

WORKING GROUP ON ACTION TO CONTROL CHEMICALS

WATCH/MIN/2005/1

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Minutes of the 3rd meeting of the Working Group on Action to Control Chemicals held on 13th – 14th January 2005 in the Kilmore Suite, Thistle Hotel, Liverpool.

Members Present

Steve Bailey
Steve Binks
Robin Chapman
David Farrar
Tony Fletcher
Alistair Hay
Rosemarie Hutchinson
Len Levy
Mark Nieuwenhuijsen
Ted Smith
Steve Williams

Invited Experts Present

Ken Donaldson (Item 3 only)
Rob Aitken (Item 3 only)
David Coggon (Item 7 only)

Apologies

None

Officials Present

Steve Fairhurst (Chair)
Nicola Gregg (Secretariat)
Mike Costigan (Secretariat)
Hayley Keating (Secretariat)
Christine Northage
Andy Garrod (Item 5 only)
John Groves
John Cocker
Damien McElvenney
Mike Topping (Items 8 & 9)
Maureen Meldrum
Andrew Smith (Items 6 & 7)
Alex Tsavalos (Item 3 only)
Steve Coldrick (Item 6 only)
Peter Howden (Items 6 & 7)
Peter Ridgway (Item 4 only)
Isla Fraser
Rob Turner
Dave Mark (Thurs only)
George Cartlidge (Item 3 only)
Lol Monaghan

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| 1 | Administrative issues |
| 1.1 | The Chairman welcomed everybody to 3 rd meeting of the Committee. |
| 1.2 | <p>WATCH secretary Nicola Gregg went through some administrative issues relating to the running of the Committee:</p> <ul style="list-style-type: none">– Outstanding on-appointment Declarations of Interest were requested by the end of the meeting.– She asked if expense forms with receipts could be sent to the Secretariat as soon as possible or at the latest within one month of the meeting.– Agendas, papers and minutes of meetings will shortly appear on the WATCH website. As part of the minutes Members names will be published but the minutes will be unattributed.– An annual report will be produced by the Secretariat and submitted to the March meeting of ACTS. |
| 1.3 | Members were invited to give feedback to the Secretariat on the administration/procedures of the “new” WATCH Committee, based on the previous two meetings. A request was made that for future meetings a provisional agenda should be sent to WATCH Members as far as possible in advance of |

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| | the meeting. |
| 1.4 | The Chairman informed WATCH Members that for the first time ad hoc Members had been invited to provide additional expertise to the discussions on nanotechnology (Professor Ken Donaldson, Edinburgh University and Dr Rob Aitken, Institute of Occupational Medicine) and formaldehyde (Professor David Coggon, Southampton University). During these items, the status of the invited experts is identical to that of permanent WATCH Members. |
| 1.5 | Adoption of agenda WATCH Members agreed to adopt the proposed agenda (WATCH/Agenda/2005/1). |
| 1.6 | Declarations of interest WATCH Members declared interests in the items on nanotechnology (Len Levy, Steve Bailey, Steve Binks, Robin Chapman), formaldehyde (Robin Chapman, David Farrar) and isocyanates (Robin Chapman). |
| 1.7 | Minutes of the 2nd meeting Members had commented on the first draft of the minutes of the second meeting (WATCH/Min/2004/2) through correspondence. They confirmed their agreement to the draft minutes now presented. |
| 1.8 | In relation to follow-up actions, it was noted that, under item 5 of the minutes, HSE had not yet provided WATCH Members with the promised current understanding of the meaning of "indicative". The Chairman apologised for this oversight and committed HSE to meeting this request. |
| 1.9 | When asked by WATCH Members, HSE responded that no feedback had been received from any Member on the paper presented by Maureen Meldrum (HSE) at the previous meeting. In relation to feedback from the COPD workshop held in July 2004, the report of the meeting is now available and copies of the report will be circulated to Members. [ACTION: HSE to provide WATCH Members with the current understanding of what "indicative" means in the context of EU Indicative Occupational Exposure Limit Values; and to circulate copies of COPD workshop report to WATCH Members] [Post Meeting Activity: Paper and electronic versions of the COPD workshop report were distributed to Members with the draft minutes to this 3rd meeting of WATCH] |
| 1.10 | A member asked about the progress of the regulatory impact assessments (RIAs) on chlorine and nitrogen monoxide foreseen by Teresa Quinn (HSE) in her presentation to WATCH in June 2004 as being necessary because it was thought that the limits proposed for these substances in the 2 nd IOELV Directive may not be practicable. HSE replied that following an initial consultation, a detailed RIA is to be undertaken on nitrogen monoxide, as industry had concerns with the proposed limit. In relation to chlorine no information had come to HSE's attention to suggest that the proposed limit is impracticable and so no further work is being done. |
| 1.11 | The Chairman then asked for views of Members on the style of the minutes produced for the previous two meetings compared with those produced for WATCH up to 2003. Members requested that for substantive items detailed minutes should be produced so that the reader could follow the arguments and understand how conclusions were derived. For less substantive items, a more succinct form of minutes would be appropriate. HSE undertook to try to meet these needs. |
| 2 | The principal strands of HSE's work on chemicals and ill-health & Clarification of the role of WATCH in this context |
| 2.1 | Steve Fairhurst gave a presentation clarifying HSE's current strategy for work on chemicals and ill-health and then led a discussion with Members about the ways in which WATCH could input into this work. |
| 2.2 | Presentation on HSE's future work on chemicals and occupational ill-health In the presentation, it was emphasised that the highest priority for HSE is meeting the Revitalising Health and Safety (RHS) targets, although clearly HSE also has other responsibilities and activity to cover. HSE aims to deliver the RHS targets via programme working, whereby a substantial amount of HSE's resource is lined up along a small number of strategic directions. Within these arrangements, |

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| | <p>HSE's work on chemicals and occupational ill-health is now described by 3 categories:</p> <ul style="list-style-type: none"> – The Disease Reduction Programme (DRP; formerly the Chemicals Programme). – Mandatory “core” activities, eg statutory responsibilities. – Other “core” activities eg the identification of new and emerging issues. |
| 2.3 | <p>The DRP is intended to contribute to the RHS targets, specifically in relation to the aim of reducing the incidence of ill-health by 20 % in 2010, relative to 2000. The available occupational ill-health statistics have directed HSE's attention towards three priority disease areas: skin disease, respiratory disease and cancer. Within each disease area, work has initiated to identify where the biggest problems occur and then to develop effective interventions. The interventions will represent risk management strategies which could, for example, involve the development of COSHH Essentials guidance. Occupational exposure limits and biological limits could also be developed as part of the risk management armoury, but in future they will be explored within the context of Disease Reduction work, rather than as a stand-alone rolling programme.</p> |
| 2.4 | <p>Mandatory “core” activities cover HSE's statutory responsibilities as the UK authority for EU-wide regulatory schemes such as Classification and Labelling, Existing Substances Regulation (ESR), Notification of New Substances (NONS), Chemical Agents Directive and Indicative Occupational Exposure Limit Values (IOELVs) Directive.</p> |
| 2.5 | <p>Other “core” activities include identification of new and emerging issues (“horizon scanning”) and helping reactively in incident investigation; it is intended that relatively modest resource will be allocated to this work.</p> |
| 2.6 | <p>It was emphasised that on this and future WATCH agendas, the source of each item, in the context of the above strategy and categorisation of work, would be indicated in the cover paper and in introducing the item at the meeting.</p> |
| 2.7 | <p><i>Discussion on the role of WATCH in the context of HSE's work on chemicals</i></p> <p>The Committee was then asked to consider paper WATCH/2005/1, which attempted to set into context the role of WATCH within the framework of HSE's work on chemicals. If agreed, this paper would then be presented to the March 2005 ACTS meeting, to provide clarity about the role of WATCH.</p> |
| 2.8 | <p>A number of Members highlighted the point made in the paper that they are nominees and not representatives. Although it was accepted that the nominating bodies should have confidence in the scientific integrity of their nominees, the use of the phrase “...secures social partner acceptance/agreement of S&T positions..” was thought to be inappropriate. It was agreed that “secures” be replaced by “supports”.</p> |
| 2.9 | <p>The following additional points were made by Members regarding the role of WATCH:</p> <ul style="list-style-type: none"> – WATCH Members could have a more active involvement in the DRP outside of WATCH meetings, for instance by attending any workshops that are planned for each of the three disease areas. – WATCH should monitor the disease burden in relation to occupational chemical exposure and identify any changes in pattern and where new issues arise. – REACH could have an impact in the workplace as it will replace ESR and NONS legislation. Issues pertaining to occupationally relevant areas of the REACH regulations should be considered by WATCH. The Chairman reminded WATCH of the current policy of the Health and Safety Commission, that HSC/HSE intends not to be a major component of the UK Competent Authority for REACH. – To assist WATCH in providing the most useful advice, a Member asked that, for any agenda item, the Committee be provided with a clear understanding of the framework in which it is intended that its recommendations will sit. – A Member also suggested the need for a mechanism for WATCH Members to input information on opportunities to improve occupational exposure in the workplace. |
| 2.10 | <p>The Chairman thanked WATCH Members for their views. A revised draft of the paper on the role of</p> |

