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1,3-DICHLORO-2-PROPANOL
(addendum)
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1,3-DICHLORO-2-PROPANOL (addendum)

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1. EXPLANATION

1,3-Dichloro-2-propanol is formed when chloride ions react with lipid components in foods under a variety of conditions, including food processing, cooking, and storage. The compound has been found as a contaminant in various foods and food ingredients, most notably in acid-hydrolysed vegetable protein (acid-HVP) and soy sauces.[1] This compound was first evaluated by the Committee at its forty-first meeting (Annex 1, reference *107*), when it concluded that it is an undesirable contaminant in food and expressed the opinion that its concentration in acid-HVP should be reduced as far as technically achievable.

1,3-Dichloro-2-propanol was re-evaluated by the Committee at its fifty-seventh meeting (Annex 1, reference *154*). Although only a few studies of kinetics and metabolism and few short- and long-term studies of toxicity and of reproductive toxicity were available for evaluation, they clearly indicated that 1,3-dichloro-2-propanol was hepatotoxic and nephrotoxic, induced a variety of tumours in various organs in rats, and was genotoxic in vitro. The Committee therefore concluded that it would be inappropriate to estimate a tolerable intake of 1,3-dichloro-2-propanol. The Committee noted that the dose that caused tumours in rats (19 mg/kg bw per day) was about 20 000 times greater than the highest estimated intake of 1,3-dichloro-2-propanol by consumers of soy sauce (1 µg/kg bw per day), and that the available evidence suggested that in soy sauces 1,3-dichloro-2-propanol was associated with high concentrations of 3-chloro-1,2-propanediol, concentrations of the latter being approximately 50 times higher than those of 1,3-dichloro-2-propanol. Therefore, in the opinion of the Committee, regulatory control of the latter would obviate the need for specific controls on 1,3-dichloro-2-propanol.

The present re-evaluation was conducted in response to a request from the Codex Committee on Food Additives and Contaminants (CCFAC) at its Thirty-seventh Session (Codex Alimentarius Commission, 2005) that JECFA review and summarize all new data on the toxicology (including new studies of genotoxicity in vivo) and occurrence of 1,3-dichloro-2-propanol. In particular, the Committee was asked to carry out an exposure assessment to readdress 1,3-dichloro-2-propanol as a separate issue from 3-chloro-1,2-propanediol.

Since the last evaluation of 1,3-dichloro-2-propanol by the Committee (Annex 1, references *154*, *155*) evaluations have been produced by other authorities (Committee on Mutagenicity, 2003; FSANZ, 2003; Committee on Carcinogenicity, 2004; National Toxicology Program, 2005).

[1] The term 'soy sauce' is used to encompass liquid seasonings made from soya beans by a range of methods including acid-hydrolysis and traditional fermentation, possibly with the addition of acid-HVP. In some countries, the term 'soy sauce' is reserved solely for fermented products.

2. BIOLOGICAL DATA

2.1 Biochemical aspects

No new data were available.

2.2 Toxicological studies

2.2.1 Short-term studies of toxicity

No new data were available.

2.2.2 Long-term studies of toxicity and carcinogenicity

No new studies were available.

(a) Dose-response modelling

Cancer dose–response data were analysed by dose–response modelling, in accordance with the International Programme on Chemical Safety (IPCS) document *Principles for modelling dose–response for the risk assessment of chemicals* (IPCS, 2004). Modelling was performed of data for neoplastic changes reported in the study by Research & Consulting Co. (1986). In this long-term study of carcinogenicity, male and female rats were given drinking-water containing 1,3-dichloro-2-propanol for up to 2 years. Treatment-related increases in the incidence of tumours were observed in the kidney of male rats (Table 1) and in the liver, thyroid gland and the tongue of both sexes (Tables 1 and 2).

Incidence data for individual tumour sites and for animals with treatment-related tumours were compiled for both sexes and used for dose–response modelling. For this purpose, only data for the groups exposed for 2 years were used; interim sacrifice groups were not considered.

Modelling

Eight models were fitted to the dose–response data. The benchmark dose was set at a 10% increase in the incidence of tumours above background (BMD_{10}) (background adjustment: extra risk). The lower confidence limit for the benchmark dose ($BMDL_{10}$) was 95%. Datasets for the two sexes were modelled independently. All datasets were found to be suitable for modelling, when models were applied using standard options as provided in the software package, without the necessity to implement additional restrictions and/or modifications of the models.

Table 3 shows the results for all treatment-related tumours in male rats. Reasonable fits, judged on the basis of visual examination of curve fits and on statistical evaluation (p values of suitable models were > 0.2), and consistent values for BMD_{10} and $BMDL_{10}$ were obtained for the eight models.

