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WATCH COMMITTEE

The use of CI Solvent Red 164 as a penetrant dye in the detection of cracks in metal components

Issue

1. What level of concern about potential ill-health consequences is appropriate in relation to the occupational use of CI Solvent Red 164 as a penetrant dye for the detection of cracks in metal components? And is it appropriate to make a recommendation in relation to potential substitutes?

Timing Considerations

2. There is current concern about this matter, such that the advice of WATCH is required at this time.

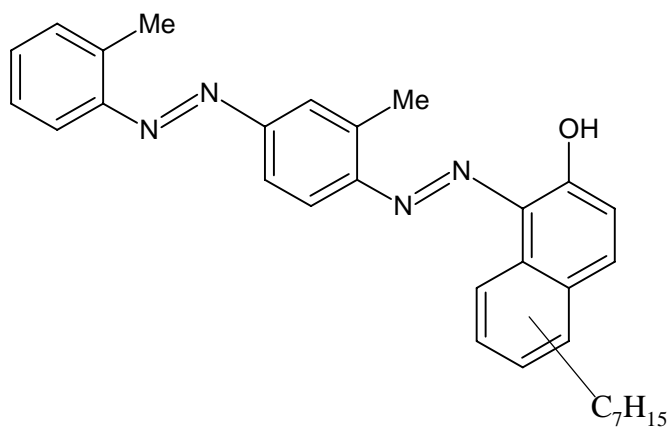
Recommendation

3. WATCH is invited to consider the issues noted in this cover paper and to respond to the actions in paragraph 17.

Background

4. Azo compounds are synthetic organic structures in which two or more aromatic rings are connected by -N=N- bonds. Their principal uses are a reflection of their strong colours and they have been widely used for many years as dyes.

5. One such compound is CI Solvent Red 164. A number of different companies make this dye commercially and at least in some cases there are substances with different chemical structures within the product (variations in the positioning of hydrogen and methyl side groups on the aromatic rings). A representative structure is given below:



6. The principal toxicological concern surrounding azo dyes is the potential for reductive metabolism, breaking the –N=N- linkages to release aromatic amines. Azo reductase activity is a component of the cytochrome P450 xenobiotic (or drug) metabolising system, which is widespread in mammalian tissues and also in many species of anaerobic bacteria commonly found in the human gastro-intestinal tract. Across the family of azo dyes there is variability in the extent to which different structures can be reductively metabolised and in the structures of (and resultant toxicological concerns about) the aromatic amines that can be generated as a result.

7. Red azo dye-containing penetrants represent a class of liquid penetrants available for use in the non-destructive testing (NDT) of metal components; they are used to check for flaws or cracks in the surface of castings, forgings or welds. It is a simple, low-cost technique – the test object is coated with the dye and any surface breakages draw in the dye by capillary action. The dye can be applied by spray application (aerosol can or air gun), brush painting or immersion of the test piece in liquid dye.

8. In the context of the Cancer Project of the Disease Reduction Programme (DRP), stakeholder concern has been raised with HSE about the appropriateness of continued use of CI Reactive Red 164 as an NDT penetrant dye. The concern arises because of the assertion that *o*-toluidine (1-amino-2-methylbenzene), classified as a category 2 carcinogen in the EU, could be released from the reductive cleavage of the azo bonds of this dye (see aromatic ring on the left-hand side of the structure above).

Argument

9. In relation to toxicological hazard, searching by HSE thus far has failed to find much toxicity data on CI Solvent Red 164. One supplier of this dye states in the accompanying safety data sheet that there is the potential for *o*-toluidine to be generated by its metabolism. However, HSE has not identified any actual data on this or indeed on many other aspects of the toxicological profile of this substance, including its ability to penetrate the skin. There is also no readily available information on the toxicological profile of the other two potential reductive metabolites of CI Solvent Red 164.

10. In relation to occupational exposure, there is clearly the potential for worker exposure by inhalation and/or via the skin during the use of crack penetrants containing CI Solvent Red 164. One of the safety data sheets seen by HSE that accompany supply of such penetrants advocates a cautionary approach to control.

11. A brief summary of the supply, formulation and use of CI Solvent red 164 is presented in Annex 1 of this paper.. However, HSE is not aware of any exposure data available for CI Solvent Red 164 used in this context.

