

This is a draft paper for discussion. It should not be quoted, cited or reproduced.

**FOR MEMBERS USE ONLY
DRAFT**

CC/03/42

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

CARCINOGENICITY OF 1,3-DICHLOROPROPAN-2-OL (1,3-DCP): REVIEW OF COC OPINION IN LIGHT OF NEW COM OPINION

Introduction

1. 1,3-dichloropropan-2-ol (1,3-DCP) is a member of a groups of chemicals called chloropropanols. 1,3-DCP can be present as a contaminant of polyamine flocculants in drinking water and some foodstuffs. 1,3-DCP was considered by the COM and the COC in 2001. COM concluded that it would be prudent to consider 1,3-DCP as potentially genotoxic *in vivo* but agreed that it should be tested for genotoxicity *in vivo* using the approach set out in the COM guidelines. Subsequently, COC advised that “it was prudent to assume 1,3-DCP is a genotoxic carcinogen and that exposure to 1,3-DCP should be reduced to as low as technologically feasible”. A copy of the COC statement on the mutagenicity of 1,3-DCP is included at Annex A.

2. New data have now been provided on the mutagenicity of 1,3-DCP, and the advice of the COM has been provided. The COC is asked to consider whether any revision of the COC statement is warranted in the light of this new information.

Further advice from COM

3. Additional *in vivo* data on the mutagenicity of 1,3-DCP commissioned by the Food Standards Agency (FSA) were discussed by the COM in May 2003. These comprised a rat bone marrow erythrocytes micronucleus test and a rat liver unscheduled DNA synthesis (UDS) assay. The COM concluded that the additional information recommended as being necessary to provide adequate reassurance that the mutagenic activity seen *in vitro* was not expressed *in vivo* had now been provided. The COM noted the uncertainties with regard to routes of metabolic activation of 1,3-DCP and agreed that the two new mutagenicity studies supported the view that reactive metabolites, if formed, did not produce genotoxicity *in vivo* in the tissues assessed. The COM therefore concluded that 1,3-DCP can be regarded as having no significant genotoxic potential *in vivo*. A copy of the revised COM statement is included at Annex B.

Public health issues

Food issues

4. 1,3-DCP is found as a process contaminant in foodstuffs where acid-hydrolysed vegetable protein has been used as an ingredient such as soy sauce and similar oriental sauces. In 1988, the Scientific Committee on Foods (SCF) considered that chloropropanols and 1,3-DCP in particular should be regarded as a genotoxic carcinogen. In 1993, the FAO/WHO Joint Expert Committee on Food Additives (JECFA) concluded that because of its carcinogenicity,

This is a draft paper for discussion. It should not be quoted, cited or reproduced.

1,3-DCP is an undesirable contaminant in food and that levels should be reduced to as low as technologically achievable. JECFA reviewed 1,3-DCP again in 2001 and concluded that it was not appropriate to estimate a tolerable daily intake (TDI) for 1,3-DCP because of the nature of the toxicity associated with this compound. These SCF and JECFA opinions were in line with previous COM/COC conclusions in the absence of *in vivo* genotoxicity data.

Drinking water

5. There are currently no statutory levels for 1,3-DCP in drinking water. However, the levels in drinking water are restricted indirectly by controlling the maximum dosing rates of polyamine flocculants to no more than 2.5 mg/L of drinking water. This is in line with limits for genotoxic contaminants, such as acrylamide and epichlorohydrin, which may arise in drinking water from the use of polymeric flocculants.

6. A European (CEN) standard for polyamine flocculants for water treatment (BS EN 1409) proposed maximum contaminant levels of 500 ppm for 1,3-DCP. However, these are not health-based values and may need to be reconsidered in the light of COC and the approach taken for other genotoxic carcinogens.

Discussion and advice from the COC

7. In view of the new COM advice that 1,3-DCP can be regarded as having no significant genotoxic potential *in vivo*, the COC is asked to consider whether its previous opinion should be revised. Specifically advice is sought as to whether 1,3-DCP can be regarded as a non-genotoxic carcinogen and a threshold-based risk assessment adopted.

8. The COC previously concluded that the spectrum of tumours observed in rats, particularly in the liver and tongue was evidence of a clear carcinogenic effect of 1,3-DCP. Tumours in the male rat kidney were possibly associated with the high rate of chronic progressive nephropathy, and thyroid follicular cell tumours could be associated with hyperplasia. [Thus it was likely that these tumours were secondary to the sustained cell proliferation in the kidney and thyroid]. Annex C contains paper COC/01/06 which includes the tumour analysis data originally seen by the COC. Significant increases in tumour incidence were observed in rats treated with the high dose of 1,3-DCP (19.31 mg/kg bw/day), but not at the low or mid dose groups (2.09 and 6.25 mg/kg bw/day).

9. The Committee previously noted that assessment of clinical biochemistry and urinalysis data suggested an hepatotoxic effect. The data in Annex C demonstrate that non-neoplastic liver findings were reported at doses below those producing a significant increase in combined hepatocellular adenoma and carcinoma. Members are asked to consider whether the evidence of hepatotoxicity, together with the negative result from the *in vivo* rat liver UDS assay, provide evidence of a non-genotoxic mode of action in the liver. Members are also asked to consider possible modes of action of 1,3-DCP in inducing tumours of the tongue.

**Secretariat
October 2003**

This is a draft paper for discussion. It should not be quoted, cited or reproduced.

CC/03/42 Annex A

Carcinogenicity of 1,3-dichloropropan-2-ol (1,3-DCP) and 2,3-dichloropropan-1-ol (2,3-DCP): COC statement COC/01/S1 – May 2001

This is a draft paper for discussion. It should not be quoted, cited or reproduced.

CC/03/42 Annex B

COM statement on the mutagenicity of 1,3-dichloropropan-2-ol –

October 2003

This is a draft paper for discussion. It should not be quoted, cited or reproduced.

CC/03/42 Annex C

COC paper CC/01/06 - 1,3-DICHLOROPROPAN-2-OL (1,3 DCP)