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| | <p>WATCH, modified to take account of comments made, will be presented to ACTS at its March 2005 meeting.</p> <p>[ACTION: HSE]</p> |
| 3 | Nanotechnology: Positions on occupational health issues raised by Nanotechnologies |
| 3.1 | <p>The Chair introduced Professor Ken Donaldson and Dr Rob Aitken, who had been invited to the meeting for this item as ad hoc expert committee members. He explained that HSE had focused attention on the potential occupational health aspects of nanotechnologies as part of its horizon-scanning activities. The opinion of WATCH on HSE's assessment of the potential human health hazards posed by nanoparticles generated by nanotechnologies, the current occupational exposure situation and the regulatory position surrounding the risk assessment and control of exposure to nanoparticles was now sought.</p> |
| 3.2 | <p>Christine Northage introduced the members of HSE's nanotechnology team who were present: Alex Tsavalos, Isla Fraser and Dave Mark. She gave an update of HSE's activities on nanotechnology, including HSE/HSL's partnership with NIOSH to organise and host the 1st International Symposium on Nanotechnologies and Occupational Health, held in October 2004. The 2nd International Symposium is to be held in Minneapolis in October 2005 and will again be sponsored by NIOSH and HSE (including HSL). She noted that the Government response to the Royal Society report '<i>Nanoscience and Nanotechnologies: opportunities and uncertainties</i>' is now expected to be published in mid-February 2005. In relation to HSE's involvement in research related to nanotechnologies, Ms Northage explained that the main activity has been on measurement techniques. HSL is currently investigating the relationship between mass, number and surface area of airborne nanoparticles. The item was then opened for discussion.</p> |
| 3.3 | <p>General comments</p> <p>WATCH Members praised the quality of the documentation. HSE's input into the Royal Society report was also commended. A WATCH Member asked about the scope of the review; the literature dealing with health effects associated with exposures to welding fume or diesel exhaust emissions, for example, was not covered. HSE responded that the focus of the review was on novel nanoparticles and that therefore only information that could usefully inform on such exposures and their potential consequences had been included.</p> |
| 3.4 | <p>Discussion on HSE's hazard assessment (Annex 1)</p> <p>The Chair then directed the discussion to the specific action points, beginning with Action Point [a]: WATCH is asked to "<i>endorse or suggest any necessary modifications to HSE's assessment of the current state of knowledge about the human health hazards of nanoparticles</i>".</p> |
| 3.5 | <p><u>Agglomeration and dose-response</u></p> <p>WATCH first considered the question of agglomeration of nanoparticles. A WATCH Member noted that the extent to which agglomeration occurs is inversely related to particle size and the rate of agglomeration increases with increasing particle concentration. He asked if this could result in a non-linear relationship between airborne nanoparticle concentration and toxicity? In response, another Member cited experimental work by Oberdorster <i>et al</i> (1992), which suggested that toxicity is diminished as a result of particle agglomeration. This Member also pointed out that agglomeration is accompanied by a reduction in the total amount of free radical activity on the particle surface and that this reduction might also contribute to amelioration in toxicity. He commented however, that in experimental work, aggregated nanoparticles consistently elicit greater toxicity on a mass basis than larger, singlet particles, i.e. agglomeration might somewhat reduce toxicity but that even with agglomeration, an effect is evident that is more related to the extensive surface area of an agglomerate than to its mass. In this context, another Member commented that a distinction should be made, when appropriate, between observations of toxicity from <i>in vitro</i> compared with <i>in vivo</i> studies. One had to be careful not to extrapolate too readily the consequences of short-term contact with cells in culture to long-term consequences of whole-animal/human exposure.</p> |
| 3.6 | <p><u>Susceptible groups</u></p> <p>A WATCH Member asked if any particular population groups were likely to be particularly susceptible to any health effects associated with exposure to nanoparticles? It was pointed out that from our</p> |

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| | <p>understanding of air pollution episodes, exposure to PM₁₀ (particulate matter < 10 µm) is associated with adverse health outcomes in susceptible populations e.g. those with pre-existing asthma or cardiovascular disease. It has been suggested that these adverse health outcomes are especially related to the nanoparticulate component of PM₁₀. If so, then these same population groups could also be particularly susceptible to any adverse health effects associated with exposure to novel nanoparticles. Another factor to consider is the presence of pre-existing airways disease, as this would affect particle deposition within the respiratory tract; so, for example, individuals with chronic obstructive pulmonary disease or other airways disease could respond differently to inhaled particles because of differences in the pattern of particle deposition in the airways. The Chair suggested that the points made in relation to susceptible populations could be borne in mind in HSE's continuously evolving view of the potential threat to human health posed by novel nanoparticles.</p> |
| 3.7 | <p><u>Viruses as nanoparticles</u></p> <p>A WATCH Member asked if any useful information could be obtained from existing knowledge on behaviours of viruses within the body, as viruses could be regarded as nanoparticles. In response, it was noted that information on the transfer of viruses via the olfactory nerve had been cited in support of very recent work that looked at axonal translocation of nanoparticles that deposited in the nasal passages.</p> |
| 3.8 | <p><u>Potential absorption and systemic toxicity</u></p> <p>A different WATCH Member noted that the potential systemic toxicity of nanoparticles was an important consideration, given that studies of pharmaceuticals had shown that even for poorly soluble substances, rendering them "nano-sized" resulted in a massive increase in bioavailability following oral administration. He suggested that this increase in absorption and bioavailability may apply to other exposure routes.</p> |
| 3.9 | <p><u>'Dose' or 'potency' as the key influence on toxicity?</u></p> <p>The question was then raised whether the differences in observed toxicity between nanoparticles and their micrometre counterparts were simply a function of dose (i.e. amount, expressed as the appropriate metric) or represented a change in toxicological potency (i.e. activity)? A response was offered that results from both <i>in vitro</i> and animal models can be explained by a two-stage model that incorporates both surface area and surface activity as important parameters in the expression of toxicity. The comment was made that the potential for apparently 'low-toxicity' micrometre-sized particles to express toxicity when in the nanometre range should be clearly emphasised.</p> |
| 3.10 | <p>Another WATCH Member pointed out that whilst surface area is an important determinant of toxicity, other factors such as chemical activity are also important. In addition, it is not clear whether the apparent relationship between particle surface area and toxicity will hold for all materials.</p> |
| 3.11 | <p><u>Additional useful data?</u></p> <p>The Chair then asked Members if they were aware of any additional useful hazard information that had not been included in the review.</p> |
| 3.12 | <p>One Member commented that very few human data are included, for example, from the wealth of epidemiological studies looking at environmental air pollution episodes, and that these may be informative. HSE responded that these data had been considered, but a detailed account of them was omitted from the document because it was not possible to separate out the contribution made by the nanoparticulate component of particulate air pollution to the observed health outcomes; this point was made in the review. Nevertheless, HSE intended to keep abreast of the literature to which WATCH had referred to inform its evolving view of the potential threat to human health posed by nanoparticles arising from nanotechnologies.</p> |
| 3.13 | <p><u>Skin absorption</u></p> <p>Another Member raised the issue of skin absorption of nanoparticles. It was noted that there was a discontinuity in this respect between the hazard assessment document and the exposure assessment; the former concludes definitively that skin absorption is negligible, certainly for poorly soluble nanoparticles, whereas the exposure assessment suggests that uptake via the skin may be an important route of exposure. It was agreed that given the paucity of informative data, a definitive conclusion on the skin absorption potential of nanoparticles could not yet be reached. HSE would therefore revise its position on this issue within its evolving view on the potential threat to human</p> |