12. In view of the general lack of data relating to hazard and exposure, HSE considers that at this moment it is difficult to express a view on the risk of ill-health that might be associated with the use of CI Solvent Red 164 in testing for cracks in metal components. The release of *o*-toluidine from CI Solvent Red in the body is a distinct possibility (the carcinogenic profile of *o*-toluidine is given in Annex 2). Very recently HSE's HSL has started to undertake biomonitoring for *o*-toluidine in 3 individuals exposed to CI Solvent Red 164 in a single foundry, a total of 12 urine samples are to be analysed. A verbal report of this work will be given to WATCH at the February meeting.

13. There are three non azo dye-based substitutes available for CI Solvent Red 164; Rhodamine B, and two metal complex-based dyes. In the time available, we have not been able to identify any toxicological information on these potential substitutes.

Link to HSC Strategy

14. This work falls under the Cancer Project of the Disease Reduction Programme (DRP) of HSE's "Fit3" Strategic Programme.

Consultation

15. No wider consultation on the content of this cover paper beyond HSE has been undertaken at this stage.

European Context

16. There are no specific links to EU procedures or activities.

Action

17. WATCH is asked to consider the issues described in this paper and to address:

(i) What level of concern about potential ill-health consequences is appropriate in relation to the occupational use of CI Solvent Red 164 as a penetrant dye for the detection of cracks in metal components?

(ii) Is it appropriate to make a recommendation in relation to potential substitutes?

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References

1. Disease Reduction Programme – Carcinogen Profiles (2007).

Annexes

Annex 1: Supply, Formulation, Use and Control of Exposure to Azo Dye Containing Crack Detection Penetrants in the UK

Annex 2: Summary of the carcinogenic potential of o-toluidine (source HSE carcinogens profile).

Supply, Formulation, Use and Control of Exposure to Azo Dye Containing Crack Detection Penetrants in the UK

1 Introduction

1.1 Azo compounds are synthetic inorganic chemical compounds. They are usually stable and have vivid colours such as red, orange and yellow and are widely used as dyes. It is the red azo compound which is used as a crack detection penetrant.

1.2 There are at least seven red azo compounds. The compound most commonly used in the UK is CI Solvent Red 24 to colour low tax diesel fuel. Solvent Red 27 is used as a staining agent in biological analysis and also to colour plastics. The compound most commonly used in the formulation of crack detection penetrants is CI Solvent Red 164 due to its greater solubility in hydrocarbons.

2 Supply of CI Solvent Red 164 concentrate

2.1 Red azo dyes are not manufactured in the UK. They are manufactured in USA, Mexico and India. At least 50 Tonnes of CI Solvent Red 164 are imported by UK industry per year, predominantly to colour automotive transmission fluids but also for blending into other colours (e.g. red + blue => purple).

2.2 Less than 3 Tonnes of CI Solvent Red 164 are imported per year for use in the formulation of crack detection penetrants.

3 Formulation of red azo dye crack detection penetrant

3.1 Approximately 1 Tonne/yr of the CI Solvent Red 164 concentrate imported is formulated into red azo dye penetrant for use in the UK. The red azo dye penetrant formulated from the remainder is exported, mainly to USA. There are five principal red azo dye formulators in the UK and it is estimated that less than thirty workers are potentially exposed to red azo dye at formulation.

3.2 CI Solvent Red 164 concentrate is delivered to formulators in 200 litre intermediate bulk containers (IBCs) and stored on site in the same container. The concentrate is then transferred to a dye penetrant solution mixing tank either by: (a) pumped transfer via a lance inserted into the bulk container; or, (b) gravity drain into a smaller container for manual transfer to the mixing tank by a worker wearing gloves and RPE. Mixing is carried out remotely.

3.3 The red azo dye penetrant solution is then transferred by sealed pumped delivery from the mixing tank to a filling point housed within a ventilated cabinet within which 440 ml aerosol spray cans are filled remotely.

3.4 It is estimated that formulators supply the UK user industries with approximately 55,000 x 440ml aerosol spray cans of red azo dye penetrant each year.

3.5 It is also estimated that formulators supply the UK user industries with approximately 13,000 litres of red dye penetrant in tins (estimated 120 x 25 litre and 2,000 x 5 litre tins) for use in immersion tanks or application to the test piece by air gun or paint brush. Typically, tins are manually filled in the open workshop by a worker wearing gloves and RPE.

3.6 The red azo dye formulation contains approximately 3.5% of CI Solvent Red 164. The highest volume constituent is odourless kerosene at approximately 70 to 75%.

