a suitable approach.</p> <p>He also believed that the portrayal of the threat posed in recent times by working with amosite to be very persuasive and this highlighted the need to make sure these exposures do not continue.</p> <p>A WATCH member commented that based on a comparison of the risks of mesothelioma across Europe, the background risk for the UK appeared to be higher than for other European countries, with an apparent four-fold increase since the 1970s. Furthermore, 15% and 50% of mesothelioma cases in men and women respectively were apparently “spontaneous”, with no obvious occupational connection. In his opinion, this indicated that background ambient exposures to asbestos, as considered for the general population as a whole, presented a small but</p>

	<p>nevertheless notable risk.</p> <p>Based on data for some of the most heavily contaminated buildings in the UK, a WATCH member emphasised his view that the spontaneous mesothelioma cases were unlikely to be due to exposures to asbestos in buildings and more likely to be due to past exposures in the 1970s and 80s following widespread environmental contamination with amosite, used in place of crocidolite.</p> <p>A WATCH member asked if, since most of the amosite imported to the UK in the 1960's and 70s originated from mines in South Africa, for which occupational epidemiological data was available, would these studies provide any insights into the characteristics of the amosite fibres most likely to be involved in the environmental contamination discussed?</p>
4.30	<p>Option (2): Further exploration of asbestos worker cohort studies</p> <p>A WATCH member wondered if more work could be done to examine if there was sufficient information in the larger asbestos worker cohort studies to demonstrate consistency in the ratio of a best estimate of "true" exposure with the exposure assessment made by the authors of the study. He was in favour of trying to generate a dose-response relationship from within a study (or a small number of more trustworthy studies), rather than fitting a model that uses every independent study to yield an independent data point, from which an overall dose-response curve is generated.</p> <p>Another WATCH member considered that reliable data to identify dose-response relationships, in terms of cancer arising at different exposure concentrations for different asbestos fibre types, are almost non-existent. Dose-response relationships can be constructed with more confidence in terms of duration of exposure (i.e. increasing cumulative dose).</p>
4.31	<p>The Chairman asked WATCH members whether they agreed with the approaches that had been used in the Hodgson and Darnton review. One member extended this further, by asking the questions :</p> <ol style="list-style-type: none"> (1) If a risk calculation was required, which of the Hodgson and Darnton or Berman and Crump approaches are better and why? (2) If there was merit in revisiting the task of reviewing the asbestos cohort data, would different approaches be considered now? If so, what would these be?
4.32	<p>John Hodgson replied that it would be of interest to factor into the Hodgson and Darnton analysis some of the concerns about the exposure measurements raised by Garry Burdett and to investigate how these may affect the risk estimates. This could be achieved using uncertainty analysis approaches, which to some extent, were applied by Berman and Crump. He expressed surprise that, having adjusted for fibre specific issues, Berman and Crump did not find that this had a major outcome on the risk estimates.</p>
4.33	<p>The previous WATCH member asked whether John Hodgson considered that additional analysis of the asbestos worker cohort data might provide a reliable indication of the level of risk associated with the current clearance limit (0.01 f/ml)? John Hodgson replied that this would require the inclusion of additional data from a wider selection of studies than that considered in the Hodgson and Darnton review.</p>
4.34	<p>With reference to Figure 2 of the Hodgson and Darnton paper, John Hodgson emphasised to WATCH his perspective that, despite the doubts about the quality of the exposure data in many of the epidemiological studies, there is an apparently good alignment between the risk estimates and the different types of asbestos fibre. Given that these relationships appear to be valid, revisiting the data using additional</p>

	<p>uncertainty analysis is warranted. Further analysis could include, for instance, available data on the environmental concentrations of asbestos from the Wittenoom cohort study, which would have contributed to total exposure.</p>
4.35	<p>A WATCH member stressed some points about risk and acceptability. He highlighted two important questions raised in the Hodgson and Darnton paper, the first being what is the relative potency of the three asbestos types studied and the second, what is the absolute potency of each fibre type? He then referred to Table 11 on page 585 of the Hodgson and Darnton paper and asked what effect the consideration of uncertainties associated with the exposure data would have on the risk estimates presented in this table and what this would imply in terms of the acceptability of these risks? Dr. Hodgson replied that in view of the discussions the risk estimates would go down but at present it was not possible to determine by how much or to address how the revised values would compare with a level of risk deemed to be “acceptable”.</p> <p>A WATCH member suggested that sensitivity and uncertainty analysis could provide helpful insights into the robustness of risk estimates associated with different exposure scenarios. He then presented a number of examples using the data from the Hodgson and Darnton paper to predict the number of deaths/million for each type of asbestos and suggested that the use of uncertainty analysis would give an indication of the potential variability in the magnitude of risk. He also gave an example using the Doll and Peto model to predict the number of deaths following a lifetime exposure to a background level of asbestos.</p> <p>The Chairman then asked WATCH members if at this stage they were confident in identifying with particular numerical values for risk? He felt that the committee had not yet reached this point, based on the discussions to date. A WATCH member commented that the available worker cohort data seemed to be informative but not reliably quantitative, in terms of making risk estimates.</p>
4.36	<p>The Chairman put to WATCH that, based on the discussion thus far, it seemed to him that there were two alternative positions they could take on the usefulness of the asbestos worker cohort data in relation to the questions that had been put to the committee. One was to consider that the whole dataset was unreliable, in relation to knowledge of exposure, and therefore unsuitable as a basis for extrapolating to low level exposure scenarios. The other was to consider that some epidemiological studies in the dataset had more reliable exposure data than others and, with further exploration, these could be potentially be used as the basis for constructing a dose-response relationship.</p> <p>In connection with the latter alternative, two WATCH members commented immediately that in their opinion the exposure data were very limited. However, John Hodgson proposed that it may be possible to improve the exposure estimates by closer examination of the data. Certainly it would be possible to select a few of the more reliable studies, or provide a better view of what the average exposures were in each study, or to supplement the dataset by looking at more recent studies of the consequences for populations of exposure to environmental asbestos.</p> <p>A WATCH member stressed that in his mind it was critical to define the problem that needs to be addressed. He was not sufficiently clear on this. He also added that it was important to bear in mind that none of the exposures experienced by asbestos workers are exclusively to a single fibre type. There are also other important issues to consider when trying to extrapolate from the observed data, including evidence of a non-linear dose response in terms of amosite, and the possibility that chrysotile and amphibole exposures can interact to enhance the overall effect.</p>
4.37	<p>Garry Burdett referred WATCH back to Annex 5 that provided an overview of the key issues affecting the exposure data associated with the quantitative asbestos cohort</p>