Akaike's information criterion (AIC) values were similar for all models. The logistic, quantal-quadratic and the probit model gave somewhat worse fits, as can be seen from residual values and chi-squared values. The $BMDL_{10}$s from these

Table 1. Number of male rats bearing tumours after receiving drinking-water containing 1,3-dichloro-2-propanol for 2 years

Tumour site	Concentration (mg/kg)			
	0	2.1	6.3	19
Kidney				
Tubular adenoma	0/50	0/50	3/50	9/50
Tubular carcinoma	0/50	0/50	0/50	1/50
Combined	0/50	0/50	3/50	9/50 [a]
Liver				
Hepatocellular adenoma	1/50	0/50	0/50	0/50
Hepatocellular carcinoma	0/50	0/50	2/50	8/50
Combined	1/50	0/50	2/50	8/50
Thyroid gland				
Follicular adenoma	0/50	0/50	2/50	3/48
Follicular carcinoma	0/50	0/50	2/50	1/48
Combined	0/50	0/50	4/50	4/48
Tongue				
Papilloma	0/50	1/50	0/49	6/50
Carcinoma	0/50	0/50	0/49	6/50
Combined	0/50	1/50	0/49	12/50
All treatment-affected sites: kidney tubular adenoma and carcinoma, hepatocellular adenoma and carcinoma, follicular adenoma and carcinoma of the thyroid, papilloma and carcinoma of the tongue				
Benign tumours	1/50	1/50	5/50	17/50
Malign tumours	0/50	0/50	4/50	14/50
Combined	1/50	1/50	8/50 [b]	29/50 [c]

From Research & Consulting Co. (1986)

[a] Male No. 274 had an adenoma and a carcinoma and was counted only once

[b] Male No. 201 had a benign and a malign tumour and was counted only once

[c] Males Nos 269 and 274 each had a benign and a malign tumour; both animals were counted only once

models were somewhat higher than from other models, but were still in a reasonable range.

BMD_{10}s and $BMDL_{10}$s varied within the range of 5.4 to 7.5 and 3.3 to 6.1 mg/kg bw per day, respectively. This proves the required independency of results from the chosen model. Modelling for malignant tumours only gave similar results (not shown) with BMD_{10} and $BMDL_{10}$ ranges of 8.3 to 10.1 mg/kg bw per day and 5.6 to

Table 2. Number of female rats bearing tumours after receiving drinking-water containing 1,3-dichloro-2-propanol for 2 years

Tumour site	Concentration (mg/kg)			
	0	3.4	9.6	30
Liver				
Hepatocellular adenoma	1/50	1/50	1/50	5/50
Hepatocellular carcinoma	0/50	0/50	1/50	36/50
Combined	1/50	1/50	2/50	41/50
Thyroid gland				
Follicular adenoma	1/50	0/50	3/50	3/49
Follicular carcinoma	0/50	0/50	0/50	2/49
Combined	1/50	0/50	3/50	5/49
Tongue				
Papilloma	0/50	0/50	0/50	7/49
Carcinoma	0/50	1/50	1/50	4/49
Combined	0/50	1/50	1/50	11/49
All treatment-affected sites: hepatocellular adenoma and carcinoma, follicular adenoma and carcinoma of the thyroid, papilloma and carcinoma of the tongue				
Benign tumours	2/50	1/50	4/50	12/50
Malign tumours	0/50	1/50	2/50	37/50
Combined	2/50	2/50	6/50	42/50 [a]

From Research & Consulting Co. (1986)

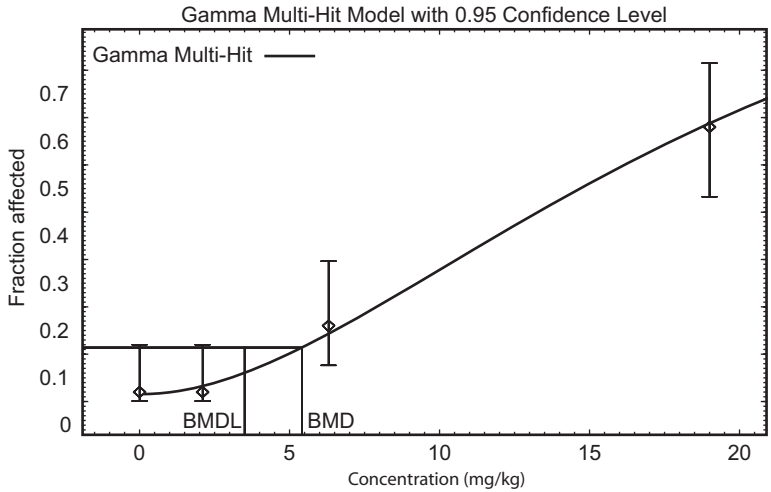
[a] Several animals had both benign and malign tumours and were counted only once.

