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ADVISORY COMMITTEE ON TOXIC SUBSTANCES

The work of HSE/WATCH in recent years on the potential for occupational exposure to organic solvents in general to produce effects on the central nervous system

A Paper by Steve Fairhurst (as WATCH Chairman)

Issue

1. Assessment of the threat of long-term neurotoxicity as a consequence of occupational exposure to organic solvents in general; the work done by HSE/WATCH in the period 1997-2002

Timing

2. Routine

Recommendation

3. That ACTS considers this information in the context of thinking about potential future issues to examine.

Background

4. At the last ACTS meeting in November 2004, there was some discussion of new and emerging issues. In this context, a member wondered if HSE and ACTS was sufficiently on top of the evidence surrounding the question of whether or not long-term occupational exposure to organic solvents could give rise to significant, long-lasting adverse effects on the nervous system; were we confident about the prevailing risk management situation, given this potential concern; and could this be an as-yet-unrealised looming health problem for the future?

5. In response, Steve Fairhurst as Chairman of WATCH reminded ACTS that HSE and WATCH had, in relatively recent times, undertaken a considerable amount of work related to this issue. He committed to update ACTS at its March 2005 meeting on the issues addressed by WATCH and the positions reached. This paper is the update.

Argument

6. Over the five year period 1997-2002, HSE worked with WATCH to develop understandings and positions on a number of issues related to the effects (alleged,

potential or established) of occupational exposure to organic solvents in general on the central nervous system (CNS).

7. Three issues were covered, via a number of papers, lines of activity and WATCH meetings. These were:

   - The evidence for the condition referred to as chronic toxic encephalopathy (CTE) arising as a result of occupational exposure to organic solvents

   - The balance of evidence for whether or not the organic solvents used in industry have the general ability to produce nervous system damage in workers that can be detected by diagnostic techniques other than neuropsychological testing.

   - An approach for the interpretation of neurobehavioural test data by benchmarking the changes reported in groups of workers or human volunteers exposed to organic solvents against the changes produced by other experiences, such as alcohol consumption, lack of sleep or ageing.

8. Only brief details are given here for what was a substantial amount of work carried out between 1997 and 2002. The positions reached by WATCH on each of the three issues were as follows, all from the May 2001 WATCH meeting:

9. **Chronic Toxic Encephalopathy (CTE) :** The conclusion reached by WATCH was that:

   "There is some evidence for a condition compatible with the current EU definition of 'CTE' having occurred in individuals occupationally exposed to organic solvents. WATCH members differed in their views of the extent of, and range of different sources for, the supporting evidence. WATCH could not agree on any form of wording that captured any collective view as to the exposure conditions believed to be associated with the production of this condition. However, WATCH agreed unanimously that more work is needed to better characterise both the condition and the exposure conditions causing it"

10. **Evidence for nervous system damage detectable by means other than neurobehavioural testing :** A review paper reflecting the position arrived at by HSE/WATCH was published in 2003 (Ridgway et al, Food and Chemical Toxicity 41, 153-187, 2003). The abstract reads:

    "The purpose of the present review is to assess the evidence published in scientific literature that industrial organic solvents as a generic group have the ability to induce long-term nervous system damage in workers that can be detected by techniques other than neuropsychological testing. The main body of evidence considered in this review was 40 studies involving the use of brain imaging, neurophysiological testing, gross autopsy or histopathology in groups of workers with long-term solvent exposure. Case reports involving both solvent abuse and occupational exposure, and experimental animal data have also been reviewed as supporting data. A number of the studies in groups of workers provide evidence of the presence of marginal atrophic abnormalities in the brain or deficits in nerve conduction velocity in solvent-exposed workers. However, there are limitations in the design of many of these studies, the

strength of association between exposure and effect is not consistently strong, no dose-response relationship can be detected, the reported changes lack specificity and there is no coherence between the human and experimental animal data. Overall, it is not possible to draw reliable conclusions with respect to the presence or absence of nervous system damage related to the common properties of organic solvents."

11. **Benchmarking of neurobehavioural test results :** The conclusion reached by WATCH was:

    - "It appears that most existing data are not currently in a form which would allow benchmarking to be carried out, at least in the immediate term

    - However, a number of courses of action can be suggested which may make such a process possible in the future – some of these relate to existing information and others wil require collection of new data"

12. Despite all of the uncertainties inherent in these positions, one logical conclusion reached was that there is a need to have each exposure situation/period controlled such that the immediate consequences of "acute" CNS disturbance/depression are avoided. It therefore follows that it is imprtant to know where the dividing line is, in terms of single exposure levels that do, and those that don't trigger such immediate disturbances. For some organic solvents the relevant data are good, but there are two significant gaps in knowledge:

    - Particular solvents that have no reliable human data in this respect; and
    - The likelihood of inter-individual variability within the potentially exposed human population, in terms of sensitivity – but the absence of significant data on this issue

    In order to develop a means of addressing these gaps, work has been undertaken by the Computational Toxicology section at HSE's HSL, using PBPK (physiologically-based pharmacokinetic) modelling techniques. The work is ongoing and has not yet advanced to the stage of an approach that is usable for regulatory decision-making.

Link to HSC Strategy

12. This information paper describes work undertaken prior to the development of the current HSC strategy.

Communication Plan

13. Not applicable.

Evaluation Plan

14. Not applicable

Consultation

15. Not applicable

Costs and Benefits

16. Not applicable

Financial/Resource Implications for HSE

17. Not applicable

Environmental implications

18. Not applicable

European implications

19. This work was undertaken at a time when there were expectations that the issue of "CTE" would become a major focus of attention within the EU. However, this expectation has not yet materialised. If it were to arise in the future, much of the work summarised above would be crucial in helping form the UK position during negotiations.

Other implications

20. None

Action

21. No action is required. It is suggested that ACTS considers the above information in the context of thinking about its potential future work programme.

Contact

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