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| | health posed by novel nanoparticles. |
| 3.14 | <p><u>GI tract absorption</u></p> <p>The issue of absorption through the gastrointestinal (GI) tract was also raised. It was noted that this aspect had not been addressed in the hazard assessment. However, given that a significant proportion of particles cleared from the lung will reach the GI tract via the mucociliary escalator, this is an important exposure route. In this context, the comments made previously in relation to potentially useful data from studies of nanoparticulate pharmaceuticals were relevant.</p> |
| 3.15 | <p><u>General applicability of hazard assessment</u></p> <p>One WATCH Member commented that the hazard assessment focuses on studies of conventional chemical structures that have been produced at the nanoscale, rather than on novel nanomaterials, because of the lack of toxicological data for the latter. However, he argued that it was not necessarily appropriate to extend the conclusions reached from investigations of the materials studied to all particles potentially arising in the future from nanotechnologies.</p> |
| 3.16 | <p><u>Deposition</u></p> <p>One WATCH Member asked for clarification in the Annex, to indicate what proportion of inhaled submicron particles is deposited in the respiratory tract. This aspect is important as it will affect the numbers of particles, and thus the particle surface area, that deposit within the respiratory tract.</p> <p>On checking this point after the meeting, HSE notes that total deposition can be inferred from Figure 2 of the Annex. The diagram shows the total deposition of particles within the airways, from which it can be inferred what percentage of particles is not deposited.</p> |
| 3.17 | <p><u>Conclusions on hazard assessment</u></p> <p>Overall, considering Action Point [a] of the cover paper:</p> <ul style="list-style-type: none"> • WATCH agreed that the HSE's hazard assessment represented an accurate appraisal of the current extent of knowledge on nanoparticles. However, HSE would take account of the comments made by WATCH in the ongoing process of keeping abreast of the potential human health hazards of novel nanoparticles. |
| 3.18 | <p><u>Discussion of occupational exposure to nanoparticles</u></p> <p>The Chair then asked members to consider Action Point [b] of the cover paper which asked WATCH to "take a position on what exposure metric(s) should be pursued in relation to assessing workplace exposure to, and control of nanoparticles (e.g. mass, surface area, particle number)" (Annex 2 of the package).</p> |
| 3.19 | <p>A Member asked if there were any methods for measurement of surface area that were suitable for use in the workplace. Another Member explained that current methods involved sophisticated and expensive techniques that were not readily applicable outside the laboratory situation. He added that indirect methods for estimating surface area from other measurements, such as particle number, are relatively easy in comparison, but consequent extrapolation cannot take account of particle agglomeration; current particle counting techniques will count an agglomeration of nanoparticles (of perhaps up to 500 particles) as a single particle, so can give misleading results. It was necessary to use a combination of information on surface area, particle number and particle mass to estimate exposure to nanoparticles.</p> |
| 3.20 | <p>An HSL representative indicated that HSL has a project underway to look at the inter-relationships between particle mass, number and surface area. Although there is a device for measuring surface area, it is not a personal monitor. However, HSL intends to trial this device in factories manufacturing novel nanoparticles.</p> |
| 3.21 | <p>Clarification of the figures in Table 5.7 on page 38 of Annex 2 was sought. A WATCH Member noted that this table reported a series of measurements expressed as particle number (Wake, 2001) whereas the remaining entries in the table referred to mass concentration. The WATCH Member noted that the numbers reported seemed low compared with background environmental particulate levels, which he understood were of the order of 10 000-20 000 particles/cc air. He asked how the measurements by Wake (2001) had been made. HSE (HSL) explained the techniques that had been used, and commented that although the numbers seemed low, it was known to be the case that particle measurements taken inside a factory could be lower than the outside levels, a reflection of</p> |

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| | the control systems in place. |
| 3.22 | HSE pointed out that DTI has allocated a great deal of research money to develop appropriate measurement methodologies, and so in the context of considering what might be the most appropriate exposure metric to pursue, WATCH need not restrict its considerations to currently available techniques. |
| 3.23 | One WATCH Member proposed that the key dose metric is surface area. Another Member added that there are two issues to consider in relation to deriving an appropriate dose metric: one is the underlying mechanism of toxicity and the other is the practicality in relation to worker protection. He noted the significant challenge of developing practical methods to measure surface area in the workplace and so felt that this aspect requires the development of reasonably reliable surrogates or indirect methods. Another Member suggested that perhaps useful lessons in risk management could be learned from experience with welding fume. If it could be ascertained that nanoparticles contribute substantially to the toxicity of welding fume, then knowledge of the standards to which it is deemed necessary to control welding fume may lead to the development of a surrogate method for assessing the appropriate standard of control for nanoparticle exposure more generally. A different Member responded that experimental work had been done to establish the underlying basis for welding fume toxicity. He felt that this had shown the toxicity to be attributable to the transition metal content of the fume rather than its nanoparticulate nature. |
| 3.24 | A number of WATCH Members then voiced the view that it is inappropriate to try to establish a single dose metric that is suitable for all nanoparticles and situations, and that a case-by-case approach is needed. So, for example, measurement of surface area may be the best dose metric for nanoparticles of inherently low cytotoxicity, but not necessarily for all nanoparticles. Another Member added that this debate on exposure had focused on inhalation, but the need to measure exposure via other routes should also be considered, as these other routes might also prove to be important. |
| 3.25 | With regard to Action Point [b], the Chair summarised and verified with WATCH the position that had been arrived at: <ul style="list-style-type: none"> • The ability to measure surface area, either directly or indirectly was important. However, it was also necessary to take a case-by-case approach to measurement, as the most appropriate metric for one type of nanoparticle may not be appropriate for another. Finally, it was noted that consideration of routes of exposure other than inhalation was important in undertaking any worker risk assessment. |
| 3.26 | <i>Discussion on risk assessment and risk management</i> The Committee was then asked to consider action points (c), relating to risk assessment and (d), relating to risk management. Specifically: (c) <i>express its opinion on the adequacy of the existing regulatory framework to accommodate the scientific and technological features of nanoparticles, and the appropriate deployment of conventional approaches, including the possible role of WELs;</i> and (d) <i>recommend whether or not new risk management approaches need to be developed and implemented (for example, approaches that can take account of the paucity of hazard and exposure data).</i> |
| 3.27 | A WATCH Member commented that there is need to act on a case-by-case basis, as different nanoparticles will require different regulatory approaches. On the point of the role of Workplace Exposure Limits (WELs), the Member noted that it would not be appropriate to contemplate a generic WEL for nanoparticles. He reflected that nanoparticles could be categorised into two types: those produced adventitiously and those intentionally manufactured. He argued that intentionally manufactured nanoparticles are likely to be very carefully controlled for commercial reasons, to preserve the product. Therefore, there may already be knowledge about and familiarity with stringent control practices with product preservation in mind, which could perhaps be enshrined in a guidance document. |
| 3.28 | Another WATCH Member commented that in relation to action point (c), the current regulatory framework broadly accommodates the issues surrounding the appropriate risk management of nanoparticles. So, under the current framework, the absence of specific hazard information on most nanoparticulate materials, together with the knowledge that there is some generic concern for toxicity, immediately places an obligation on producers to consider the potential risks and the need for risk management measures. The issue then is with the available risk management measures, and whether or not the current technology is adequate to effectively control exposure to nanoparticles. In |

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| | <p>response to this point, a WATCH Member offered the view that in principle, current control technologies should be adequate to control exposure to nanoparticles; for example, for inhalation exposure, filtration-based control systems should work well in principle. However, there is very little data to show that these technologies are effective in practice. Respiratory Protective Equipment (RPE) will be prone to leakage, because of the mobility of nanoparticles. He also commented that airborne nanoparticles will distribute widely which raises the issue of widespread deposition on surfaces and consequent potential skin and ingestion exposure, and the need for control measures to take account of these routes. In this respect, a WATCH member commented that generic research into control measures for these routes, particularly the skin, was required.</p> |
| 3.29 | <p>A WATCH Member commented that one area where there may be shortcomings in the current regulatory framework is in relation to the development of nanoparticulate forms of existing materials, where the need to consider differences in toxicity and consequently different control measures may not be obvious to the developer. He also added that factors other than occupational health considerations may drive risk management decisions in a precautionary direction for example, compliance with environmental legislation.</p> |
| 3.30 | <p>A different WATCH Member expressed an opinion that the regulatory framework is adequate, but that in the climate that can be predicted to prevail in the future, there may be a need to change approaches to gathering the necessary hazard data, for example, to make more use of <i>in vitro</i> tests of toxicity. Another WATCH Member pointed out that research funds to develop such approaches had been made available at the EU level, and that this issue was also recognised by NIOSH in the US.</p> |
| 3.31 | <p>HSE mentioned that NIOSH had suggested taking a control banding approach to the control of nanoparticles, along the lines of COSHH Essentials, and canvassed WATCH Members' views on the feasibility of such an approach. WATCH endorsed exploring this possibility.</p> |
| 3.32 | <p>The Chair then summed up the discussion on Action Points [c] and [d]. He verified with WATCH its agreement to the following statements. With regard to Action Point [c]:</p> <ul style="list-style-type: none"> • WATCH agreed that in principle, the existing regulatory framework can accommodate all nanoparticles but on a case-by-case basis. As such, there is a need to look at the way each individual case fits within the regulatory framework, such that different elements of the framework may be more or less appropriate for different situations. For example, the regulatory approach to the control of nanoparticulate silica would be different to that for nanoparticulate titanium dioxide. Nevertheless, as new particles and technologies are developed, there should be an obligation on producers to understand the hazards and risks of their products. |
| 3.33 | <p>With regard to Action Point [d]:</p> <ul style="list-style-type: none"> • There is no need for new risk management approaches, as existing control approaches should be applicable, although again, each situation needs to be considered on a case-by-case basis. In addition, in view of the paucity of data, pragmatic approaches such as assignment to hazard and control bands may be worth pursuing. |
| 3.34 | <p>The Chair thanked Ken Donaldson and Rob Aitken for their helpful and expert contribution to the discussion.</p> |
| 4 | <p>Portland Cement: Assessment of the respiratory and carcinogenic hazards of Portland cement</p> |
| 4.1 | <p>The Chair introduced Peter Ridgway (HSE), responsible for putting together the package on Portland cement, to the Committee. He pointed out that this work was undertaken in relation to the Occupational Respiratory Disease and Cancer elements of the Disease Reduction Programme.</p> |
| 4.2 | <p>General comments on the hazard assessment document (Annex 1)</p> <p>WATCH considered that overall, the quality of the epidemiological database for Portland cement was poor. It was noted that some studies didn't appear to have data on duration of exposure. HSE responded that although exposure duration was not always stated in the studies, most did include information on mean duration of employment (around 10 – 15 years), which, because of the stability of the employee population in this industry, could be regarded as being equivalent to exposure duration. Another observation was made that the information on the control populations used in the studies was, in general, less than one would want. HSE indicated that all available information had</p> |