8.4 mg/kg per day, respectively. Figure 1 shows the dose–response data and the curve fit for the gamma model, as an example.

Modelling results for female rats (animals with treatment-related tumours) are shown in Table 4. As for male rats, several models gave reasonable fits and BMD_{10}s and $BMDL_{10}$s varied only within a narrow range: the ranges obtained were 7.6 to 10.3 mg/kg bw per day for BMD_{10} and 6.6 to 7.7 mg/kg bw per day for $BMDL_{10}$. Figure 2 shows the dose–response data for female animals and the curve fit for the Weibull model as an example.

Table 5 gives a summary of the modelling of data for individual tumour sites. Modelling was performed on incidence data for tumour-bearing animals for benign and malign kidney tumours (males only), hepatocellular tumours (males and females) as well as tumours of the tongue (males and females) (see Table 1 and 2 for incidence data for males and females, respectively). Incidence data for thyroid

Figure 1. Dose–response data (incidence of animals with treatment-related tumours) and adjusted gamma model for male rats



tumours showed no clear dose–response relationship and were unsuitable for modelling.

Table 3. BMD_{10}, $BMDL_{10}$ and statistical parameters obtained from fitting models to dose–response data for male rats with treatment-related tumours after receiving drinking-water containing 1,3-dichloro-2-propanol for 2 years

Model	*p* value	Chi-squared	AIC	BMD_{10} (mg/kg bw per day)	$BMDL_{10}$ (mg/kg bw per day)
Gamma	0.507	0.44	138.1	5.4	3.5
Logistic	0.248	2.79	138.5	7.5	6.1
Logistic (log dose)	0.534	0.39	138.0	5.4	3.5
Probit	0.366	2.01	137.7	6.8	5.6
Probit (log dose)	0.731	0.12	137.7	5.4	3.6
Quantal-quadratic	0.493	1.42	136.9	6.5	5.6
Weibull	0.620	0.43	138.3	5.4	3.4
Multistage (2nd degree polynomial, betas ≥ 0)	0.343	0.90	138.6	5.7	3.3

AIC: Akaike's information criterion; BMD_{10}: benchmark dose for 10% extra risk of tumours; $BMDL_{10}$: 95% lower confidence limit for the benchmark dose. Extra risk is defined as the additional incidence divided by the tumour-free fraction of the population in the controls. Multistage stands for a specific mathematical model applied.

Table 4. BMD_{10}, $BMDL_{10}$ and statistical parameters obtained from fitting models to dose–response data for female rats with treatment-related tumours after receiving drinking-water containing 1,3-dichloro-2-propanol for 2 years

Model	*p* value	Chi-squared	AIC	BMD_{10} (mg/kg bw per day	$BMDL_{10}$ (mg/kg bw per day)
Gamma	0.967	0.00	120.2	10.2	7.2
Logistic	0.810	0.42	118.6	9.4	7.5
Logistic (log dose)	0.953	0.00	120.3	10.1	7.4
Probit	0.588	1.06	119.2	8.5	6.9
Probit (log dose)	0.996	0.00	120.2	10.1	7.7
Quantal-quadratic	0.41	1.77	120.1	7.6	6.7
Weibull	0.888	0.02	120.3	10.3	7.0
Multistage (3rd degree polynomial, betas ≥ 0)	0.854	0.03	120.3	10.3	6.6

AIC: Akaike's information criterion; BMD_{10}: benchmark dose for 10% extra risk of tumours. $BMDL_{10}$: 95% lower confidence limit for the benchmark dose. Extra risk is defined as the additional incidence divided by the tumour-free fraction of the population in the controls.

Figure 2. Dose–response data (incidence of animals with treatment-related tumours) and adjusted Weibull model for female rats