	<p>studies. Based on this, he highlighted some criteria that could be used to assess the quality of studies on the basis of their exposure data. He pointed out that some of the epidemiological studies would not have measured the peak airborne asbestos levels associated with particular tasks and thereby may have underestimated exposure. There were other systematic biases in the data that indicated that the exposure assessment had not been accurately derived. For example, many of the cohorts did not have any data on exposure levels in their early years of operation and therefore the authors of the study made assumptions about what these were likely to be. Exposures in these studies may have been subject to systematic under-estimation.</p>
4.38	<p>Option (3): exploring directly the risks of cancer in different contemporary occupational exposure scenarios</p> <p>A WATCH member suggested that the questions posed to WATCH in paragraph 15 of the cover paper would be better addressed in the context of the risk involved in specific exposure scenarios, preferably those for which some data exists. He suggested that consideration of the risk involved in specific occupations is important (e.g. the mesothelioma risk for carpenters has been estimated at 6%). In understanding risks associated with other scenarios, for example, risks posed by asbestos in buildings, consideration of historical data for air levels of asbestos in such buildings would be useful, alongside analysis of the associated risks. He considered that the focus of further analysis should be mesothelioma rather than lung cancer. The Chairman asked if it was possible to derive a reliable estimate of asbestos (amosite) exposure for carpenters. A WATCH member suggested that this would be possible by simulating what they did. Another WATCH member asked Professor Peto if part of his study presented earlier had included asking individual cases about their exposures? Professor Peto explained that it was not possible to get the required level of detail. Another member added that it was difficult for people diagnosed with mesothelioma to remember what they were doing 20-30 years ago in terms of their exposure.</p>
4.39	<p>A member suggested that, since the focus of interest was low-level exposure to asbestos, a possible exposure situation to explore could be that of teachers potentially exposed to asbestos in school buildings.</p>
4.40	<p>Extending the discussion of the issue of risk, the Chairman asked whether some key questions could be derived which could be put to WATCH to address at future meetings.</p> <p>Several WATCH members helped to suggest the following key questions :</p> <ol style="list-style-type: none"> (1) What is the number of mesothelioma cases which are plausibly due to exposure to ambient asbestos (based on current models and knowledge of the fibres types likely to be involved)? (2) What plausible risk estimate can be derived for mesothelioma based on the re-evaluation of past studies (with and without considering biases associated with the exposure data)? (3) Are concerns about potential contamination of the environment with amosite justified and what risks does this pose to people who may have been exposed with and without knowing? (4) To what extent are the uncertainties associated with the exposure data likely to influence the dose-response relationships (in terms of orders of magnitude) and what impact is this likely to have when using these relationships to extrapolate to low exposure scenarios? (5) What is the relative importance of different asbestos type; the relative risk by

	<p>concentration and fibre type and the relative and absolute risk by exposure?</p> <p>(6) Is it possible to characterise the high, medium and low risk exposure groups in the mesothelioma case-control study to help determine a dose-response relationship?</p>
4.41	<p>The Chairman sought and received confirmation from WATCH that its position was that, despite the large package of information and data that had been provided, this did not consist of the type or quality of data that would allow the Committee to derive scientifically robust statements on the level of risk associated with any specific exposure level/fibre type. The Committee had not yet identified any epidemiological studies for which it had confidence in the associated exposure assessment. Nevertheless, WATCH considered that the asbestos worker cohort data should be revisited to better determine its usability in terms of furthering understanding of risks, dose-response relationships and the scope for extrapolating to low level exposure scenarios.</p> <p>WATCH members agreed that further exploration of the existing cohort studies was warranted. A number of comments were raised in this respect. Garry Burdett reiterated that since measurement data and associated information was available in other published papers, relating to many of the cohorts studied, scope did exist to further assess the exposure levels involved in individual studies. He pointed out however, that the purpose of carrying out meta-analysis on epidemiological data, as opposed to considering individual studies separately, was to account for biases and provide an overall balanced position. A WATCH member commented that if separate analysis of individual studies and exclusion of those deemed to be of poor quality yielded the same findings as that for the entire dataset, this would essentially validate the conclusions of the Hodgson and Darnton paper. If on the other hand, exclusion of the more unreliable studies produced different findings, this may indicate that a meta-analysis approach may not be appropriate given the range of data quality issues affecting the cohort studies. Andy Darnton commented that Berman and Crump had attempted to look across the cohort study data, to explain sources of variability and to address uncertainties; ultimately, however, expert judgement rather than data had been used when adjusting for fibre length.</p>
4.42	<p>The Chairman thanked WATCH, and particularly the ad hoc members, for their comments and contributions to the extensive discussion. He said that he would work with the WATCH secretariat to try to capture from the notes taken a succinct portrayal of the position to which the discussions had led. This would then be offered to WATCH for comment, alongside the draft full minutes of the whole meeting.</p> <p>He also referred to the ACTS meeting on 15 November, which he would attend as WATCH chairman to deliver to ACTS a report from WATCH; he would need to give an account of the “asbestos” item and its outcome.</p> <p>For both purposes, the following text was suggested:</p> <p>WATCH indicated that in its view there were substantial concerns about the reliability of some aspects of the data within the occupational epidemiological studies included in the key assessments made by Hodgson & Darnton and Berman and Crump. The major concern was the quality of the asbestos fibre exposure data presented in many of these studies.</p> <p>WATCH considered that further work was needed before statements about dose-response relationships and/or the level of risk for different fibre types and different cancers can be made with confidence.</p>

	<p>A number of approaches were suggested for how the issue of characterising what can be said about the levels of risk involved in low level exposure to asbestos could be taken further forward by WATCH:</p> <ul style="list-style-type: none"> • There was scope for looking more closely at the individual occupational epidemiological studies included in the Hodgson and Darnton (and Berman and Crump) reviews, with a view to distinguishing those which are of better quality (and hence contain more reliable information) from those which have identifiable serious deficiencies in respect of exposure data quality. Any overall analysis might then lean more heavily on the more reliable data. • Given that the Hodgson and Darnton analysis was performed almost a decade ago, there might be merit in revisiting it. In doing so, alternative approaches to viewing and utilising the data from the original epidemiology studies could be considered, for example, using uncertainty analysis techniques such as those applied by Berman and Crump in their analysis. • As an alternative or supplementary approach to extrapolation from higher-level exposure, it might be possible to identify better the risks involved in lower level asbestos exposure by investigating directly such “lower-level” occupational exposure scenarios. One example might be to explore the situation for carpenters who have worked with amosite asbestos insulation board. If any exposure data are available for such work, these could be compared with the data we have on mesothelioma and lung cancer occurring in this workforce. • During the discussion it was stated that there is an indication that the incidence of ‘non-attributable’ mesothelioma has increased in the general population; this <i>might</i> be causally associated to past asbestos exposures in the general air, particularly near to sites of asbestos use. Further work could be carried out to investigate the apparent relationship between the data for environmental air asbestos levels (historically and currently) and the risk of mesothelioma in the general population. Any apparent relationship so derived might then be “reality checked” against predictions for this exposure scenario that would be made by extrapolating from data relating to higher levels of asbestos exposure. <p>In post-meeting clearance of the draft minutes WATCH agreed with this description of the position at which it had arrived.</p>
4.43	The chairman then asked the ad hoc members if they were willing to remain involved (as WATCH members) in the envisaged continuation of this work in WATCH; all the ad hoc members present indicated that they were and the chairman thanked them for this response.
4.44 ACTIONS	HSE to formulate a plan for taking the issue of estimating the risk involved in low level exposure to asbestos further forward at WATCH, the plan needing to incorporate the key points portrayed above that emerged from the discussion.
	Day 2 : 8th November
5	Introductions (day 2)
5.1	The Chairman welcomed WATCH members who had not attended day 1 to the 11 th WATCH meeting.
6	Administrative issues (day 2)