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| | been included in the study summaries. |
| 4.3 | The point was also made that any references to 'total dust' should be assumed to refer to total inhalable dust, as measured by the American convention. |
| 4.4 | <i>Discussion of the assessment of the non-cancer respiratory effects of Portland cement</i> It was noted that in most studies the measurement of respiratory function and identification of functional deficits appeared to have been performed well. However, it is unclear from the studies if factors other than Portland cement dust played a causal role in the development of the respiratory deficits reported in them. |
| 4.5 | A WATCH Member referred to the study by Mwaiselage <i>et al.</i> , (2004), in which deficits in pulmonary function had been observed in association with a cumulative dust exposure of 300 mg.m ⁻³ .year. He questioned the conclusion that had then been drawn from this, namely that pulmonary function deficits could occur with exposures to 10 mg.m ⁻³ Portland cement dust for 30 years. Given that the average duration of employment for the workers in the Mwaiselage <i>et al</i> study was only 12 years, it was more likely that the observed deficits were associated with exposure to dust levels considerably higher than 10 mg.m ⁻³ over a shorter period of time. |
| 4.6 | WATCH Members acknowledged that the quality of the exposure information was generally poor. In addition, there was the potential for secondary exposures from dusty clothing. Consequently, it difficult to construct a reliable dose-response curve for the observed respiratory effects. |
| 4.7 | In terms of respirable dust measurements, the Committee considered the study by Yang <i>et al.</i> , (1993) to be the best available. A Member suggested modifying the final sentence of HSE's summary of this study to reflect the statistically significant differences in prevalence of cough between the high exposure group and the medium and low exposure groups. |
| 4.8 | Members then commented that the two studies by Yang <i>et al.</i> , (1993, 1996) appeared to use the same exposure data (given that the highest value in the range of respirable dust concentrations was the same, apparently very precise number in both studies). In the 1993 study, the population was divided into three exposure groups, yet in the 1996 study only two groups were defined. It was speculated that the study authors may have taken the most significantly exposed subjects from the 1993 study and tested their pulmonary function, reporting this data in the 1996 study. |
| 4.9 | Another Member commented that the conclusions of the 1993 study related to an increase in the subjective reporting of symptoms while the 1996 study provided objective evidence for an effect, based on spirometry; the latter was therefore potentially of more value. Although personal monitoring was performed in the 1993 study, it was noted that this would not be a true reflection of past exposures, particularly as the mean duration of employment was 17 years. Thus, the possibility that higher previous exposures produced the observed effects could not be excluded. |
| 4.10 | In response to a question regarding the possible inappropriateness of the control group used in the Yang <i>et al.</i> , (1996) study, HSE replied although it was a weakness of the study that the control group may have differed from the exposed workers in terms of socio-economic status, overall it was felt that this would not be sufficient to render the result invalid. |
| 4.11 | Members were then asked to consider the statement in paragraph 12 of the cover paper, which read "...it would seem reasonable to conclude from the data available that respiratory deficits would start to develop with long-term average exposures to respirable cement dust above 1 but below 4 mg.m ⁻³ ". This statement implied that the current OES for Portland cement is not completely protective against adverse respiratory effects and so could have significant downstream consequences if it were to be agreed by the Committee. The HSE authors commented that the basis for the conclusion that respiratory deficits occur at exposures below 4 mg.m ⁻³ was the study by Yang <i>et al.</i> , (1996). |
| 4.12 | A Member commented that whilst there appeared to be no significant effects on respiratory function at exposure levels below 1 mg.m ⁻³ , it is unclear at what level above 1 mg.m ⁻³ effects on respiratory function start to appear. It was suggested that additional analysis of all the data could be performed, for example in a meta-analysis or by a simple study-by-study plot of exposure against the degree of respiratory deficit, to give a better indication of the dose-response relationship. In response, the point was made that at the level of exposure at which respiratory effects just begin to appear, a large study population would be needed before one could achieve statistical confidence in the data. The usefulness of further in-depth analysis was questioned, also because of the poor quality of the |

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| | original data. |
| 4.13 | HSE then asked whether the Committee considered 1 mg.m ⁻³ (8h TWA) to be a NOAEL for respiratory effects, drawing attention to the study by Fell <i>et al.</i> , (2003). In this study, there were no differences in respiratory health between a survivor population of workers exposed to cement dust and a comparable group of non-exposed workers. Contemporary measurement of workplace air samples indicated a mean respirable dust concentration of 0.9 mg.m ⁻³ (8h TWA). In addition, it was pointed out that there are three studies cited in the 1994 HSE review of Portland cement dust (Annex 2) that showed no significant respiratory deficits below 1 mg.m ⁻³ . |
| 4.14 | A member responded that the key studies in Annex 1 are those by Fell <i>et al.</i> , (2003) and Yang <i>et al.</i> , (1993, 1996). The Fell study shows no respiratory deficits at a mean 8h TWA exposure level of 0.9 mg.m ⁻³ . However, in the studies by Yang <i>et al.</i> , statistically significant increases in the prevalence of cough compared with controls were reported at mean exposure concentrations of 1.2 and 3.5 mg.m ⁻³ . Given that there is evidence for an effect at 1.2 mg.m ⁻³ , and that no real precision can be put on the exposure estimates, he did not agree that there was robust evidence that exposures below 1 mg.m ⁻³ can be considered to have no effect on respiratory function. |
| 4.15 | There was a discussion about possible sources of information on the current incidence of respiratory disease associated with Portland cement dust exposure. It was suggested that data may have been available from THOR (The Health and Occupation Reporting Network). However, after checking this, HSE informed the Committee later in the meeting that no useful data were available on this issue from THOR. |
| 4.16 | Overall, in response to Action Point [i] of the cover paper, WATCH agreed that: <ul style="list-style-type: none"> • <i>It is clear that occupational exposure to Portland cement dust has produced deficits in respiratory function. However, the evidence available at the present time is insufficient to establish with any confidence the dose-response relationship for these effects.</i> |
| 4.17 | <i>Discussion on the evidence for a causal association between Portland cement dust exposure and cancer</i> Action Point [ii] was then considered, in which "...the opinion of WATCH is sought on the interpretation of the evidence from the case-control studies on laryngeal and pharyngeal cancer." |
| 4.18 | Several Members of the Committee clearly felt that, based on the data presented, a risk of laryngeal and pharyngeal cancer associated with Portland cement dust exposure could not be excluded. |
| 4.19 | In relation to stomach cancer, a WATCH Member questioned why HSE had suggested in the paper that there was the biological plausibility for an association with Portland cement dust exposure. HSE explained that its thinking was that there is the potential for cement dust to be swallowed following clearance from the lung via the mucociliary escalator, and there is literature suggesting that exposures have been associated with stomach cancer. The WATCH Member was not convinced about this plausibility argument. |
| 4.20 | In response to Action Point [ii] of the cover paper, the Committee agreed that a modification of the statement in Annex 1 of the documentation was an appropriate conclusion, ie: <ul style="list-style-type: none"> • <i>A causal association between Portland cement exposure and cancer has not been established. Nevertheless, the findings of the recent study maintain the uncertainty concerning a possible risk of cancer raised by the earlier data reviewed by HSE (1994).</i> <p><i>As a highly alkaline substance, cement can cause irritation at sites of contact, such as the mouth, throat and lungs. Persistent chronic irritation will cause repeated cycles of cell death, cell proliferation and other inflammatory responses. It is recognised that this process can be a step on the pathway to cancer. Thus, it is biologically plausible that cement dust could have the potential to cause cancers at sites of contact in the respiratory tract.</i></p> |
| 5 | Proposal for an isocyanates biological monitoring strategy: Establishment of a biological monitoring guidance value (BMGV) for isocyanate metabolites in urine |
| 5.1 | The Chair introduced Andy Garrod and John Cocker, the authors of the isocyanates WATCH |