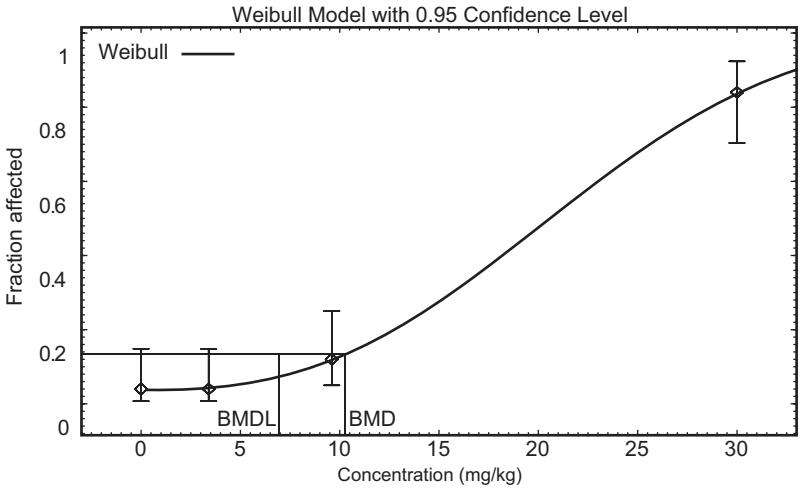


Table 5. Result of dose–response modelling (BMD_{10}, $BMDL_{10}$) for various treatment-affected tumour sites for male and female rats receiving drinking-water containing 1,3-dichloro-2-propanol for 2 years

Tumour site and type	Models with acceptable fits	Range of BMD_{10}s (mg/kg bw per day)	Range of $BMDL_{10}$s (mg/kg bw per day)
Males			
Renal adenoma and carcinoma	Gamma, log logistic, log probit, Weibull, multistage	11.1–12.2	7.2–7.7
Hepatocellular adenoma and carcinoma	Logistic, probit, log probit, quantal-quadr., multistage	14.4–16.0	10.3–12.3
Tongue papilloma and carcinoma	Gamma, logistic, log logistic, probit, log probit, quantal-quadratic, Weibull, multistage	12.4–17.9	8.7–11.6
Females			
Hepatocellular adenoma and carcinoma	Gamma, logistic, log logistic, probit, log probit, Weibull, multistage	11.2–14.6	9.1–10.1
Tongue papilloma and carcinoma	Gamma, logistic, log logistic, probit, log probit, quantal-quadratic, Weibull, multistage	17.1–22.8	11.5–19.1

BMD_{10}: benchmark dose for 10% extra risk of tumours. $BMDL_{10}$: 95% lower confidence limit for the benchmark dose. Extra risk is defined as the additional incidence divided by the tumour-free fraction of the population in the controls.

Software

Modelling was carried out using the US EPA BMDS (benchmark dose software), version 1.3.2.[2]

2.2.3 Genotoxicity

In a test for micronucleus formation in bone marrow of rats in vivo, which was conducted according to OECD guideline No. 474, groups of six male Han Wistar rats were given 1,3-dichloro-2-propanol orally at a dose of 0, 25, 50, or 100 mg/kg

[2] The BMDS is freely available at <http://cfpub.epa.gov/ncea/>.

bw per day for two consecutive days. The high dose produced piloerection, weight loss and lethargy. Bone marrow was harvested 24 h after the final dose. The ratios of polychromatic to normochromatic erythrocytes (PCE/NCE) varied amongst individual animals of the control group, but the mean value was within the range of data from historical control groups. Rats treated with 1,3-dichloro-2-propanol at any dose had group mean PCE/NCE ratios that were comparable to those of the control group and that were within the normal range. Thus toxicity to the bone marrow was not demonstrated. There was no statistically significant increase in the frequency of micronucleus formation with 1,3-dichloro-2-propanol at any dose, while the positive-control agent, cyclophosphamide, was clearly active (Howe, 2002).

In a study of unscheduled DNA synthesis in rat hepatocytes in vivo, which was conducted according to OECD guideline No. 486, groups of three Han Wistar male rats were given a single oral dose of 1,3-dichloro-2-propanol at 0, 40, or 100 mg/kg bw. In the 2–4 h experiment, piloerection and lethargy were observed. Hepatocytes were isolated at 2–4 h and 12–24 h after dosing and cultured in the presence of [^{3}H]thymidine; the incorporation of [^{3}H]thymidine during unscheduled DNA synthesis was measured autoradiographically. No information on liver toxicity was provided. 1,3-Dichloro-2-propanol did not elicit unscheduled DNA synthesis, while the positive-control compounds, 2-acetylaminofluorene and dimethylnitrosamine, were clearly active (Beevers, 2003).

2.2.4 Reproductive toxicity

No new data were available.

2.3 Observation in humans

No new data were available.

3. ANALYTICAL METHODS

3.1 Chemistry

Chloropropanols are chemicals formed when glycerol reacts with chlorine under acidic conditions. 1,3-Dichloro-2-propanol (CAS Registry No. 96-23-1) boils at 175 °C at normal pressure and its solubility in water at 20 °C is 15.2 g per 100 g.