6.1	The Chairman asked for any declarations of interest related to the items on the agenda from members who has not attended day 1. David Farrar declared an interest in metal working fluids and low toxicity dusts.
7	Comparison between the dose-response relationship for the respiratory effects of respirable coalmine dust with similar relevant data available for other poorly soluble dusts of limited toxicity
7.1	The Chairman introduced the item by reminding WATCH that the dose-response relationship for the respiratory effects of coalmine dust (as a potential representative “poorly soluble, limited cytotoxicity” dust) had been considered at the February 2007 meeting of WATCH; and that the conclusions about coalmine dust then reached had been presented to ACTS at the May 2007 ACTS meeting. At the February 2007 WATCH meeting, other more general recommendations were also made and further progress on these was now the subject of this item. In this respect, HSE had now made a comparison between the derived dose-response relationship for the respiratory effects of respirable coalmine dust and similar relevant data available for other poorly soluble dusts of limited toxicity. The Chairman thanked Dr. Helen Ferguson (HSE) for conducting and documenting this analysis (WATCH/2007/9). He then referred members to paragraph 26 of the cover paper and asked WATCH to consider what conclusions could be drawn regarding how the dose-response data for the respiratory effects of respirable coalmine dust compare with the data for other poorly soluble dusts of limited toxicity? He added that the objective was to derive a view on the potential to use coalmine dust (and/or other dusts deemed to have reliable data on them) as a benchmark(s) for deciding on appropriate control standards for other poorly soluble dusts of limited cytotoxicity for which there is little or no information. He opened the item for discussion, initially inviting any general observations.
7.2	<p>Several WATCH members commented that the paper was helpful and had provided a clear and concise comparative analysis of dose-response relationship for the respiratory effects of coalmine dust and other poorly soluble dusts of limited cytotoxicity.</p> <p>A WATCH member expressed surprise at the observations of lung function reported in polyvinyl chloride (PVC) workers, particularly in relation to the prediction that 17% of workers exposed for a working lifetime to 4 mg/m³ would have a decrement in lung function of 3 litres. He thought that this prediction was excessive and wondered about the accuracy of these findings</p>
7.3	<p>Defining the scope of “dusts”</p> <p>A WATCH member pointed out that when this topic was first addressed by WATCH, the focus had been on dusts in general. The scope had subsequently been narrowed to “poorly soluble” dusts. The Chairman asked WATCH whether considering only poorly soluble dusts was still appropriate or whether it was necessary to broaden the scope to include other dusts? A WATCH member replied that broadening the scope may be necessary if the current reference levels for airborne concentrations of dust in general (10 mg/m³ inhalable dust and 4 mg/m³ respirable dust) were revised in the future. Another WATCH member agreed that it was important to define the scope of any positions derived by WATCH for “dusts”, particularly as this is an issue of interest to ACTS in relation to exposure control.</p> <p>A WATCH member commented that the expansion in building indicates that the use of cement is increasing. He wondered whether more data should be sought from the cement industry, given the comments made in the paper about the lack of reliable dose-response data for the effects of cement dust on lung function. He also questioned whether it was legitimate to include workers exposed to pulverised fuel</p>

	<p>ash (PFA) in the analysis of “poorly soluble, limited cytotoxicity” dusts presented in the paper, given that PFA generation occurred in a specialised sector of industry. However, it was clarified that PFA is then used in other industries, for example in specialist brick-making. The Chairman explained that the objective was to inform on appropriate control of dusts generated, for example, in building demolition or in recycling operations on hard materials, involving crushing and other dust-generating tasks.</p>
7.4	<p>A WATCH member commented that when addressing the scope of the “dusts” issue to be progressed by WATCH and how much further work should be done, it was important that the committee weighs up the potential benefits of the time and refinements involved in any further analysis, against the benefits of deriving positions now that could help immediately in developing appropriate control solutions.</p>
7.5	<p>Significance of lung function metrics</p> <p>A WATCH member commented that in the analysis presented in the cover paper, forced expiratory volume in 1 second (FEV₁) had been used as the only measure of lung function. This WATCH member and others asked for clarification as to why other metrics (e.g. forced vital capacity, FVC and FEV₁/FVC) had not been used in addition to FEV₁? Had other metrics of lung function been used in the studies but had been included in the paper presented to WATCH? Helen Ferguson replied that most of the studies used in the HSE analysis had used FEV₁ as the measure of lung function; there had been insufficient data available for any other endpoints or lung function metrics to enable any meaningful cross-comparison to be carried out for the dusts. The WATCH member returned to the apparently anomalous (excessive) reduction in FEV₁ for exposure to PVC dust and wondered if it could have arisen because of the (inappropriate) choice of lung function metric used? The Chairman pointed out that in the Institute of Occupational Medicine (IOM) report, concerns had been expressed over the quality of the PVC exposure data and it was to this that the apparently anomalous result had been attributed.</p> <p>Another WATCH member commented that the lung function metric(s) used in studies should be related to the health outcomes that were being investigated. For example, if the study was investigating restrictive lung disease, then FVC would be an important lung function metric to include. If on the other hand, the study was focused on obstructive disease of the lungs (e.g. chronic obstructive pulmonary disease) then FEV₁ or the ratio of FEV₁/FVC would be important metrics to include. He wondered if more analysis should be done on the types of effects on the lung that each of the various dusts investigated might have.</p>
7.6	<p>A WATCH member commented on lung function metrics based on his knowledge of carbon black studies. He highlighted that although various lung function metrics had been assessed for carbon black (e.g. FVC and forced expiratory flow 25-75% : FEF), measures of FEV₁ had tended to be more reliable and sensitive than other metrics to the effects of carbon black.</p> <p>Based on his knowledge of other studies of carbon black, he informed WATCH that additional data were available for the respirable and inhalable dusts of carbon black and for the effects of the respirable dusts on FEV₁ and FVC. Although these studies were unpublished, they were documented in a PhD thesis and were therefore publicly available. He informed WATCH that three cross-sectional studies had been conducted from the late 1980s to mid 1990s. The exposure conditions for workers were known to have differed across this time span; for example, the ratio of respirable to inhalable carbon black dust ranged from 20% in the earlier studies to 50% in the later studies. Recognising that respirable dust in these studies had been measured at relatively low levels (around the detection limit of the analytical methods used), these ratios of respirable to inhalable dust broadly agreed the assumption made in</p>

	<p>paragraph 12 of the cover paper that the ratio of respirable/inhalable dust was 50%. In terms of the effects on FEV₁, related specifically to measured <i>respirable</i> carbon black, a decrement of 60 ml per100 mg. months. m⁻³ was observed. Based on these observations, the WATCH member estimated that the mean loss of FEV₁ associated with a 40 year exposure to 2 mg.m⁻³ respirable carbon black dust would be 575 ml; with a mean loss of FEV₁ of approximately 1000 ml with lifetime exposure to 4 mg.m⁻³ (in comparison with the estimated mean loss value of 386 ml presented in the cover paper).</p>
7.7	<p>A WATCH member wondered how precise the various lung function metrics were in terms of providing insights into the respiratory effects of dusts and what was known about how variable were measurements made for these metrics? The Chairman pointed out that the available studies had used different approaches to assess the effects of dusts on lung function, and had done so at different points in time and to different standards. In addition, the extent and quality of the various data sets was variable. This given, the variability of measurements of lung function metrics was difficult to determine.</p>
7.8	<p>Considering the outcomes of the comparative analysis of dusts</p> <p>A WATCH member pointed out the observations across the data sets examined in the comparative analysis had been strikingly consistent, given the range of industries and dusts considered. This was suggestive of a general effect of dusts, rather than specific effects and further work to establish the common or generic features involved underlying this would be helpful. He proposed that this raised three key questions:</p> <ol style="list-style-type: none"> (1) Is more information needed on the ratio of respirable to inhalable fractions of different dusts? (2) Have health outcomes emerged that may be linked to dusts, other than those respiratory effects already observed? (3) Has any contradictory data emerged for dusts that may challenge the position that respirable, poorly soluble dusts in general induce respiratory effects with exposure at and around 4mg.m⁻³?
7.9	<p>In relation to point [3], the Chairman noted that HSE was not aware of a reliable “dusts” data set where respiratory effects had not been observed to some extent.</p>
7.10	<p>Another WATCH member suggested that, in addition to the European studies discussed earlier on carbon black (point 7.3), data from a study of USA carbon black workplaces, discussed at previous WATCH meetings in 2002, could be considered. The USA study had included a range of plants and was of similar quality to the cross-sectional studies discussed in point 7.3. The findings of this USA study were also in agreement with the findings reported in the WATCH cover paper and supported the argument that effects observed for dusts are consistent.</p>
7.11	<p>A WATCH member commented that if consistent findings in the responses of other metrics of lung function were also observed, this would reinforce the evidence for consistency of response to different dusts, based on responses in FEV₁. He wondered if there might be other studies available that could provide insights into this?</p> <p>Another WATCH member commented that if it was found that some, but not all such dusts produced responses in other lung function metrics in addition to FEV₁, then this might indicate that some dusts may be associated with more severe respiratory effects than others.</p> <p>In response to these comments, the Chairman pointed out that the paper presented for the item (WATCH/2007/9) encompassed pre-existing WATCH positions on the</p>