3.7 There are no exposure data currently available for workers employed to formulate red azo dye mixtures. At the beginning of January however, three workers, from one azo dye crack detection penetrant formulator, had submitted twelve urine samples for analysis for the presence of metabolised o-toluidine.

3.8 Results of the analysis are not yet available but will be reported to WATCH subject to availability.' If a positive result is recorded then this will indicate that one of three possible exposures has occurred:

1. exposure to a red azo dye has occurred; it has been absorbed, metabolised to o-toluidine (and conjugates) and excreted in urine;
2. exposure to a red azo dye has occurred; it has been absorbed and then excreted in urine in a form that yields o-toluidine during analysis;
3. exposure to o-toluidine has occurred from another source (smoking, diet, environment, etc.)

4 Use of red azo dye crack detection penetrant

4.1 Red azo dye containing penetrants are one of several liquid penetrants available for use as part of the non destructive test (NDT) of metal components. They are used to check for flaws or cracks in the surface of castings, forgings or welds.

4.2 Consultation with both the British Institute of Non Destructive Testing (BINDT) and The Welding Institute (TWI) indicate that approximately 60% of liquid penetrant testing is carried out using red azo dyes. It is a simple, low-cost technique for detecting surface breaking flaws. The test object is coated with the dye and any surface breaking imperfection draws in the dye by capillary action. Coating of the surface of the test piece can be carried out by:

- Spray application by aerosol can;
- Immersion of the test piece in a holding tank;
- Application by paint brush; or,
- Application by air gun.

4.3 After cleaning away excess dye from the surface, a developer is used to act like blotting paper and draw the dye away from the imperfection, thus revealing the defect.

4.4 NDT of metal components is carried out in a wide range of metals industries including:

- Founding and forging of metal components;
- Welding and subsequent in-service inspection of fabrications and structures such as pressure vessels, pipelines designed to convey hazardous materials, ships and fairground rides.

4.5 Testing can be carried out by surveyors and assessors employed by the user industry, specialist sub-contractors or insurance companies. BINDT estimate there to be at least 17,000 registered testers in Britain. It is likely that all will have worked with red azo dyes at some point in their career. BINDT advise that usage will vary greatly. Those however who are fully engaged in work with red azo dyes are likely to use at least two aerosol cans per week. This equates to approximately 40m of weld inspection.

4.6 The ONS Labour Force Survey of May 2005 identifies there to be some 200,000 welders in GB. Consultation with both BINDT and the Insurance industry Safety Assessors Federation (SAFed) indicates that liquid penetrant is used by many such workers to simply

check surface finish before engaging a specialist NDT surveyor to formally test a metal component. A reliable estimate of the potential number of workers so exposed however cannot be provided.

4.7 There are no exposure data currently available for any workers employed to use red azo dye penetrants in NDT. Usage can vary greatly from as little as two or three brief (less than ten seconds) aerosol spray applications per year to the use of at least two aerosol spray cans per week.

4.8 Users are advised to take a cautionary approach to the use of red azo dye containing penetrants and wear suitable respiratory, skin and body protection. The nature of the dye (brightness and permeability) makes any staining on the skin or clothing obvious and should encourage the worker to take immediate action to clean away any residue and seek to avoid further exposure.

5 Discussion

The use of azo dye containing products for crack detection testing in the metal industries does not occur in all cases. There are two red non azo dye containing substitutes currently available plus a third now under development as well as alternative test methods, notably:

- Visual examination;
- Liquid penetrant testing using fluorescent dyes
- Magnetic particle inspection;
- Radiography;
- Ultrasonics; or
- Eddy current.

5.1 One supplier's CI Solvent Red 164 Safety Data Sheet (SDS) clearly describes CI Solvent Red molecule to the potential to be metabolised to o-toluidine; because of this possibility, the supplier has self-classified the substance as a category 3 carcinogen and assigned the R40 phrase "Limited evidence of a carcinogenic effect".

5.2 Consultation with the formulators and user industries however presents a picture of widespread use of red azo dye containing penetrants and little awareness or evidence of any associated health considerations. Several red azo dye containing liquid penetrant SDSs have been reviewed and they do not supply the user enough information to adequately assess the risk of possible metabolism of the absorbed azo compound into a carcinogen.