3.2 Description of analytical methods

1,3-Dichloro-2-propanol can be measured by using gas chromatographic separation and mass spectrometric detection (GC/MS) with an automated headspace procedure (HS GC/MS). The in-house validation methods developed by the Central Science Laboratory (CSL) of the United Kingdom Government Department for Environment Food and Rural Affairs (Crews et al., 2002) and also by the Center for Food Safety and Applied Nutrition (CFSAN) of the United States Food and Drug Administration (FDA) are available and published. The results from the two-method comparison showed that, in spite of a limit of detection (LOD) that was higher for the United Kingdom (UK) method than the FDA method (3.000 versus

0.055 ng/g), the recoveries for the spike-test portions, as well as the amounts of 1,3-dichloro-2-propanol found in the retail products, were comparable for 1,3-dichloro-2-propanol at concentrations of of ≥ 10 ng/g in soy and related sauces.

The CSL method has the advantage of being faster and simpler than the FDA modified method, which is more labour-intensive, but the FDA method has the advantage that it allows extraction and analysis of 1,3-dichloro-2-propanol and 3-chloro-1,2-propanediol in the same GC/MS run.

In a paper published in 2006, the Chinese authors also proposed a methodology that allows the simultaneous separation and determination of chloropropanols (1,3-dichloro-2-propanol, 2,3-dichloro-2-propanol, 3-monochloro-propane-1,2-diol and 2-monochloro-1,3-propanediol) in soy sauce and other flavouring, using GC/MS in negative chemical and electron-impact ionization modes, at low concentrations of around 0.6 µg/kg (Xiamin Xu et al., 2006).

4. LEVELS AND PATTERNS OF CONTAMINATION OF FOOD COMMODITIES

4.1.1 Surveillance data

Chloropropanols are a group of chemical contaminants formed under certain processing and storage conditions; 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol are primary members of this group. 1,3-Dichloro-2-propanol is formed during the production of acid-HVPs such as soya beans from the reaction of hydrochloric acid and residual vegetable fat from the raw materials used. As a result of the use of acid-HVP, 1,3-dichloro-2-propanol has now been found as a contaminant in various foods and food ingredients, most notably in acid-HVPs and soy sauces[3] (Codex Commission on Food Additives and Contaminants, 2006).

4.1.2 *National occurrence of 1,3-dichloro-2-propanol*

Data on the occurrence of 1,3-dichloro-2-propanol were submitted by member states of the European Union (European Union, 2004), Australia (FSANZ, 2003), Hong Kong Special Administrative Region of China (SAR) (FEHD, 2005), and Japan (MAFF, 2005 and 2006). Data on soy sauces and related products were also available for the United States of America (USA) from the literature (Nyman et al., 2003b).

Table 6 describes the summary of the distribution-weighted concentration of 1,3-dichloro-2-propanol in soy sauce and soy-sauce based products, in other foods products and in food ingredients from those countries, from 2001 to 2006.

[3] The term 'soy sauce' is used to encompass liquid seasonings made from soya beans by a range of methods including acid hydrolysis and traditional fermentation, possibly with the addition of acid-HVP. In some countries the term 'soy sauce' is reserved solely for fermented products.

4.1.3 Soy sauce and soy sauce-based products

(a) Australia

Australia submitted occurrence data for 39 individual samples of different soy and oyster sauces, based on food surveys conducted in 2001 and 2002 (FSANZ, 2003). Sampling was undertaken of selected soy and oyster sauces and a range of other foods available at Australian retail outlets. The method used for quantitative analysis of 1,3-dichloro-2-propanol was based on the Association of Official Analytical Chemists (AOAC) Method No. 2000.01. The limit of quantification (LOQ) was 0.01 mg/kg. The majority of soy and oyster sauces did not contain detectable levels of 1,3-dichloro-2-propanol. 1,3-Dichloro-2-propanol was detected only at less than 1 mg/kg in those sauces that also contained 3-chloro-1,2-propanediol, that is, mainly soy seasoning sauce.

- The highest contamination level was reported for the seasoning soy sauce product, with a maximum of about 0.6 mg/kg.
- The average was calculated by assigning a value of half the reporting limits to the 26% of samples for which the reported value was less than the limit.
- The average concentration of 1,3-dichloro-2-propanol in the soy sauce and soy sauce based products was reported to be 0.07 mg/kg.

(b) Hong Kong SAR

Hong Kong SAR submitted the results of occurrence data in aggregate samples of different soy sauce and sauce-based products using the Global Environment Monitoring System—Food Contamination Monitoring and Assessment Programme (GEMS/Food) reporting format. Sampling was performed in 2003 and included the results of the analysis of 84 samples. Based on the very low limits of detection and quantification, 0.5 and 1.5 µg/kg respectively for 1,3-dichloro-2-propanol, analyses were performed using GC/MS. No indicator of analytical quality assurance was described in the submission data (FEHD, 2005).