	respiratory effects of the different dusts analysed - no new evidence had been presented.
7.12	A WATCH member stated his view that FEV ₁ provided one of the most powerful indicators of lung function and he supported the analysis presented in the paper. To him the findings appeared to be valid and there was no viable alternative argument to explain the pattern of results. Another WATCH member commented that in his view, the observations for coalmine dusts had suggested that the validity of the level of 4 mg/m ³ as a key discriminatory point for exposure to respirable dusts was questionable. Given that consistent findings had also now emerged from studies on other dusts, he agreed with the first member's comment but added that consideration of any additional data that might be available was perhaps necessary to further strengthen the evidence base.
7.13	<p>Solubility of dusts</p> <p>A WATCH member expressed an interest in soluble dusts such as those encountered in the pharmaceutical industry. As soluble dusts, these presented very different toxicological profiles to the poorly soluble dusts that had been considered so far. The Chairman added that there were other soluble dusts of occupational relevance that pose concerns in relation to respiratory effects, such as those that dissolve to produce extremes of pH (e.g. sodium hydroxide dust). However, the processes by which such soluble dusts could induce respiratory effects were different to those by which poorly soluble dusts affected the lungs. The WATCH member agreed that for soluble dusts, the effects were chemically induced and therefore these dusts could not be grouped with poorly soluble dusts that induce effects by means of their physical properties. He emphasised the importance, therefore, of defining what 'poorly soluble dusts' means.</p>
7.14	A WATCH member asked if <i>in vitro</i> laboratory tests could be used to help group dusts together on the basis of solubility characteristics? He stressed that solubility in water was not necessarily the key issue; a more physiologically relevant approach might be to use synthetic lysosome solution to assess the solubility of different dusts. Another WATCH member agreed that the solubility of dusts in lysosomes was as important as their solubility properties in water.
7.15	<p>Benchmarking</p> <p>To focus the discussions, the Chairman gave a recap on the progress to date that had been made on the "dusts" topic and the issues WATCH had been asked to address. When this topic had initially emerged as a priority "new and emerging issue" for WATCH, the aim had been to examine the appropriateness of the existing regulatory stance on exposure to such dusts in workplace air. In terms of the progress made, he referred members to the two points in paragraph 26 of the cover paper. In relation to point (i), a dose-response relationship had been established for coal mine dust and further comparative analysis had now been carried out for a wider range of similar dusts. The Chairman asked WATCH what conclusions could now be drawn from this analysis?</p> <p>The aim of point (ii) was to consider what advice could be offered in situations where there was limited information about the particular dust involved in an exposure situation. In this context the Chairman asked: whether there was scope to 'read-across' from dusts for which there were good datasets to dusts for which little was known; to what scenarios could this be applied to and would bringing together information on groups of similar dusts be helpful?</p>
7.16	A WATCH member suggested that the best approach to point (ii) could be scrutiny of the available data and using expert judgement to select the values that could inform

	read-across from dusts with good datasets to those with poor datasets.
7.17	<p>Deriving a position on low toxicity dusts</p> <p>The Chairman suggested that, based on the analysis presented and the comments made during the discussion, a consensus had not emerged. Furthermore, he noted that members had stressed the importance of balancing the benefits of any further analysis against the benefits of making an informative position statement now, that could be used in deriving a stance on appropriate control. He therefore asked WATCH members</p> <ul style="list-style-type: none"> • Whether there was an outcome from the analysis that was sufficiently reliable to use to inform a wider position on the control of exposure to poorly soluble dusts of limited cytotoxicity? • Whether, if such an outcome were supported, it should be put to the next ACTS meeting on 15 November?
7.18	A WATCH member replied that a position could be taken now, but he did not think the full range of lung function parameters potentially affected by exposure to dust had been considered in the analysis. He re-iterated the view that if data were available on lung function parameters other than FEV ₁ , then these data should be examined before a final position is adopted by WATCH. Another WATCH member agreed that further assessments of different lung function parameters could be carried out, but that the primary aim of such work should be to further quantify the scale of effects of different dusts. In this respect, the Chairman suggested that, from what he had heard, further analysis could be carried out using the full extent of data available for carbon black. Another WATCH member commented that WATCH could derive a position now, based on the current assessment of data, but he would prefer the derivation of a final position to be informed by further exploration of all of the available relevant data.
7.19	A WATCH member commented that for any given dust, it was reasonable to accept a certain degree of uncertainty about the extent and nature of the respiratory effects that might be produced as a result of exposure. He felt that a generic position for exposure to such dusts could be derived, allowing the issue of appropriate control measures to be moved further forward.
7.20	A WATCH member wondered if we knew enough about current levels of exposure to such dusts? He suggested that the further work was needed to determine current standards of occupational hygiene, if the reference points of 4 mg.m ⁻³ and 10 mg.m ⁻³ were to be changed in seeking to improve the control of exposure.
7.21	<p>A WATCH member suggested that a meta-analysis of studies on dusts could be performed that included an analysis of uncertainties. Derivation of confidence intervals around normalised values could be derived for individual studies. Based on the observation range for each study, questions could address whether a no-effect level was apparent. In this context, he asked whether dose-response relationship had been observed for the individual studies. The Chairman replied that whilst a dose-response relationship had been established in some studies, there was insufficient data to do so in others.</p> <p>The Chairman expressed a concern about the scale of the work being suggested (refer to 7.4 and 7.18) and asked WATCH members to reflect on the importance/necessity of HSE and WATCH taking on this further work.</p>
7.22	In terms of any input WATCH could provide to the next meeting of ACTS, a WATCH member felt that the comparative analysis of a range of dusts in the paper WATCH/2007/9 should be presented to ACTS in the present format. He added that it would be helpful for ACTS to consider this analysis and provide WATCH with