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| | <p>package, to the Committee. The work forms part of the asthma strand of the Disease Reduction Programme. WATCH was asked to consider a BMGV for isocyanates by the COSHH Essentials Working Group of ACTS in May 2004. Members were reminded that following a discussion by WATCH in 2002, it was agreed that alongside the specific criteria already available a more flexible approach to the setting of BMGVs could be taken, on a case-by-case basis. The Chair also pointed out to Members that comments on the proposals in the paper had been received from industry and these had been tabled. The Committee was asked to consider first Action Point [i]: “<i>To recommend that biological monitoring is required to assess the effectiveness of control measures for isocyanate exposure.</i>”</p> |
| 5.2 | <p>A typographical error on page 5, ie the limit of detection should be 0.1 rather than 1 nmol/l, was acknowledged.</p> |
| 5.3 | <p><i>Discussion on the role of biological monitoring in assessing the effectiveness of control measures for isocyanate exposure</i></p> <p>WATCH Members did not think the phrase “...<i>is required.</i>” was appropriate and asked whether or not this apparent compulsion was what was intended; if so, what would be the legal implications of using such a phrase? The HSE authors responded that from a risk management perspective, a respirator is used to control exposures to isocyanates. They suggested that biological monitoring is the only way to assess the effectiveness of the respirator in preventing isocyanate exposure. Therefore, the phraseology used in Action Point [i] was intended to signal a strong recommendation to use biological monitoring to assess the effectiveness of the respirator. The need for routine biological monitoring as a measure of respirator effectiveness was questioned by WATCH Members. They argued that respirators are standard exposure control devices in the chemicals industry and there is no routine practice of performing biological monitoring to check they are working correctly. A Member commented biological monitoring has a role, as part of a structured risk management programme. However, he felt it is probably not the most effective way to routinely measure the effectiveness of exposure control and that compulsory biological monitoring is not feasible in practice in the workplace.</p> |
| 5.4 | <p>The availability and robustness of the analytical methods involved was also questioned, in relation to the concept of widespread biological monitoring for isocyanate exposure. In response it was acknowledged that HSE’s HSL was the only UK establishment that offered a biological monitoring service for isocyanate exposure. HSL carefully monitors quality control and for isocyanates, the assay is robust, the precision is good and the method is validated and published in the literature.</p> |
| 5.5 | <p>HSE was then asked what guidance was envisaged on the use of biological monitoring in workplaces where isocyanate exposure occurs? HSE suggested that it would stipulate that at least one biological monitoring survey should be carried out and if isocyanate metabolites were detected in the urine then there would be a need to look at the control measures in place. In addition, it would be suggested that new employees might routinely undergo biological monitoring in their first period in work to gather baseline data, to be used for comparative purposes if further samples were then taken from them in the future. A WATCH Member asked if HSE felt that it would be necessary to perform biological monitoring for every individual at the end of every shift? HSE indicated that as a tool to measure the efficiency of control measures, biological monitoring was not necessarily something to use at the end of every shift. A WATCH Member asked how might it be ensured in a compulsory scheme that urine samples provided were legitimate? HSE responded that it was not envisaged that there would be a legal requirement to do biological monitoring for isocyanate exposure. However, experience to date suggests that if a workplace believes its control measures are good then there is a willingness to collect biological monitoring samples appropriately.</p> |
| 5.6 | <p>Overall, WATCH was clearly not happy to recommend that biological monitoring for isocyanate exposure is “required”, because of the apparent compulsion involved, which WATCH felt was inappropriate. Instead on Action Point [i], WATCH recommended:</p> <ul style="list-style-type: none"> • That biological monitoring is used as appropriate, within a well-considered risk management strategy, to assess the effectiveness of control measures for isocyanate exposure. |
| 5.7 | <p><i>Discussion on the proposed BMGV</i></p> <p>The Committee then discussed action point (ii): “To agree that a biological monitoring guidance value (BMGV) at 0.5 µmol urinary diamines/mol creatinine released by hydrolysis of protein conjugates of</p> |

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| | HDI, TDI, MDI or IPDI, is appropriate as a Benchmark value. This amount represents an equivalent monomeric isocyanate exposure below 5% of the current Maximum Exposure Limit and the envisaged future Workplace Exposure Limit (20 µg/m ³ , 8-hour TWA)." |
| 5.8 | A Member began the discussion by indicating that he had similar concerns to some of the points that had been raised by industry in the tabled submission, these being: the potential variability in absorption of isocyanates; whether or not there was a truly linear relationship between airborne levels of isocyanates and urinary output of diamines; the potential inter-individual variation in excretion times of amines, which could result in significant isocyanate exposures being missed in some individuals; and whether or not other free amines could interfere with the assay. Although there was some good quality hygiene data in the WATCH package, there still appears to be many gaps in our knowledge of the overall picture of occupational exposure to isocyanates. In addition, he felt that the BMGV proposed (0.5 µmol urinary diamines/mol creatinine) might be unduly stringent, given that it is equivalent to exposure at 5 % of the current MEL |
| 5.9 | The HSE authors responded that one should avoid making unduly precise correlations between airborne exposure and biological measurements. The proposed BMGV was based primarily on the detectability of urinary metabolites, which would be indicative of significant exposure having occurred, rather than on a correlation with any specified airborne concentration of isocyanates. HSE suggested that biological monitoring against a BMGV was important to pick up human behavioural aspects to exposure control, such as a body sprayer lifting his mask to check how a paint spraying job is looking and being unintentionally exposed to isocyanates as a consequence. |
| 5.10 | A Member asked whether it is reasonable to set a BMGV at a level which is effectively at the limit of detection of the analytical technique? He suggested that a BMGV should be set at some point above the detection limit to allow some latitude for interpreting different results. Another Member questioned whether, with a philosophy that detection indicates overexposure, an actual BMGV figure was needed? The thinking seemed to be that detecting metabolites in the urine would indicate that significant isocyanate exposure had taken place; therefore, the target of a biological monitoring survey would be no metabolites detectable. |
| 5.11 | A WATCH Member questioned whether it was appropriate to aggregate all isocyanates in a single BMGV value of 0.5 µmol urinary diamines/mol creatinine? Based on the information provided in the WATCH package in table 2 of Annex 1, this value is well below the 90 th percentile values quoted for 3 of the isocyanates for which biological monitoring data has been reported. HSE replied that these data represent urine samples where the particular isocyanates involved were known; however, the quality of control measures in these workplaces was not assessed. From other survey data, HSE knows that where good control measures are in place, the urinary amine levels are likely to be less than 0.5 µmol urinary diamines/mol creatinine. It was suggested that including a table of values in workplaces where it is known that there was good control and where there was bad control would be useful in helping the Committee decide on an appropriate BMGV. |
| 5.12 | A Member asked whether there were any data sets from plants/factories where good control measures are in place and measurements have been taken? HSE responded that this type of data is available for HDA and it had proved useful to factory managers in showing that the control measures in place were preventing significant exposure to isocyanates. A WATCH Member responded that biological monitoring results are not necessary to identify where there is evident bad hygiene practice. However, HSE responded that the use of biological monitoring data has led to the identification of a problem with isocyanate exposure in the construction industry, which had previously only been suspected. At present within the UK there are approximately 10, 000 motor vehicle sprayers, who are potentially routinely exposed to isocyanates and the likelihood is that in a significant number of cases the control of exposure is poor. Biological monitoring could prove a useful technique in identifying the extent of the problem and provide evidence of bad practice to operators. |
| 5.13 | The Chair then asked the Committee if it was comfortable with recommending a value of 0.5 µmol urinary diamines/mol creatinine as a Benchmark BMGV, to be included in a future version of EH40? It was clear that WATCH did not endorse this proposal. A Member commented that a Benchmark BMGV is portrayed as the boundary between good control and bad control and as such he felt that a value closer to the equivalent of exposure at the current MEL was warranted. Another Member indicated that the proposed value might have a role as a reference point but that, as a published BMGV, it would complicate the assessment of compliance/non-compliance with the MEL, in terms of reasonable practicability of control below the MEL. |