- The average was calculated by assigning a value of half the reporting limits to the 84% of samples for which the reported value was less than the limit.
- The average concentration of 1,3-dichloro-2-propanol reported to be present in soy sauce and sauce-based products was less than 1.0 µg/kg.
- Of the 84 samples, two samples were reported to have tested positive for 1,3-dichloro-2-propanol: these were concentrated soup (2.7 µg/kg) and soy-sauce product (2.4 µg/kg).

(c) European Union

Individual occurrence data for 1,3-dichloro-2-propanol were available from four member states of the European Union (Austria, Finland, Germany and the UK) from the reports on tasks for Scientific Cooperation on levels of 3-chloro-1,2-propanediol and related substances in foodstuffs (European Union, 2004). The Joint Research Centre of the European Commission assisted in the task by providing advice on analytical methodology. Participants agreed that only occurrence data

obtained after 1997 until the year before the publication report in 2004 should be submitted as there was concern about the robustness of data acquired before that date. Some occurrence data provided by participants were from targeted sampling of products suspected of containing high levels of chloropropanols.

Of the 2035 soy sauce and related samples available, 282 were analysed for 1,3-dichloro-2-propanol. These were of the following origins: Austria (n = 10), Finland (n = 35), Germany (n = 114), and UK (n = 123). The limit of quantification for soy sauce and soy-sauce based products was between 0.005 mg/kg and 0.15 mg/kg.

- The average was calculated by assigning a value of half the reporting limits to the 80% of samples for which the reported value was less than the limit.
- The weighted average concentration of 1,3-dichloro-2-propanol in soy sauce and sauce-based products was reported to be 0.092 mg/kg. For the different types of soy sauce, the average concentrations of 1,3-dichloro-2-propanol were reported as follows: mushroom soy sauce, 0.43 mg/kg; soy sauce and seasoning sauce, 0.08 mg/kg; dark soy sauce, 0.036 mg/kg; and light soy sauce, 0.027 mg/kg. Other average concentrations of 1,3-dichloro-2-propanol reported for sauce-based products were less than 0.01 mg/kg.

(d) Japan

Using the GEMS/Food reporting format, Japan submitted the results of occurrence data on levels of 1,3-dichloro-2-propanol in aggregate and individual samples of soy sauce containing acid-HVP. Sampling was performed in 2005–2006 and included results of the analysis of 40 samples of soy sauce made with acid-HVPs. The method used for analysis of 1,3-dichloro-2-propanol was validated in-house using GC/MS, and was published in a paper cited in MAFF (2005 and 2006). [4]The LOD and LOQ were 0.002 mg/kg and 0.004 mg/kg, respectively.

- The results of 83% of analyses of samples of soy sauces made with acid-HVP indicated that concentrations of 1,3-dichloro-2-propanol were below the LOQ. Samples containing quantified levels of 1,3-dichloro-2-propanol also contained 3-chloro-1,2-propanediol (at or above 3.4 mg/kg). The highest level reported was 0.022 mg/kg and the average was 0.005 mg/kg.

(e) USA

Results of occurrence data for individual samples of 39 different soy sauce and sauce-based products purchased from retail outlets in metropolitan areas in 2002 were published by the FDA (Nyman et al., 2003a). The method used for quantitative analysis of 1,3-dichloro-2-propanol was based on a modified version of AOAC Method No. 2000.01. Based on this modified method, validated in-house, an LOQ of 0.025 mg/kg was established for 1,3-dichloro-2-propanol. The authors concluded that all samples that contained 1,3-dichloro-2-propanol at a concentration of greater than 0.05 mg/kg were from products manufactured in Asia, indicating that at the time of their study some Asian manufacturers had not made

[4] *Journal of Food Hygienic Society of Japan* 1995, 36(3):360–364.

the necessary processing changes to control the formation of chloropropanols in acid-HVP.

1,3-dichloro-2-propanol was detected in 36% of those sauces that also contained 3-chloro-1,2-propanediol, mainly in samples of soy sauce. The highest concentration reported was 9.84 mg/kg, for a soy sauce.

- The average was calculated by assigning a value of half the reporting limits to the 64% of samples for which the reported value was less than the limit.
- The average concentration of 1,3-dichloro-2-propanol was reported to be 0.62 mg/kg.

4.1.4 Food ingredients

(a) European Union

Results of the analysis of 1,3-dichloro-2-propanol in over 24 samples of food ingredients were available from the reports on Tasks for Scientific Cooperation on levels of 3-chloro-1,2-propanediol and related substances in foodstuffs, but it was not possible to precisely identify from which member states the data were derived (European Union, 2004). 1,3-Dichloro-2-propanol was investigated in malt products only. Of these samples, 13% were found to contain 1,3-dichloro-2-propanol at a concentration that was greater than the LOQ, set at 0.010 mg/kg. The weighted average concentration of 1,3-dichloro-2-propanol for this food category was reported to be 0.009 mg/kg in quantified samples.