	feedback on any additional data or information that should be gathered to inform on further progressing the issue.
7.23	<p>The Chairman thanked WATCH members for their comments and endeavoured to bring the item to a close. He reminded WATCH that the control of exposure to dusts in general is also currently being raised by ACTS. The next meeting of ACTS would be on 15 November and, as WATCH chairman, he would attend to report on the activity and outcomes of the last two WATCH meetings. <u>He suggested that the consideration of “dusts” by WATCH had now reached a stage where it would be appropriate to ask for a steer from ACTS about what direction should be taken for any further work by WATCH on this issue.</u> In this context he proposed the following summarisation of the position WATCH had now reached and said that, with WATCH’s agreement, he would report this to ACTS at its 15 November meeting:</p> <p>“WATCH had initially approached the issue of ‘poorly soluble, limited cytotoxicity’ dusts and the appropriate standard of control for exposure to dusts of this type by considering the data available on coalmine dust, given that this is the best dataset for a dust of this type. The dose-response relationship agreed by WATCH for the effects of respirable coalmine dust on lung function and the associated observations and recommendations from WATCH made at its February 2007 meeting were presented to ACTS at the May 2007 ACTS meeting. As a follow-on to this and discussions held at the June WATCH meeting, further analysis had been carried out to compare the dose-response relationship for the respirable effects of coalmine dust with similar relevant data available for other poorly soluble dusts of limited cytotoxicity (e.g. carbon black and kaolin). This analysis was considered by WATCH at its November 2007 meeting.</p> <p>Such analysis indicated to WATCH that, for the different dusts examined, there was some variability in the data for the estimated reduction in FEV₁ that would arise from exposure to 4 mg.m⁻³ of respirable dust; and there were a number of variable factors between the dusts (e.g. variable degrees of solubility within the “poorly soluble” general characteristic; distribution of particle size within the respirable range) that could influence their properties. Nevertheless, two important general points are that for each of the dusts examined, a significant effect on FEV₁ with exposure to 4 mg.m⁻³ respirable dust is apparent; and that notwithstanding some variability, the scale of reduction in FEV₁ under such conditions is of the same general order as that for coalmine dust. These findings reinforce the conclusion that a range of dusts of the “poorly soluble, limited cytotoxicity” type are predicted to produce reductions in FEV₁ on long-term exposure to 4 mg.m⁻³ respirable dust.</p> <p>Several suggestions for potential further work were made by WATCH at its November meeting:</p> <ul style="list-style-type: none"> • Exploration of the effects of dust exposure on lung function parameters other than FEV₁, such as FVC, to gain a more comprehensive picture of the total range and degree of effects. • Meta-analysis of the total data available from all of the individual studies, to further probe issues such as relative quality of data, consistency, uncertainty etc. • Advocacy of experimental work aimed at producing a solubility test that would be a reliable indicator of the relative solubility of different dusts in the lung; this might be useful in assessing the degree to which the unknown toxicological properties of a dust with respect to the lung might correspond to the properties of the poorly soluble dusts studied

	<p>here.</p> <ul style="list-style-type: none"> • Further development of benchmarking methods that might be used to find “best fit” approaches to connect a poorly soluble dust of limited cytotoxicity that has very limited data on it, with the dose-response data available for a more thoroughly studied dust with the most similar physicochemical characteristics. <p><u>WATCH agreed with this portrayal of the position and with the proposal that, via the WATCH chairman, a steer from ACTS was now needed to determine the future course of action.</u></p>
8	Registration, Evaluation and Authorisation of Chemicals(REACH) – update on activities of UK REACH CA
8.1	Nicola Gregg chaired this session and opened by inviting Steve Fairhurst to update WATCH on the activities of the UK Competent Authority (CA). Steve Fairhurst explained to WATCH that a large part of his job was to manage the UK REACH CA function housed within HSE. He would present WATCH with an outline of the current UK REACH CA arrangements and activity and suggest how WATCH may contribute to REACH-related activity in the future.
8.2	<p>Outline of UK REACH CA</p> <p>He started his presentation with a reminder of the different aspects of REACH including Registration, Pre-Registration, Evaluation and Authorisation. He then explained the role of a national REACH CA and emphasised that this role differs in its features from other familiar CA roles. Under REACH, very few decisions will be made at the national level. Instead, almost all decision-making will be carried out centrally by the European Chemicals Agency (EChA), based in Helsinki, assisted by REACH Committees which will comprise nominees from the EU Member States. As an example, national REACH CAs, including that of the UK, will have no part to play in the direct transaction between a company and EChA in registering a substance (although national REACH CAs will have a duty in securing compliance with registration). Another point he emphasised was that HSE, as host of the UK REACH CA, has a coordination role to link together the various UK regulatory authorities that will have roles in the REACH enforcement arrangements being established in UK.</p>
8.3	At present the key roles for the UK REACH CA are to raise awareness of REACH amongst potential UK duty-holders and to operate a helpdesk to provide advice to industry. Steve Fairhurst said that about 65% of the total UK REACH CA resource is currently being spent on these two aspects. A WATCH member commented that this work was appreciated by industry.
8.4	<p>Role of WATCH in REACH-related activity</p> <p>One member asked for clarification on the role WATCH might have in relation to work to be done by the UK REACH CA. Steve Fairhurst responded by saying that any input from WATCH would need to be within the committee’s terms of reference. One potential example would be that WATCH could become involved in substance <i>evaluations</i> under REACH, offering its perspective on a draft evaluation which would assist the UK nominees in their input to the relevant EU REACH committee deliberations.</p>
8.5	Another WATCH member asked for clarification on why it would be desirable to achieve a “UK position” (utilising WATCH) on the evaluation of a particular chemical if all decision-making would be carried out by the EChA and its committees? Steve Fairhurst replied that although the EChA would coordinate the programme of evaluations, individual Member States would be asked to carry out the much of the work via a “rapporteur” role. He hoped that the UK would be able to choose to

	<p>evaluate substances of particular interest to the UK. The WATCH member commented that the process described sounded similar to that operating in the OECD High Production Volume (HPV) chemicals programme.</p>
8.6	<p>A WATCH member commented that under REACH, the responsibility for chemical hazard assessment had shifted from government to industry. This given, control measures would most likely be based on caution and socio-economics, rather than scientific analysis. If this was the case, he was unsure what role WATCH could adopt in REACH work. In response Steve Fairhurst reiterated that he felt that it was important to retain a strong scientific basis for REACH decision-making and in this sense WATCH might be able to provide valuable input on substance evaluations and possibly on some generic technical issues.</p>
8.7	<p>A WATCH member supported this idea by stating that a lot of the work under REACH will be similar to the work carried out by WATCH in the past. For example, WATCH might be able to contribute helpfully to the ongoing considerations of different approaches that might be used to determine Derived No-Effects Levels (DNELs) for us in identifying an appropriate risk management regime for a substance under REACH.</p>
8.8	<p>Prioritisation and authorisation</p> <p>Several WATCH members asked how substances would be prioritised for evaluation under REACH and the chair for this session asked whether or not the UK REACH CA would be able to provide any input? Steve Fairhurst replied that discussions on this issue had not yet taken place.</p>
8.9	<p>A WATCH member asked about the <i>authorisation</i> aspect of REACH; specifically, if it was the EChA or an EU committee that would be responsible for interpreting the prioritisation criteria in terms of the candidacy of a substance for authorisation and deciding on the authorisation list. A WATCH member expressed his opinion that there needed to be set criteria for determining priority lists for authorisation and highlighted industry concerns that ‘unofficial grey lists’ of candidate substances could arise, which may influence how some substances are viewed by business and society. Another WATCH member considered that the criteria are clear and it was up to industry to interpret them appropriately. In his opinion a competent company would be able to identify how particular substances should be processed through REACH.</p>
8.10	<p>Steve Fairhurst clarified that the substances requiring authorisation will be category 1 and 2 carcinogens, mutagens and reproductive toxicants, those that meet the criteria for a PBT or vPvB substance, or a substance possessing “properties of equivalent concern” to these. He added that another role of the UK REACH CA would be to put forward to EChA candidate substances for authorisation. No decision had yet been made on how substances put forward for authorisation would be ranked.</p> <p>The chair for this session asked if substances had to be evaluated before being put forward for authorisation? Steve Fairhurst replied that they did not.</p>
8.11	<p>Time-frame for registration</p> <p>Steve Fairhurst then described the time-frame for registration of existing substances that fall within the scope of REACH. He explained that the registration process would be staggered, depending on tonnage per annum and chemical classification, and would run up to 1st June 2018. However, to qualify for such “phase-in” registration status, a substance had to be <i>pre-registered</i> with the EChA before the end of November 2008. If a substance is not pre-registered, then from 1 December 2008 it will need to be fully registered in order for its manufacture and/or supply in the EU to continue.</p>