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| 5.14 | Overall in respect of Action Points [ii] and [iii], WATCH felt that the available position was such that the proposed BMGV value could not be recommended for inclusion in EH40 at this point. |
| 5.15 | <p>Overall Conclusions on the isocyanates package</p> <p>The Chair ended the discussion by summing up the statements agreed by WATCH. In relation to Action Point [i], WATCH recommended:</p> <ul style="list-style-type: none"> • That biological monitoring is used as appropriate, within a well-considered risk management strategy, to assess the effectiveness of control measures for isocyanate exposure. |
| 5.16 | <p>In relation to Action Points [ii] and [iii]:</p> <ul style="list-style-type: none"> • WATCH could not recommend a value for a Benchmark BMGV. |
| 6 | Outcome Relationship Mapping: defining Disease Reduction Programme (formerly known as Chemicals Programme) activity & Evidence base and logic for the Skin Disease sub- programme of the Disease Reduction Programme |
| 6.1 | The Chairman introduced Steve Coldrick, Programme Director for the Disease Reduction Programme (DRP). This item took the form of 2 presentations, one by Steve Coldrick, defining new project management principles that were to be used in the DRP to help deliver targets and ensure clear accountability; the second from Steve Fairhurst, on how these principles could apply to the Skin Disease element of the DRP and on the potential future role of WATCH in contributing to this work. |
| 6.2 | Steve Coldrick began by explaining that the new name for what had been known as the “Chemicals Programme” - the DRP – had been chosen to more clearly identify the aim of the programme. To ensure consistency in the management of the different strands of the DRP, the principles of project management set out by the Office of Government Commerce (OGC) will be applied. As part of these project management principles, the use of Outcome Relationship Maps (ORM) is being introduced. An ORM will be developed for each project within the DRP. |
| 6.3 | In each case, the ORM will clearly set out the target to be achieved and will define the intermediate steps that need to be taken to achieve this target. It will then identify the series of activities necessary to deliver the intermediate stages and so achieve the final target. |
| 6.4 | Work on restructuring the work of the DRP along the lines of the OGC principles is underway, and plan should be finalised at the end of March. He felt that there is clearly the potential for a significant role for WATCH within the DRP; and also a potential role for individual WATCH Members to contribute their knowledge and experience to particular activities that help towards delivery of the Programme. |
| 6.5 | It was emphasised that it is hoped that key stakeholders will play a proactive role in the activities identified to deliver disease reduction in a particular area. The level of stakeholder commitment will have an impact on the level of resource that HSE allocates to a particular disease area, in the sense that without stakeholder commitment it is more difficult to see the benefit that will arise from HSE expending much resource on an issue. |
| 6.6 | Steve Fairhurst then gave a presentation on how these project management principles could be developed within the skin disease element of the Programme. |
| 6.7 | <p>There are four aspects to the planned work on skin disease and WATCH conceivably has a role in each: measuring the baseline statistics; deciding what intermediate steps are needed to achieve the target; identifying and undertaking specific activities to complete the steps; and evaluating the effectiveness of these activities in achieving the target. Of these areas:</p> <ul style="list-style-type: none"> – The baseline statistics used at present are those of the current reporting schemes EPIDERM and OPRA (contained within THOR, The Health and Occupation Reporting network) and undoubtedly underestimate the true incidence of skin disease, but by an unknown quantity. Therefore, there is a need to generate ideas for improving the baseline statistics against which to measure progress. – The sub-programme will need to establish priorities and identify specific activities to pursue; both these elements need to have a transparent and logical basis. WATCH could have a role |

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| | <p>here.</p> <ul style="list-style-type: none"> – The Committee could have a role in progressing activities to deliver the targets. This will become clearer once the ORM has been finalised. – There is a need to identify the best methods to evaluate the effectiveness of activities in delivering the targets. |
| 6.8 | <p>The Chair then asked for comments on the presentations. The following points were raised and addressed during the discussion:</p> <ul style="list-style-type: none"> – In response to a question on the timelines for the DRP activity, HSE indicated that the overall top priority was to achieve the RHS targets by 2010. It is envisaged that key stakeholders will be engaged over the next few months, particularly with regard to skin and asthma, when the ORMs have been established. – The question of evaluating the commitment of stakeholders to engage in the programmes was raised. HSE responded that once stakeholders are identified their commitment to the programme can be measured by the extent to which they contribute to a particular activity. The ORM is a good way of encouraging stakeholders to commit to the programme, as it clearly identifies the path to achieving a particular outcome and their position on it. – A member asked if large-scale studies of levels of disease incidence or prevalence in industry were being conducted. HSE responded that this is a key research objective in the skin disease work. HSE will be commissioning research with the aim of establishing incidence and prevalence rates in 2005 in some industries for which a significant skin disease problem has been identified. This will be used to benchmark the THOR data, to estimate the degree of under-reporting of skin disease, and so establish a more reliable baseline for 2005; this will also then be extrapolated back to previous years, including 2000 – the year against which progress in disease reduction by 2010 will be assessed. – The breadth and potential flexibility of the role of WATCH in the DRP was questioned. HSE responded that WATCH's role as a Scientific Advisory Committee is clearly defined, ie it will deal with scientific and technical matters only. Its more specific role in the DRP awaits finalisation of the ORMs. However, in addition to serving their "WATCH Committee" role, individual Members could have additional involvement in communicating messages or persuading stakeholders to be involved in elements of the DRP, if they so wished in the context of their individual jobs. – One member proposed that WATCH look at an example of one disease area (once the relevant ORM is completed) and discuss ways the Committee could make a contribution. HSE considered this to be an excellent idea and undertook to further develop this idea in the context of the agendas for the following two WATCH meetings in 2005. <p>[ACTION: HSE]</p> |
| 6.9 | The Chair thanked Members for their thoughts and closed the discussion. |
| 7 | The Carcinogenicity of Formaldehyde: Position on the strength of evidence that formaldehyde has caused cancer in humans |
| 7.1 | The Chair welcomed Professor David Coggon of the MRC Environmental Epidemiology Unit, who had been invited to join the Committee as an ad hoc expert for this item. David Coggon had been a Member of the IARC Working group that had reappraised its position on formaldehyde carcinogenicity in 2004. The HSE personnel involved in the formaldehyde work were also introduced to the Committee: Isla Fraser, Mike Costigan and Damien McElvenny. |
| 7.2 | The Chair explained that the initial stimulus for HSE's appraisal of formaldehyde carcinogenicity was the "emerging issue" of a possible link between formaldehyde exposure and leukaemia in humans. Subsequently, during 2004 there was the IARC reassessment of the overall carcinogenic potential of formaldehyde, with a particular emphasis on nasopharyngeal cancer; and now the French Competent Authority has announced its intention to submit a Classification and Labelling (C&L) proposal on formaldehyde carcinogenicity to the EU C&L Working Group (WG), possibly in Spring 2005. As yet HSE is not aware of what will be the proposal. Given the widespread occurrence of formaldehyde and the substantial regulatory attention that has been paid to its carcinogenic potential, a view on the |