(b) Japan

Using the GEMS/Food reporting format, Japan submitted to the JECFA secretariat the results of occurrence data on the levels of 1,3-dichloro-2-propanol in acid-HVPs from aggregate and individual samples. Sampling was performed in 2005–2006 and included results of the analysis of 40 samples of acid-HVPs. The method used for analysis was validated in-house using GC/MS. The analytical method has been published in a paper cited in MAFF (2005 and 2006).[4]The LOD and LOQ were 0.002 mg/kg and 0.004 mg/kg, respectively.

- Results of the analysis of 1,3-dichloro-2-propanol in more than 30 out of 40 samples of acid-HVPs from other production processes showed that concentrations of 1,3-dichloro-2-propanol were below the LOQ. The average concentration was reported to be 0.008 mg/kg in acid-HVPs.

4.1.5 Other food products

Only Australia and the European Union submitted occurrence data for foods and food groups likely to contain 1,3-dichloro-2-propanol as a result of processing or storage conditions. Analysis of several products included in the diet, e.g. cereals, meat and meat products, dairy products, fish and seafood products, was reported.

(a) Australia

Australia submitted occurrence data for 204 individual samples of other foods based on food surveys conducted in 2001 and 2002 (FSANZ, 2003). Sampling was performed in selected other foods and a range of other foods available at Australian retail outlets. The method used for quantitative analysis of 1,3-dichloro-2-propanol was similar that used to analyse this compound in soy and oyster sauces and was based on AOAC Method No. 2000.01. The LOD and LOQ were 0.003 mg/kg and 0.005 mg/kg, respectively. Analyses were performed for the following food categories: meat and meat products (99 samples), fish and fish products (29 samples), chicken eggs (8 samples), cereals (37 samples), infant food (3 samples), infant formulas (3 samples), cheese, cheddar and processed (12 samples), starchy vegetables (3 samples), roasted coffee and cocoa paste (6 samples), vegetable oils and fat (4 samples). Of these samples, 25% were reported to contain 1,3-dichloro-2-propanol at concentrations greater than the LOQ.

- *Fish and fish products.* 1,3-Dichloro-2-propanol was quantified in three samples: two samples of fish fillets, battered and fried, 0.024 mg/kg; and in one sample of battered fish fillet, fried, at a concentration that was slightly greater than the LOQ of 0.006 mg/kg. The weighted average concentration of 1,3-dichloro-2-propanol for this food category was reported to be 0.0025 mg/kg.
- *Meat and meat products, including poultry and game.* 1,3-Dichloro-2-propanol was quantified in 48 out of 99 samples: 25 out of 44 samples of beef, minced products, fried, raw or cooked, from 0.011 to 0.11 mg/kg; in 22 out of 43 samples of sausages, meat products, fried, raw or cooked and leg ham, from 0.015 to 0.069 (sausages, meat products, fried, raw or cooked) and from 0.014 to 0.021 (leg ham) mg/kg, respectively**;** and in one sample of chops, lamb raw product, 0.091 mg/kg. The weighted average concentration of 1,3-dichloro-2-propanol for this food category was reported to be 0.019 mg/kg.

(b) European Union

Results of the analysis of more than 42 samples of products other than soy sauce and soy sauce-based products were available from the European Union report (European Union, 2004). 1,3-Dichloro-2-propanol was investigated in the following food categories: cereals and cereal products, excluding bakery (two samples), meat and meat products (16 samples), fish and fish products (14 samples) and in salts, spices, soups, sauces, salads and protein (10 samples). Only 2 out of 42 samples were found to contain 1,3-dichloro-2-propanol at a concentration greater than the LOQ, set at 0.010 mg/kg; these were two samples of edible sausage casing found to contain 1,3-dichloro-2-propanol at 0.5 and 1.5 mg/kg.

4.1.6 Co-occurrence of 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol

Few studies have analysed 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol in the same food samples. The USA reported a study in 55 samples in 2003. Hong Kong SAR reported 84 samples in 2003, the UK reported 51 samples in 2000/2002, European Union member states reported 232 samples

in 2004, Australia reported 39 samples in 2000 to 2002 and Japan reported 80 samples in 2005–2006.