8.12	A WATCH member asked if pre-registration required the submission of preliminary data? Steve responded that only very basic details are needed for pre-registration, as the main aim of pre-registration is to put parties with a common interest in the same substance in contact with each other, to facilitate a subsequent collaborative effort
8.13	In terms of <i>when</i> WATCH might be involved in REACH work, he explained that it was difficult to predict but, since the first deadline for registration of “phase-in” substances was 1st December 2010, significant involvement of WATCH in individual substance evaluations was not expected before then. However he suggested that there was the potential for WATCH involvement in issues before then. For example, one or two Member States may want to look at restricting the use of particular substances earlier than this, because they view a substance as posing a particular threat. He also added that the first list of substances for authorisation would be clarified in June 2009. In addition he said that there maybe generic issues to be addressed at WATCH before 2010 and referred to the presentation at the November 2006 WATCH meeting by Susy Brescia (HSE) on DNELs and risk assessment under REACH, the valuable comments provided by WATCH at that time having now been incorporated into the current EU guidance on DNEL derivation.
8.14	A WATCH member expressed concern that the EChA will receive a vast amount of information after 1 June 2008 and wondered how this would be processed. Steve Fairhurst acknowledged that there will be a huge amount of work required to process pre-registrations submitted from all of the companies associated with the estimated 30,000 eligible substances in the EU.
8.15	A WATCH member commented that there will be other work to do before the end of the first phase-in period, including work on the unfinished Risk Reduction Strategies under the EU Existing Substances Regulation (ESR) which will now be progressed under REACH.
8.16	Steve Fairhurst informed WATCH that member states’ nominations were now being requested for the various EU REACH committees. One of these, the Risk Assessment Committee, will also become involved in future EU classification and labelling work. It was possible that in the future WATCH could be asked to consider classification and labelling issues, as it had in the past.
8.17	A WATCH member asked how REACH will affect “new substances” from December 2008. Steve Fairhurst explained that if the substance is new to the EU market it will face a similar approach to that under current EU “7 th Amendment”/UK Notification of New Substances (NONS) legislation, in that under REACH the substance will need to be registered with EChA before it is manufactured or placed on the market. As with NONS, the quantity of pre-marketing information required is dependent on the tonnage, although in general there will be less data required under REACH than currently required under NONS.
8.18	The Chair brought this item to a close by thanking Steve Fairhurst for the presentation and members for the associated discussion.
9	Metal working fluids – update on progress within HSE since June meeting
9.1	The Chairman introduced this item, reminding WATCH that health risks posed by metal working fluids (MWF) had been identified as a ‘new and emerging issue’ at the November 2006 WATCH meeting and subsequently had been discussed further at the June 2007 WATCH meeting. He referred WATCH members to the actions from the June meeting (point 5.14 of the cover paper) and introduced Ian Gardner and Simon Edwards (HSE) who are involved in developing and delivering HSE’s plan of action on this issue. The Chairman then handed over to Ian Gardner to provide an

	overview of the work carried out since the June meeting and work that is planned for future delivery.
9.2	Ian Gardner informed WATCH that following the June WATCH meeting, HSE enforcement, inspection and regulatory specialists and HSL scientists had considered the key points and recommendations that had emerged from the discussion and had proposed a programme of research to take the issue further forward. There are two key strands of activity: (1) further investigation of ill-health associated with exposures to MWF; and (2) investigation of potential contaminants of MWF.
9.3	<p>Initiatives already approved for funding by HSE</p> <p>Ian Gardner informed WATCH that proposals for two initiatives recommended at the June WATCH meeting had been submitted to HSE and had been approved for funding. Proposals for the delivery of this work were currently being prepared. He gave a brief summary of the two initiatives:</p> <ol style="list-style-type: none"> 1. A critical review of outbreaks of respiratory disease associated with MWF will be carried out. The aim of the review will be to examine outbreaks in the UK, Europe and elsewhere to understand why these have occurred at some MWF plants, but not in others. The review will also consider potential aetiological agents (microbial, immunological and chemical) and the different strategies used to control contamination of, and exposure to MWF. 2. A case definition of respiratory ill-health (including extrinsic allergic alveolitis and asthma) associated with MWF work will be carried out. The case definition will be reviewed, finalised and submitted for publication by a study group including clinicians from GORDS (Group of Occupational Respiratory Disease Specialists)
9.4	<p>Additional proposals</p> <p>In addition to the initiatives that had already been approved, Ian Gardner informed WATCH that the programme of work on MWF also included proposals to address a number of other specific topics. The business case for these proposals would be considered by HSE during November. He then summarised these topics in the anticipated order of delivery and priority :</p> <ol style="list-style-type: none"> 3. Work has been proposed to develop an action plan for managing and further investigating any future outbreaks of respiratory ill-health associated with MWF. This will involve HSE inspectors, occupational hygienists, clinical and laboratory investigators, in consultation with MWF users, producers and relevant trade bodies. It will include consideration of data handling and dissemination of results. 4. A workplace study of micro-organism growth, endotoxins, immunogenic proteins and chemical contaminants in aging conventional and “bio-concept” MWF products. The aim of this work will be to understand the factors that can influence contamination and help inform guidance for the use and management of conventional and “bio-concept” MWF. 5. Investigations have been proposed for alternative methods to the widely used approach of using dip slides for monitoring contaminants in MWF. Work is also needed to establish a robust method to monitor inhalation exposure to mists of MWF to help inform exposure assessment. 6. A workplace research study of MWF-exposed workers has been proposed. A large well-designed workplace research study is required to improve understanding of the relationship between exposures to chemical and biological agents and respiratory ill-health.

	<p>7. Little information is available about the immunological response to biological contaminants associated with MWF. A study has been proposed to investigate the role of bacterially derived proteins to determine whether common DNA/protein epitopes in closely related bacteria (<i>Pseudomonas</i> and related genera) exist and whether exposed workers carry immunological markers of response to these molecules.</p>
9.5	<p>Timescales for planned research activity</p> <p>The Chairman thanked Ian Gardner, commenting that it appeared that the HSE team were planning to address the key points that had been raised at the June 2007 WATCH meeting. He reminded WATCH that a consensus view had emerged at the June WATCH meeting that MWF was an appropriate issue for the committee to address, as it involved assessing and controlling chemical entities. He asked Ian Gardner to indicate the expected timeframes for delivery of each of the projects.</p> <p>Ian Gardner replied that some of the proposals had specific milestone and end-dates: the outcome of the critical review of respiratory disease was expected in April 2008 and the workplace study of MWF contaminants was planned for the next 3 years. He informed WATCH that the aim was to complete most of the proposed projects by April 2009 and he would confer with HSE colleagues to obtain further information in this respect.</p>
9.6	<p>A WATCH member asked whether the timing of the research projects would be staggered? He anticipated that the outcome of the critical review of respiratory disease associated with MWF would influence the activities carried out in some of the other projects. Ian Gardner confirmed that the outcomes from projects that had already been approved would be used to directly inform the other projects.</p>
9.7	<p>A WATCH member commented that the plan to conduct workplace investigation of respiratory ill-health linked to MWF was highly appropriate. He pointed out that had a similar incident to that at the Powertrain Ltd plant occurred in the USA, a major investigation of other workplaces would have been instigated. He asked if there were plans to include small-to-medium-sized enterprises (SMEs) as well as larger firms in the study? He also commented that workplaces with poorer standards, and hence a greater potential for disease to occur, should be included in the study. Ian Gardner agreed that it was important to include workplaces with poorer hygiene standards in the study. He added that since the Powertrain Ltd incident there had been a number of other sporadic cases of respiratory ill-health in sites using MWF which indicated that this may be an on-going problem at the number of workplaces.</p> <p>Another WATCH member commented that occupational hygiene resources in the UK are limited. He suggested that, during the proposed studies, it would help to secure proper maintenance and control of MWF if HSL scientists visiting engineering workshops to collect spot samples could provide information about the husbandry and stewardship issues relating to MWF.</p>
9.8	<p>A WATCH member asked whether there was any potential for disease to occur following dermal exposure to MWF? Ian Gardner replied that no such concerns had emerged. The proposed studies only intended to consider exposure via the inhalation route.</p>
9.9	<p>There being no further points made, the Chairman brought this item to a close by affirming with WATCH that the proposed programme of research on MWF had been well received and would address the key points raised at the June 2007 WATCH meeting. He asked Ian Gardner, on behalf on the HSE/HSL project team on MWF to provide WATCH with the expected timescales for conducting the projects in the programme. He highlighted that a key milestone in the programme - the outcome of the critical review of respiratory disease associated with MWF - was expected to be</p>

