

DRAFT

**COMMITTEE ON THE MUTAGENICITY OF CHEMICALS IN FOOD,
CONSUMER PRODUCTS AND THE ENVIRONMENT**

2,3-DICHLOROPROPAN- 1-OL (2,3 DCP)

INTRODUCTION

1 2, 3 Dichloropropan-1-ol (2,3 DCP) is a member of a group of compounds known as chloropropanols, which includes 3-MCPD (recently reviewed by the COM) and 1,3 DCP (the subject of a companion paper, MUT/01/06 and currently under review by COM). 2,3 DCP co-exists with both 3-MCPD and 1,3 DCP as a contaminant in certain foodstuffs and in polyamine flocculants used in the treatment of drinking water.

2 Compared with 1,3 DCP there is very little toxicity and genotoxicity data for 2,3 DCP.

3 The public health issues for 2,3 DCP are the same as those described for 1,3 DCP (see MUT/01/06).

4 In terms of regulatory issues, while JECFA have looked both 3-MCPD and 1,3 DCP, there appears to be no intention to look at 2,3 DCP. A draft CEN standard for polyamine flocculants for drinking water treatment contains a maximum impurity limit for 2,3 DCP of 1000ppm in the finished product. At current permitted maximum application rates a theoretical concentration of upto 2.5µg/litre may arise in drinking water. There appears to be no toxicological basis for the maximum impurity level

5 To assist in future health risk evaluations of this substance which might be required by the Food Standards Agency or the Drinking Water Inspectorate, COM are invited to consider and comment on the available toxicity and genotoxicity data for 2,3 DCP.

CHEMICAL AND PHYSICAL PROPERTIES

9 2,3-Dichloro-1-propanol is a member of a family of a group of chemical substances known as chloropropanols or alternatively chlorohydrins. It is a viscous, liquid with a boiling point of 184°C. It is soluble in water (upto 10mg/l) and soluble in ethanol, ether and acetone. The specific gravity is 1.36 at 20°C

10 Common synonyms include: dichlorohydrin, β-dichlorohydrin and glycerol alpha beta dichlorohydrin. Its CAS number is 616-23-9 and its molecular weight is 128.99.

SUMMARY OF EXPERIMENTAL STUDIES

METABOLISM

11 There are very little data on the absorption, distribution, and excretion of 2,3-DCP. Theoretically, 2,3 DCP could be metabolised to produce epichlorohydrin (and subsequently glycidol) and therefore has structural alerts for genotoxicity and carcinogenicity. Additionally, a pathway to 3-MCPD is possible with potential effects upon the kidney and male reproductive performance

TOXICOLOGY

Acute toxicity

12 Acute toxicity data are as follows (HSDB, 2000)

- Rat oral LD₅₀ : 90 mg/kg
- Rat inhalation LCL₀ (4hr) : 500ppm (2600mg/m³)
- Rabbit skin LD₅₀ : 200 mg/kg

13 week study - rats

13 Four groups of male and female rats (30/sex/group) were dosed orally with 0, 10, 35, or 100 mg/kg/day of 2,3-dichloropropanol. (USEPA 1989). Rats scheduled for the interim sacrifice were dosed for 28 to 29 days, while the rats scheduled for the final sacrifice were dosed for 91 to 92 days. The toxicological evaluations of this study included body and organ weight changes, food consumption, clinical-pathological evaluations, and histopathological evaluations of target organs. The results of this study indicated significant dose-related hypoactivity and mortality attributed to myocardial degeneration in rats dosed with 100 mg/kg/day. Other organs affected were kidney and liver, showing hypertrophy of both organs and karyomegaly and bile duct proliferations in the liver. Hematological and serum enzyme changes seen in the mid- and high-dose groups in this study were also considered to be treatment-related. Myocardial degeneration, as well as other toxic effects, were observed to a lesser extent at the intermediate dose of 35 mg/kg/day. The 10 mg/kg dosage produced no apparent adverse effect.

GENOTOXICITY STUDIES

Salmonella typhimurium

14 Nakamura et al (1979) described an increase in the direct mutagenicity of 2,3-DCP at concentrations of 0.1 to 100µmole/plate with and without rat S9 for the strains TA 100 and TA 1535, and was weakly mutagenic in the strain TA 98. However, negative results were obtained with TA 1537 and TA 1538, indicating that base substitutions had been produced but not frameshift mutations.(Data table for 2,3 DCP results provided in MUT/01/06 ;Annex A)

15 Zeiger et al. (1988) also reported that 2,3-DCP at concentrations of 333 to 3333µmole/plate also produced a positive result in the Ames test. Although this test was carried out both in the presence and absence of metabolic activation, the

conditions producing a positive result is not clear from the table of results.(see data table in MUT /01/06 ; Annex A)

E. coli

16 An indirect assay for DNA damage, the SOS chromotest, produced negative results both with and without metabolic activation with the strain PQ37 under standard conditions (von der Hude et al 1988). Doses were not given in the paper.

Mammalian cells

17 In the sister chromatid exchange (SCE) with Chinese Hamster V79 cells, 2,3-DCP tested at doses of 1.0 to 6.0 mM produced dose-related increases in the frequency of SCEs both with and without S9 (von der Hude et al.1987). The addition of S9 metabolic activation resulted in an increase in the SCE rate. (see data table in MUT/01/06 ; Annex B).

Summary of genotoxicity studies

18 In a limited amount of studies conducted, 2,3 DCP is genotoxic *in vitro* with and without metabolic activation in bacterial and mammalian cells. No *in vivo* studies in mammalian systems have been conducted.

COMMITTEE ADVICE

19 The opinion of COM is sought on the following statement :

(i) 2,3 DCP has been shown to produce gene mutations in studies in bacteria, both in the presence and absence of metabolic activation. Positive results were also obtained in an assay for sister chromatid exchange. The in-vitro data indicates that 2,3 DCP has mutagenic potential

(ii) There are no in-vivo data to assess whether this potential can be expressed in the whole animal. In view of this it is prudent to regard 2,3 DCP as having genotoxic potential in vivo.

(iii) Data from in-vivo assays in bone marrow and liver would be needed to evaluate whether the activity seen in vitro was expressed in vivo.

**Secretariat
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REFERENCES

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MUT/01/07

This paper has been prepared for consideration by the COM and does not necessarily represent the final views of the Committee.

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