5.3 The SDSs reviewed do however already advocate a cautionary approach to the use of red azo dye containing penetrants and advise suitable respiratory, skin and body protection. Such a cautionary approach would include:

- Avoid all skin contact by changing the way the azo dye is used and wear gloves which are classed as suitable for use with organic chemicals;
- Frequent changes and good maintenance of gloves as essential. A specialist safety equipment provider should be consulted;
- Avoid spray application;
- Use of effective extraction systems where vapours or spray may be released. Extreme care should be taken with disposal of contaminated material, cleaning off the dye from the test piece, maintenance of extraction system, etc. All workers carrying out these tasks, or working nearby should be informed of the need for particular care to be taken.

Summary of the carcinogenic potential of *o*-toluidine

The carcinogenic potential of *o*-toluidine has been investigated in humans in a single case control study. The most comprehensive information on carcinogenic potential comes from standard studies in rats and mice, along with supportive information from non standard studies in rats and mice.

Human data

Exposure to chemicals including *o*-toluidine in the dyestuffs industry and more recently in the rubber industry has been reported to be associated with an increased incidence of bladder cancer. For example, expected and observed cases of bladder cancer were recorded in a thorough, well conducted retrospective cohort study at a rubber chemical plant in upstate New York (Ward et al., 1991). The cohort consisted of all 1749 male and female workers employed at the plant between 1973 and 1988. These workers were exposed primarily to *o*-toluidine and aniline. In 1988, airborne *o*-toluidine and aniline levels were <1 ppm (<4.4 mg/m³ for *o*-toluidine).

Based upon 13 identified cases of bladder cancer among all 1749 employees, compared with 3.61 cases expected (estimated from the rate in the population of the state of New York, excluding New York City), the standardized incidence ratio (SIR) was 3.6 (90% confidence interval [CI] = 2.13-5.73). The SIRs for bladder cancer among workers "definitely exposed" (*n* = 708), "possibly exposed" (*n* = 288), and "probably unexposed" (*n* = 753) to *o*-toluidine and aniline were 6.48 (90% CI = 3.04-12.2; 7 observed cases), 3.66 (90% CI = 1.25-8.37; 4 observed cases), and 1.39 (90% CI = 0.25-4.39; 2 observed cases), respectively. The risk of bladder cancer increased with duration of exposure and time since first exposure. The SIRs for bladder cancer among the "definitely exposed" workers with <5, 5-9.99, and ≥10 years of exposure to these chemicals were 0 (0 observed cases), 8.8 (90% CI = 0.45-41.7; 1 observed case), and 27.2 (90% CI = 11.8-53.7; 6 observed cases), respectively. The SIRs for bladder cancer among workers with <10, 10-20, and >20 years since their first employment in the "definitely exposed" department of the plant were 0 (0 observed cases), 2.03 (90% CI = 0.10-9.64; 1 observed case), and 16.4 (90% CI = 7.13-32.3; 6 observed cases), respectively. It was calculated that smoking was unlikely to account for the increased incidence of bladder cancer in this group of workers. The mean latency period for the group of seven "definitely exposed" workers with bladder cancer was 23 years. However, it is not possible to conclude that *o*-toluidine alone was responsible for the observed increase in tumour incidence, as exposures were mixed.

Studies animals

In one study, F344 rats were given diets containing 0, 3000 or 6000 ppm *o*-toluidine hydrochloride for 101-104 weeks (equivalent to intakes of approximately 150 and 300 mg/kg body weight per day) (NCI, 1979; Goodman et al., 1984). In the control, low-dose, and high-dose groups, the combined incidence of sarcomas, angiosarcomas, and osteosarcomas of the spleen was 0/20, 9/49, and 12/49, respectively, in females and 0/20, 8/49, and 4/42, respectively, in males. The combined incidence of sarcomas, fibrosarcomas, angiosarcomas, and osteosarcomas in multiple (unspecified) organs was, among females, 0/20, 3/50, and 21/49 and, among males, 0/20, 15/50, and 37/49, for animals in the control, low-dose, and high-dose groups, respectively. In females, the incidence of transitional cell carcinomas of the urinary

bladder was 0/20, 9/45, and 22/47, respectively; the incidence of this tumour was not significantly increased in the male rats. The incidence of malignant mesothelioma of the testicular tunica vaginalis was 0/20, 10/50, and 6/49 in the control, low-dose, and high-dose groups, respectively. Although not observed among control animals, splenic fibromas were noted in the exposed animals; however, the incidence was significantly increased only for males in the low-dose group (10/49). For animals in the control, low-dose, and high-dose groups, the incidence of skin fibromas among males was 0/20, 28/50, and 27/49, respectively, and the incidence of mammary gland fibroadenomas among females was 6/20, 20/50, and 35/49, respectively.