	delivered in April 2008.
9.10 ACTIONS	HSE to provide WATCH with an outline of the expected timeframes for the projects within the research programme on MWF. HSE to provide the WATCH Secretariat with regular updates on the progress of individual projects within the research programme.
10	New and Emerging Issues – Horizon Scanning within HSE and a review of 2 years experience of this process at WATCH
10.1	<p>The Chairman opened the item by introducing HSE’s Chief Scientific Adviser, Dr Patrick McDonald, to the Committee and inviting him to give a presentation on the topic.</p> <p>Patrick started his presentation by outlining his roles in HSE. These include his responsibilities for HSE’s “analytic services” which provide the science and engineering evidence base to support HSE planning of its business; and his responsibilities as head of HSE’s “science and engineering” profession, which includes providing HSE with the specialist resource it needs, managing the professional development of such specialists, and the procurement of new scientific work (mainly from HSL) needed by HSE.</p> <p>He explained that one of the major challenges facing HSE is deciding on its science and technology priorities, given the breadth of responsibilities of HSE. The use of horizon-scanning techniques is an attempt to help with this prioritisation process.</p> <p>He then described the different horizon-scanning categories used in HSE including four key areas - the workplace; political climate; science and technology; and socioeconomic trends. He explained that each of these key areas is associated with a number of drivers and a number of uncertainties. In terms of science and technology, drivers include energy (including climate change, security of supply, increasing demand and its different forms), computer dependency, genetically modified organisms, UK technical capability and UK industry competitiveness. Uncertainties include disasters such as Buncefield; the public perception of HSE; and geopolitical issues.</p> <p>Many of the drivers and uncertainties affecting the workplace reflect changes in the economy, for example many traditional industrial diseases have disappeared or reduced but the emergence of new sectors such as the waste reclamation industry have led to new health problems being identified including a high incidence of physical injury and fatality and the potential for the development of respiratory diseases arising from exposure to materials in waste.</p> <p>Patrick McDonald then described the formal scenario-casting techniques used in HSE to test different propositions and highlighted one of the outputs from this process that suggested that in future HSE should have an increasing role in education, awareness-raising and guidance. Therefore it will be necessary to maintain and further develop this capability. However it also raises questions as to how HSE can combine the roles of regulator and advisor.</p> <p>He also outlined an alternative approach to horizon-scanning in which specific topics are investigated, such as the potential for future use of performance enhancing drugs by workers in high-hazard workplaces, to increase their attention span.</p> <p>He concluded his presentation by highlighting the current challenge facing HSE of how to incorporate the outputs of HSL’s horizon scanning team that is endeavouring to address issues in 10+ years time into HSE’s business planning process that</p>

	<p>traditionally looks ahead only 3 years. He asked members for their comments and views on what issues may be important in the future and offered WATCH the ability to interact further with HSL's horizon scanning facility.</p>
10.2	<p>The Chairman thanked Patrick McDonald for his presentation and asked members for their comments.</p> <p>Several WATCH members acknowledged the difficulties associated with trying to predict future health and safety issues but believed that WATCH had a role to play in horizon scanning and expressed an interest in working with HSL's horizon scanning team. They also suggested that WATCH may need to adopt a more flexible way of working in the future to deal with the identification of new and emerging issues, such as the provision of views by correspondence on issues requiring an immediate reaction.</p>
10.3	<p>A member suggested that HSE may find it helpful to engage with other committees/bodies carrying responsibilities for horizon-scanning in other areas, on matters common to both, such as those relating to applied ethics.</p> <p>Another member commented that in his opinion certain ethical issues will need to be addressed in the future, such as balancing a person's right to work against the need to maintain a fit workforce by preventing sensitive sub-populations from working with specific substances.</p>
10.4	<p>A WATCH member considered that gauging public attitudes to particular subjects was important and noted that the acceptability of situations and circumstances can be amplified or attenuated depending on public perception. He felt that sometimes "new" issues were not new but simply re-branded existing issues; he felt that nanotechnology and nanoparticles had some such features. Patrick McDonald agreed that public attitude was important but suggested that it is very difficult to predict.</p> <p>In the context of public perception, a couple of members highlighted the issue of newspaper reports incorrectly portraying health and safety regulations as the reason for certain activities being prevented and the problems that this causes health and safety regulators when trying to convince the public of the need for action in respect of serious occupational health and safety issues.</p>
10.5	<p>On a different topic, a member asked if information was available on the predicted demographic trends for the UK workforce, in relation to chemical exposure? He highlighted the problems associated with communicating health risks and appropriate control measures to workers in sectors that employ largely migrant workers. Peter Elwood (HSE - HSL horizon-scanning team) said that his unit had produced a general report on UK workforce demographics, available on the HSL website, and suggested that this might be looked at in more detail with WATCH.</p>
10.6	<p>John McAlinden (HSE) informed WATCH that the identification of situations where migrant workers comprise a substantial proportion of the relevant workforce was included as a consideration in the prioritisation work done within the Cancer Project of the Disease Reduction Programme and seen recently by WATCH. The only sector identified thus far as having a significant number of migrant workers is the foundry sector.</p> <p>A member highlighted the problem of workers in the transportation industry who are not UK residents being unaware of the standards required in the UK in relation to the transport of chemicals.</p> <p>The Chairman suggested to WATCH that if, in delivering its horizon-scanning responsibilities, members identified a need for particular reference material that might</p>

	<p>be available (eg demographic trends), then they should submit these requests to the WATCH Secretariat who would find out if this information was available and, if so, provide it.</p>
10.7	<p>The Chairman reminded members that WATCH had had “new and emerging issues” sessions at two previous WATCH meetings (in 2005 and 2006) and asked members if, prior to undertaking a third horizon-scanning session, WATCH might benefit from a structured horizon-scanning workshop delivered by Peter Elwood’s team sometime in 2008? This was welcomed by the committee.</p> <p>The Chairman then asked members if they considered that horizon-scanning modelling techniques could be applied to specific substances, such as asbestos, to make predictions of future outcomes in terms of disease incidence, based on a particular exposure scenario and the planned course of action? A WATCH member thought that this should be explored; one always had to consider questions being asked in the future as to why nothing was done to prevent future cases of ill health when the tools enabling this outcome to be predicted were available at the time that no action was decided upon. He suggested that it might be helpful to look back at the regulatory actions taken in relation to asbestos in the 1970’s and try to assess whether or not, with the data available at the time and the modelling techniques now available, the outcome seen in current cancer statistics could have been predicted?</p> <p>Another member highlighted the issue of occupational asthma caused by isocyanate exposure and the fact that data highlighting the scale of the problem was available for 20 years prior to any tough regulatory action being taken. He added that in his opinion a similar situation was now evident in relation to flour dust. He also believed that there should be more feedback on the impact of regulatory decisions to guide future decision-making. Another WATCH member reflected on the potential for a future public backlash in relation to the amount of asbestos that is still in UK buildings and health risks arising from exposure, particularly to carpenters and maintenance workers but also more generally to members of the public – questions might be asked in the future about why it was not removed? Patrick McDonald confirmed that these techniques can be used to look at past decision-making processes to inform future decisions and referred to the lessons learned after the foot and mouth outbreak in 2001.</p>
10.8	<p>A WATCH member suggested that in such considerations in the future it might be possible to utilise information from a number of EU projects that are developing models to assess the impact of EU regulations on environmental pollutant emissions.</p>
10.9	<p>The Chairman suggested that it might be worth considering the predicted impact of REACH on the UK chemical industry over the next 10 years, in terms of changes in the way industry might do its business? For example, will there be fewer small companies? Will downstream users act differently because they are provided with a higher quality safety data sheet and detailed control specifications?</p>
10.10	<p>A WATCH member asked Patrick McDonald to clarify where he sees the split between “blue sky” future-gazing activities and shorter-term tactical work based on what is happening in industry now and in the near future? Patrick McDonald responded by saying that there is an overlap between these activities. He would appreciate any WATCH contributions to this process, even if it were restricted to predictions for the next 3-5 years; this would still be important in helping to determine how HSE resources are best distributed.</p>
10.11	<p>No other points were made. The Chairman brought this item to a close by thanking Patrick McDonald and Peter Elwood for their contributions and members for the associated discussion.</p>