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| | <p>strength of evidence that it has caused cancer in humans was now sought from WATCH to help inform the UK position to be taken forward into the envisaged forthcoming EU debate. The Chairman pointed out to Members that comments on the proposals in the paper had been received from industry and these had been tabled. Members were asked to firstly consider action point (i), ie “to construct a description of what it feels is the strength of evidence for formaldehyde having caused cancer in humans.” The Chairman suggested that the discussion should concentrate first on nasopharyngeal cancer.</p> |
| 7.3 | <p><i>Discussion of the overall pattern of evidence for formaldehyde having caused nasopharyngeal cancer in humans</i></p> <p>A Member began the debate by offering a synthesis of the evidence on this matter. He argued that epidemiological data should be interpreted in the context of all other surrounding information. He said that it is clear that formaldehyde is an animal carcinogen and the mechanism involved is likely to be relevant for humans. In humans nasopharyngeal tissue is exposed directly to inhaled formaldehyde and formaldehyde-DNA crosslinks have been found in relevant tissues in exposed humans and monkeys.</p> |
| 7.4 | <p>He continued by emphasising that nasopharyngeal cancer is a rare cancer in humans, particularly in Western populations; and that although formaldehyde is a widely used chemical, high levels of exposure such as those found in some of the cohort studies reviewed in this WATCH package are rare in the general population. Because of these factors, the statistical power of each epidemiological study to detect an increase in nasopharyngeal cancer will be low and so it is not surprising that there are inconsistencies in the results emerging from different studies. Therefore, he argued that one should look at the overall pattern of results from all of the available studies in reaching a conclusion, rather than just dissecting each individual study in isolation.</p> |
| 7.5 | <p>The Member went on to say that where excesses of nasopharyngeal cancer have been reported the Relative Risks (RR) for nasopharyngeal cancer that have been found are not particularly large even among those subjects with relatively high peak and cumulative formaldehyde exposures. This observation, together with the low background incidence for this cancer indicates that the absolute numbers of nasopharyngeal cancers arising from formaldehyde exposure are very small.</p> |
| 7.6 | <p>Overall, he felt comfortable with a position similar to that of IARC; he suggested that the epidemiological evidence for formaldehyde having caused cancer in humans is not as strong as that for chemicals such as asbestos, nickel and chromium, but is comparable with that for dioxins or sulphuric acid mist.</p> |
| 7.7 | <p>Another WATCH Member made the point that the study of Hauptmann <i>et al.</i>, (2004; an update of the “NCI study”) was very important in shaping an overall decision. He suggested that there are questions surrounding this study and the appropriate interpretation of its findings. The Member sought a view on what conclusion IARC might have reached if this study had not been available; in reply it was ventured that an IARC classification of 2a would have been reached. The Member pointed out that it is unlikely that in the future a better study than that of Hauptmann <i>et al.</i>, (2004) will become available, which would lead IARC to reconsider its position. He also suggested that, given that any nasopharyngeal cancer produced by formaldehyde would be very rare, one would not wish to see intense and burdensome risk management action on the basis of higher carcinogenicity hazard classification than formaldehyde currently has.</p> |
| 7.8 | <p>Another WATCH Member asked David Coggon about his study in a UK cohort which showed no excess of nasopharyngeal cancer in formaldehyde-exposed workers. The Member offered the view that perhaps one could consider formaldehyde to be a “low potency” human carcinogen. In response it was suggested that in any single study one could fail to see an effect of formaldehyde on nasopharyngeal cancer by chance; one could see this by considering the size of the confidence intervals for nasopharyngeal cancer findings in the available studies.</p> |
| 7.9 | <p>Following a comment that the nasal epithelium is the site at which formaldehyde produces cancer in animal carcinogenicity studies, whereas nasopharyngeal cancer appears to be the site of concern in humans following formaldehyde exposure, a Member replied that generally nasal cancer in animals is the site-equivalent of sinonasal cancer in humans. However, exposure-modelling studies have shown that in humans inhaling formaldehyde the nasopharyngeal tissues receive much higher levels of exposure than the nasal sinuses, and this might explain the site of action.</p> |
| 7.10 | <p><i>Points made on the details of the Hauptmann and Marsh studies</i></p> |

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| | The WATCH package indicated that the study of Hauptmann <i>et al.</i> , (2004; Annex 4 of the documentation) suggested an association between formaldehyde exposure and nasopharyngeal cancer based on an analysis of 10 factories in the USA. Many of the cases of nasopharyngeal cancer were found in one plant only and this data was investigated in some detail in Marsh <i>et al.</i> , (2002; Annex 5 of the documentation). The analysis of the data from this one plant subsequently raised questions about the findings presented by Hauptmann <i>et al.</i> , (2004). |
| 7.11 | A WATCH Member pointed out that the fact that 5 of the total of 9 cases of nasopharyngeal cancer in the Hauptmann study occurred in a single factory (Wallingford) should not be considered unusual. This concentration of cases could well have arisen by chance and no other significant confounding factors, in terms of other known causes of nasopharyngeal cancer were identified. He then questioned the interpretation of the results presented in the Marsh study. An additional 2 cases of nasopharyngeal cancer were identified within the Wallingford factory, that were not included in Hauptmann <i>et al.</i> , (2004), and the results presented in the Marsh analysis showed a consistent exposure-response relationship between cumulative formaldehyde exposure and nasopharyngeal cancer. The estimates of formaldehyde exposure made in the Marsh study were approximately ten times lower than those made by the authors of the Hauptmann study. Although this clearly reflects a difference in opinion between the exposure assessors involved in the two studies, it does not affect the interpretation of the cancer data in respect of hazard assessment, since there remains evidence of an exposure-response relationship. |
| 7.12 | A WATCH Member asked which feature of exposure – cumulative, peak or duration – was likely to exert greatest influence on the expression of toxicity with exposure to airborne formaldehyde. The reply was that theoretically risk would be expected to increase with higher peak exposures because of the irritancy associated with formaldehyde. Based on data in animal studies risk of nasopharyngeal cancer is likely to be increased when peak exposure occurs above 1 – 2 ppm. In the Hauptmann study and in epidemiology studies generally there are limitations in the retrospective assessment of peak exposures; therefore the more usual exposure metric is cumulative exposure. |
| 7.13 | <u><i>Consideration of potential confounding factors</i></u> WATCH Members asked whether exposure to wood dust or cigarette smoke could be considered potential confounding factors for the risk of nasopharyngeal cancer following formaldehyde exposure. It was noted that wood dust was a significant confounder for interpretation of sinonasal cancer data but not for nasopharyngeal cancer. |
| 7.14 | With regard to smoking, it was the opinion of a Member that there is no evidence that smoking is associated with nasopharyngeal cancer; and if it is associated, then the increase in RR must be very small, such that it has not become apparent in the many studies conducted. If smoking was a significant confounding factor in the formaldehyde studies it is more likely that increases in cancers at other sites associated with cigarette smoking eg cervix, bladder etc. would have been observed. Although formaldehyde is a contaminant in rooms where cigarettes have been smoked, the level of exposure to formaldehyde in exhaled smoke is relatively low. |
| 7.15 | <i>Conclusion on the evidence for formaldehyde having caused nasopharyngeal cancer in humans (part of Action Point [ij])</i> On invitation from the Chairman for views on the strength of evidence for formaldehyde having caused nasopharyngeal cancer in humans, a WATCH Member expressed a view that the Hauptmann study provided the strongest evidence, but that there was also consistency in the finding of an association between nasopharyngeal cancer and formaldehyde exposure in 5 out of 7 separate case-control studies. This represented multiple independent sources of evidence. In addition, there was biological plausibility for the findings. He offered the statement “ Formaldehyde has probably caused nasopharyngeal cancer in humans ” as the most appropriate description of the strength of evidence. |
| 7.16 | This was agreed by WATCH. |
| 7.17 | The Chair reminded Members that these discussions would be important in informing the view of HSE, as the UK regulatory authority, to take forward to the EU C&L WG. Formaldehyde is currently classified as a category 3 carcinogen in the EU; the conclusion now reached by WATCH would be compatible with category 1 or category 2 status. Either position would entail a (similar) step change in regulatory consequences. |
| 7.18 | One WATCH Member questioned if there was a potential for misinterpretation of this conclusion, in |

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| | that it could be interpreted as meaning formaldehyde is only a “probable” human carcinogen, whereas it appeared to him that Members considered the strength of the evidence to be reasonably compelling for nasopharyngeal cancer. The Chairman clarified that HSE recognised the clear difference between describing a substance as a “probable” human carcinogen in a predictive sense, based on experimental animal data, and concluding that a substance was the probable cause of an actual increase in human cancer seen in epidemiology studies. It was the latter conclusion that WATCH had agreed. |
| 7.19 | <p><i>Discussion and conclusion on the evidence for formaldehyde having caused leukaemia in humans (another component of Action Point [i])</i></p> <p>With regard to any apparent association between formaldehyde exposure and leukaemia, a Member commented that there is no mechanistic basis for such a link. He felt that the epidemiological evidence for this cancer type is much weaker than for nasopharyngeal cancer, with the main evidence coming from one study; he suggested that this might well have been just a chance association. Members were asked if they were content with wording in paragraph 17 of the cover paper. Members indicated that it was wrong to say there was “no basis for concern” and that text should be modified to take account of this. Consequently, the following wording was agreed:</p> <ul style="list-style-type: none"> • In relation to the apparent association seen in some studies between formaldehyde exposure and leukaemia, based on recent reviews of the evidence, and also considering biological plausibility, there is no basis for any significant concern for this cancer. |
| 7.20 | <p><i>Discussion of Action Point [ii]: mechanistic and dose-response considerations and their implications for potential risk management</i></p> <p>Members were then asked to address Action Point [ii], to set the answer to Action Point (i), “...into context with the available experimental animal data on carcinogenicity and the overall toxicological profile for formaldehyde”. Could anything be said about dose-response relationships, thresholds, the mechanism by which the tumours arise or any other issues that impact on risk management?</p> |
| 7.21 | <p>The Committee discussed the mechanisms by which nasopharyngeal tumours following formaldehyde exposure could arise. A WATCH Member commented that, based on the animal carcinogenicity data, there is biological plausibility to suggest that tumours arise through a mechanism involving both irritation and genotoxicity components. Although the animal carcinogenicity data suggests that nasal tumours arise only under conditions of chronic inflammation, the evidence in humans does not allow any conclusions to be drawn about the relative balance of the contributions of irritation versus genotoxicity in the development of nasopharyngeal tumours. Members agreed with the following statement:</p> <ul style="list-style-type: none"> • It is probable that formaldehyde exposure has caused nasopharyngeal cancer in humans, via a mechanism to which it can be predicted that both chronic inflammation (provoked by irritancy) and genotoxicity contributed. |
| 7.22 | Members then considered the available information on dose-response relationships. Because of the quality of the exposure data in the epidemiology studies, WATCH Members did not consider that a confident assessment could be made of the dose-response relationship or the identification of a possible threshold for nasopharyngeal cancer in humans following formaldehyde exposure. |
| 7.23 | The Committee then offered thoughts about the risk of nasopharyngeal cancer at current occupational levels of formaldehyde exposure. One perspective would be to consider that current occupational exposures will be up to 2 ppm (the current MEL). It was suggested that there might be a significant increase in risk above the background level at exposures around 2 ppm; and that with an anticipated contribution to the carcinogenic process from irritancy, one might expect that the risk of cancer would rise steeply with exposures substantially above 2 ppm. |
| 7.24 | A Member commented that there are potential problems associated with measurement of formaldehyde exposure. Formaldehyde is used in a wide range of industries, often involving concurrent exposures to other aldehydes. The methods used historically to measure formaldehyde have been non-specific and for aldehydes in general. Concurrent exposures to particulates can also occur and one could get artificially low measurements when exposures occur in the presence of particulates. |
| 7.25 | <i>Views on priority for risk management action</i> |