F344 rats received 0 or 62 mg *o*-toluidine hydrochloride in the diet each day for 72 weeks (~ 470 and 130 mg/kg bodyweight per day at the beginning and end of the study, respectively), followed by a 16-week recovery period, exposure to *o*-toluidine reduced survival (6/30 and 18/30 survivors in the exposed and control groups, respectively) (Hecht et al., 1982). Incidences of the following tumours (in the control and exposed groups, respectively) were: bladder epithelial cell tumours, 0/30 and 4/30; skin fibromas, 1/30 and 25/30; splenic fibromas, 0/30 and 10/30; mammary tumours, 0/30 and 13/30; and peritoneal tumours, 2/30 and 14/30. Although the statistical significance of these results was not discussed in this report, the results reveal an increased occurrence of a variety of tumour types in animals administered *o*-toluidine hydrochloride for 72 weeks.

Male Charles River CD rats were given diets containing *o*-toluidine hydrochloride at concentrations of 8000 or 16000 ppm for 3 months (estimated intakes of approximately 800 and 1600 mg/kg body weight per day), (Weisburger et al., 1978). Excessive toxicity (increased mortality and reductions in bodyweight), resulted in the concentrations being reduced to 4000 and 8000 ppm (with estimated intakes of 400 and 800 mg/kg bodyweight per day) for a further 15 months, followed by a 6-month observation and recovery period. Only animals that survived 6 months or more were necropsied. There was a statistically significant increase in the incidence (0/16, 18/111, 18/23, and 21/24 in the matched control, pooled control, low-dose, and high-dose groups, respectively) of subcutaneous fibroma and fibrosarcoma in *o*-toluidine-exposed animals. The incidence of bladder transitional cell carcinoma was 0/16, 5/111, 3/23, and 4/24 in the matched control, pooled control, low-dose, and high-dose groups, respectively.

Statistically significant increases in hepatocellular carcinomas and adenomas, as well as haemangiosarcomas, were observed in a study in which groups of B6C3F₁ mice were given diets containing 0, 1000 or 3000 ppm *o*-toluidine hydrochloride (estimated intakes of 110 and 340 mg/kg bodyweight per day) for 101-104 weeks (NCI, 1979). In the control, low-dose, and high-dose groups, the incidences of hepatocellular carcinoma (in females), hepatocellular adenoma (in females), and haemangiosarcoma (in males) were 0/20, 2/49, and 7/50; 0/20, 2/49, and 6/50; and 1/19, 1/50, and 10/50, respectively.

Significantly increased incidences of haemangiosarcomas and haemangiomas were observed in a study in which CD-1 mice were given diets containing *o*-toluidine hydrochloride at concentrations of 16000 or 32000 ppm (estimated intakes of 1800 and 3600 mg/kg body weight per day) for 3 months (Weisburger et al., 1978). Excessive toxicity, based upon increased mortality and reductions in body weight, resulted in the concentrations being reduced to 8000 and 16000 ppm for a further 15 months, followed by a 3-month observation and recovery period. Only animals that survived 6 months or more were necropsied. In the matched control, pooled control, low-dose, and high-dose groups, the incidence of abdominal haemangiosarcomas

and haemangiomas was 0/14, 5/99, 5/14, and 9/11 (in males) and 0/15, 9/102, 5/18, and 9/21 (in females), respectively.

O-Toluidine has been reported clastogenic in mammalian cells *in vitro* but only in the presence of metabolic activation. Although it has generally tested negative in the *in vivo* mouse micronucleus test, there is evidence for *in vivo* genotoxicity from a Comet assay in which oral dosing led to positive Comet responses in the liver and urinary bladder of mice and the urinary bladder of rats (Sasaki et al, 2000).

Summary

A retrospective cohort study found that occupational exposure to o-toluidine may be associated with an increased incidence of bladder tumours in humans, however, this study is confounded by co exposure to other aromatic amines such as aniline. Studies in rats and mice indicate that o-toluidine causes clear increases in tumour incidence, most notably in rats. In addition, there is some evidence that o-toluidine may be genotoxic *in vivo*. Overall, it is probable that o-toluidine is a genotoxic carcinogen.