10.12 ACTIONS	HSE to develop a horizon-scanning workshop as a component of a 2008 WATCH meeting.
11	Global Harmonised System for Classification and Labelling (GHS) – update on progress towards implementation and impact on current system
11.1	Nicola Gregg chaired this session. Steve Fairhurst introduced the item by reminding WATCH that it had undertaken to keep under consideration progress on the adoption by the EU of the GHS. This was to be an update on the current situation.
11.2	<p>Overview of progress of the GHS in the EU</p> <p>Steve began a brief presentation with a reminder of the history of GHS which started in 1992 with an international commitment to develop a global system to harmonise classification and labelling and culminated in the agreement of a United Nations Globally Harmonised System 15 years later. The EU has now decided to adopt much of GHS into EU law via the proposed new Classification, Labelling and Packaging of Substances and Mixtures Regulations, a draft of which was published in June 2007. A public consultation has been held and Member State negotiations, which began in July 2007, are expected to continue up to late 2008. The European Commission has hopes that the new regulations can be brought into force by 2009 because one of the conditions of REACH requires the application of a classification and labelling system to substances and mixtures thereof. It was therefore preferable to have the new GHS regulation in place when use of classification & labelling rules are required under REACH. The current draft regulation proposes transitional arrangements such that from 1 December 2010 substances should be classified under the new system and also according to the current EU system, but should be labelled and packaged only in accordance with the new system. From 1 June 2015 substances and mixtures shall be classified, labelled and packaged according to the new regulation only. The Helsinki EChA will be the centre for the new EU classification & labelling work, in addition to REACH.</p> <p>He then highlighted a number of key issues that had been raised by Member States, including:</p> <ul style="list-style-type: none"> • The necessity, not yet assured in the new draft regulation, for consistency with REACH (especially in regard to terminology, confidentiality rules, language provisions) • Concerns over whether or not the transition period is too ambitious • The need to ensure all other EU legislation affected by changes to classification & labelling rules and positions is amended prior to entry into force of the new regulation. • Concern over possible ambiguity by the proposed shift away from classification of ‘what is placed on the market’ to ‘the form or state in which a substance/mixture to be used or reasonably be expected to be used’. • The need to clarify the roles and responsibilities within the supply chain. <p>Steve concluded the presentation with an outline of future plans in relation to the proposed new regulation.</p> <ul style="list-style-type: none"> • Member State Council negotiation meetings are planned until end 2007.

	<ul style="list-style-type: none"> • HSE consultation within the UK on the proposed regulation and the accompanying regulatory impact assessment ended on 2 November. • There is an EU “correspondence group” charged with reviewing the technical annexes to the draft regulation, to which HSE has put a number of comments. It is unclear as to how this work will be progressed. • REACH Implementation Project (RIP) 3.6 – ‘Guidance for industry on GHS’ is being developed concurrently with other GHS work. There may be difficulties in the EU co-ordinating ongoing parallel progression of the draft regulation itself, its technical annexes, and RIP 3.6 guidance on how to use the new system. <p>There is a UN sub-committee of experts in GHS that will hold regular 6 monthly meetings to review and, if necessary, amend and update the GHS.</p>
11.3	<p>A WATCH member expressed concern that under the proposed new EU classification & labelling system, there was more scope for a company using its own judgement when classifying and labelling a substance; there would be no standardisation by the regulatory system of classification and labelling for some toxicological endpoints. He asked Steve Fairhurst to clarify if regulatory authorities would develop any systems for the selection of appropriate toxicological approaches in these circumstances?</p>
11.4	<p>Steve Fairhurst responded by saying that according to the proposed new regulatory framework, regulatory authorities will standardise classification and labelling for the human health endpoints of carcinogenicity, mutagenicity and reproductive toxicity. Beyond this, via REACH Substance Information Exchange Forum (SIEF) arrangements companies will be expected to resolve and agree among themselves the appropriate classification and labelling of a substance for other endpoints such as eye irritation. Another WATCH member clarified this point, suggested that classification and labelling decisions may be made by industry consortia rather than by SIEFs. He also offered a view that whilst some industries will act responsibly in regard to classification and labelling, others may seek to exploit the system and choose to take toxicological positions to their advantage. In his opinion, a system of rules and guidance needed to be in place to prevent this.</p>
11.5	<p>Two WATCH members commented that industry does not expect there to be globally harmonised labels in the foreseeable future. The concern is that each country will endeavour to create a national position.</p>
11.6	<p>GHS & COSHH Essentials</p> <p>A WATCH member asked if the new EU classification and labelling system would have an impact on COSHH Essentials in regard to control banding? Steve Fairhurst responded by saying that inevitably it would. Within the features proposed to assist with introduction of the new classification & labelling regime there is a proposition that a semi-automatic conversion of existing to new (“GHS”) classification can be made, without the need for detailed re-evaluation of individual substances. Inevitably there will need to be a change in COSHH Essentials terminology because the GHS does not have the same labelling phrases, nor term them “R-phrases”. Steve also suggested that if REACH works as planned then there would not be the same need for COSHH Essentials in some areas.</p> <p>A WATCH member informed the committee that both the current EU and future EU “GHS” classification systems had been used in parallel at a recent EU classification and labelling meeting, an account of which could be found on the European</p>

	<p>Chemicals Bureau (ECB) website. He added that the REACH draft guidance RIP 3.2.2 advocates a “COSHH Essentials” style approach to risk control, but disappointingly from a UK perspective it cites the German version of COSHH Essentials in support of this position.</p> <p>Another WATCH member commented that although COSHH Essentials is an excellent system to use, unfortunately it disappoints for the control band of highest concern, when it goes no further than suggesting that the user “seeks expert advice”. He believed that this aspect needed to be improved if COSHH Essentials is to have a valuable role in the longer term.</p>
11.7	<p>One member also suggested that there should be training provided for workers and the general public on the correct interpretation of the new hazard symbols. Steve Fairhurst responded by saying that it is anticipated that Member States will be required to provide a helpdesk/awareness raising function for the new EU classification & labelling system, similar to that now being provided for REACH.</p>
11.8	<p>The Chair brought the item to a close by thanking Steve Fairhurst for the presentation and WATCH members for their comments.</p>
12	Date of next meeting
12.1	<p>The Chairman thanked everybody for their contributions. The Secretary reminded WATCH that the next meeting will be held on the 13th February 2008 at the Health and Safety Executive, Rose Court, London,</p> <p>The meeting closed at 15.00.</p>