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| | <p>The Chair pointed out that formaldehyde is on a list of 15 substances with existing MELs that will be reviewed as the new Occupational Exposure Limit framework comes into effect. Prioritising substances on this list will involve key questions regarding dose-response relationships, contemporary levels of exposure and an overall view of the level of risk. A Member commented that the potential change in the classification of formaldehyde will in itself have significant downstream regulatory consequences. However, in terms of overall disease burden in the UK workforce, when one considers the background incidence of nasopharyngeal cancer in the UK population, the excess relative risks reported in the key epidemiology studies, and contemporary levels of occupational exposure, one might predict that only 1 new case of nasopharyngeal cancer per year would be expected as a result of occupational formaldehyde exposure. Members suggested that based on this, it was important to avoid unnecessarily precipitate and onerous risk management. One Member suggested, that given the major impact that the position taken by the Committee with respect to the nasopharyngeal cancer hazard could have in the workplace, HSE should issue some sort of note to clarify the position and to reassure workers exposed to formaldehyde about the risk situation.</p> <p>[ACTION: HSE to consider the points raised in the development of the regulatory position on formaldehyde]</p> |
| 7.26 | <p>General points made in relation to presentation of epidemiology data</p> <p>An opinion was given that in addition to considering epidemiology data on a study-by-study basis, it is necessary to undertake and present a synthesis of all the data. This could be done in a variety of ways, such as by performing a meta-analysis of the relevant studies or more simply by separately tabulating data from the cohort and case-control studies (to include observed and expected numbers of deaths and the exposure metric). Members suggested that while meta-analyses generally work well for randomised control trials they are less useful for looking at cohort study data and even less useful for looking at case-control study data. In general, it was agreed by WATCH and HSE that in future WATCH packages with a heavy emphasis on epidemiological data more investment would be made in constructing an overall synthesis of the available information.</p> <p>[ACTION: HSE to undertake and present an overall synthesis of data for future WATCH packages which have a heavy emphasis on epidemiological data]</p> |
| 7.27 | <p>Another WATCH Member pointed that IARC use indicative criteria to facilitate consistency in its decision-making process. The Member then suggested that similar criteria should be developed by WATCH to ensure that a consistent approach is taken with different chemicals.</p> |
| 7.28 | <p>Overall Conclusions on Formaldehyde Package</p> <p>The Chair ended the discussion by summing up the statements that WATCH had agreed. In relation to Action Point [i] WATCH agreed that:</p> <ul style="list-style-type: none"> • Formaldehyde has probably caused nasopharyngeal cancer in humans; and • In relation to the apparent association seen in some studies between formaldehyde exposure and leukaemia, based on recent reviews of the evidence, and also considering biological plausibility, there is no basis for any significant concern for this cancer. |
| 7.29 | <p>In relation to Action Point [ii], WATCH agreed that:</p> <ul style="list-style-type: none"> • It is probable that formaldehyde exposure has caused nasopharyngeal cancer in humans, via a mechanism to which it can be predicted that both chronic inflammation (provoked by irritancy) and genotoxicity contributed. |
| 8 | <p>Early identification of new and emerging issues and review of existing advice: Annual consideration</p> |
| 8.1 | <p>Members were asked to agree to the document outlining Committee procedures for dealing with new and emerging issues (WATCH/2004/12). The changes that had been made by the Secretariat were agreed although clarification of the text at bullet point 1 was considered necessary.</p> <p>[ACTION: HSE to redraft text at bullet point 1 in WATCH/2004/12 and seek to clear with WATCH by correspondence]</p> <p>[Post Meeting Activity: WATCH/2004/12 was distributed to members with the draft minutes to this 3rd meeting]</p> |

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| 8.2 | <p>Members were asked if there were any new or emerging issues that they felt may warrant consideration by the Committee. The following points were raised:</p> <ul style="list-style-type: none"> – On a procedural note, in addition to suggesting issues meriting attention, Members indicated that they could also suggest how best such issues might be progressed. It was also requested that HSE should provide feedback to members on the consequences of recommendations made by WATCH. – HSE was asked to explore in future WATCH papers its suggestions for improving the presentation and analysis of epidemiological data (see minutes on formaldehyde, Portland cement dust). It was also suggested that more scrutiny should be given to the robustness of exposure assessments in epidemiology studies. – WATCH could look at approaches to the assessment of the effects of high exposures to acute toxins in accident situations. A discussion on the use of a banding approach to develop guidelines on acceptable levels of exposure for workers in the period following a terrorist chemical attack may also be useful. – In terms of C&L, explore and clarify what is meant by normal handling and use? – Find out what work other countries are undertaking on setting exposure limits and reviewing substances. Check for consistency in the setting of occupational and environmental limits. Look at the effect of shift patterns on exposure, and the adequacy of risk management standards in this context. Finish the work started in 2001-02 on establishing a framework for dealing with toxicological uncertainty. – Explore the potential for making more use of <i>in vitro</i> testing, SAR and computer modelling in regulatory decision-making. |
| 9 | Evaluation of the impact of eCOSH Essentials |
| 9.1 | <p>The Chairman introduced Michael Topping (HSE) who delivered a brief presentation on the issues involved in seeking to evaluate the impact of eCOSH Essentials (CE) and asked members for ideas.</p> |
| 9.2 | <p><i>Ideas for evaluation of CE</i></p> <p>The following ideas were put forward by members:</p> <ul style="list-style-type: none"> – Target industries within two or three specific areas/groups of concern to find out if they have heard about CE and how to access it; assess the working conditions at this point and direct the operators towards CE; then assess this group again after a suitable interval to evaluate whether CE has had any impact. – The total number of hits on the CE site represents a small percentage of the potential target audience. Perform a random survey of UK workplaces to ascertain the reasons why people do or don't access CE. – Investigate whether people actually use the guidance sheets once they have accessed them, although there are "access anonymity" issues here. – Develop a questionnaire on CE to be completed as part of routine, planned visits to workplaces by Field Inspectors. <p>Identify workplaces that are known to have improved controls in recent years and ask whether or not this was a result of using CE.</p> |
| 9.3 | <p><i>General comments on CE</i></p> <p>The following comments on CE were also made during the discussion:</p> <ul style="list-style-type: none"> – It might be worth exploring setting up sites for specific groups of workers eg hairdressers, to provide targeted information for that group. – Optimise the search engines to increase the number of hits on the website. – Include CE in the ongoing HSE project on the provision of Occupational Health Support Services. |

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| | <ul style="list-style-type: none"> - Involve Local Authorities in any survey of CE. - Use Trade Fairs to promote the use of CE. - Include references to CE in every HSE activity involving chemical exposure. |
| 9.4 | The Chairman thanked Members for their thoughts and closed the discussion. |
| 10 | Date of next meetings |
| 10.1 | The next meeting dates for 2005 were set for May 5 th in Rose Court and October 5 & 6 th in Buxton. |
| 11 | AOB |
| 11.1 | There were no items of AOB The meeting closed at 15.00. |