Analysis of the study of co-occurrence described below includes cases where quantifiable amounts of both 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol were measured in the same sample of soy sauce and soy sauce-based products and in food ingredients such as acid-HVPs. Figure 3 shows a plot of the percentage of 1,3-dichloro-2-propanol/3-chloro-1,2-propanediol contained in samples of different types of soy sauce (53 samples of soy sauce, 11 samples of seasoning soy sauce, 3 samples of oyster sauce, 11 samples of other sauces and 19 samples of mushroom sauce) and 10 samples of acid-HVPs found to contain both substances at quantifiable concentrations greater than 0.4 mg/kg of 3-chloro-1,2-propanediol.

Based on a limited number of data, some trends were apparent:

- Food ingredients such as acid-HVPs contain less 1,3-dichloro-2-propanol/3-chloro-1,2-propanediol than do mushroom soy sauce or seasoning soy sauce—0.1% versus 1.3–1.4%, respectively.
- Other soy sauces and oyster soy sauce contain more 1,3-dichloro-2-propanol/3-chloro-1,2-propanediol the highest percentage compared to than do other types of soy sauce, at 2.4% and 8.3% respectively.

(a) Soy sauce and soy sauce-based products

Co-occurrence of 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol in the same food samples was reported in 102 samples of soy sauce and soy sauce-based products, including 14 samples from the USA, 2 samples from Hong Kong SAR, 7 samples from Japan, 12 from the UK, 58 from the European Union and 9 from Australia.

1,3-Dichloro-2-propanol was detected only in those soy sauces that contained 3-chloro-1,2-propanediol, which suggests that, in this product, 1,3-dichloro-2-propanol is derived from 3-chloro-1,2-propanediol. Co-occurrence was found when samples contained 3-chloro-1,2-propanediol at a concentration greater than 0.4 mg/kg (82% of samples). When 3-chloro-1,2-propanediol is present at a concentration of less than 0.4 mg/kg, 1,3-dichloro-2-propanol is generally rarely detected, but this is reliant on the performance of the analytical method (LOD and LOQ) for analysis of 1,3-dichloro-2-propanol.

The statistical analysis of co-occurrence and the relationship between the two substances includes the analysis of 102 results for which quantifiable amounts of 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol were measured in the same sample. As shown by the regression linear depicted in Figure 4, the relationship between 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol is highly significant with a very good Pearson correlation (r = 0.9209). The formula given below describes the linear relationship for predicting the concentration of 1,3-dichloro-2-propanol from a quantified level of 3-chloro-1,2-propanediol of greater than 0.4 mg/kg in soy sauce and sauce-based products:

[1,3-dichloro-2-propanol]= 0.00949866 [3-chloro-1,2-propanediol]

Table 6. Summary of the distribution-weighted concentration of 1,3-dichloro-2-propanol in soy sauce and soy sauce-based products, in other foods and in food ingredients from various countries, 2001 to 2006

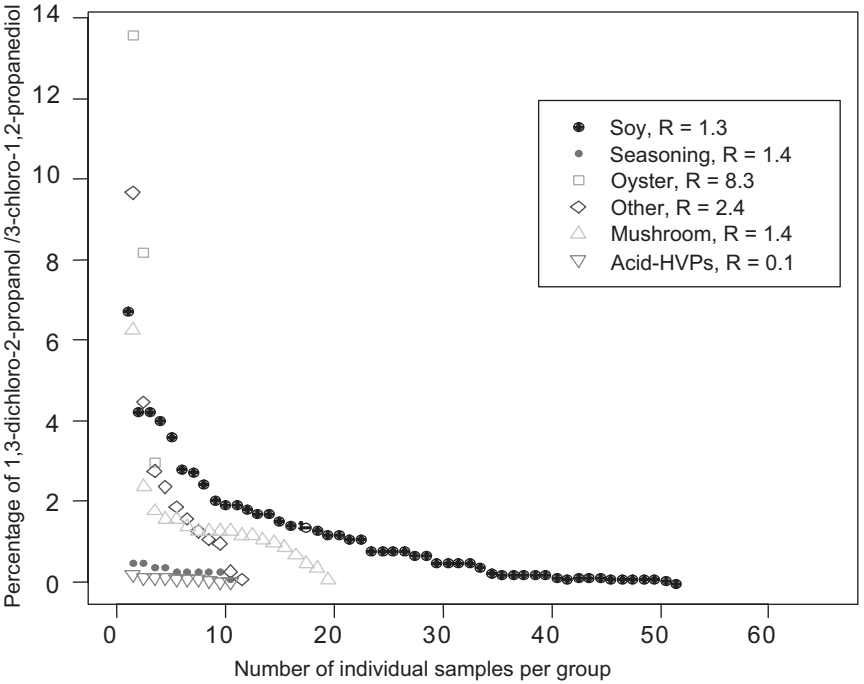
Products		Country and date	LOQ (mg/kg)	No. of samples	No. of samples with concentration < LOQ	Mean[a] (mg/kg)	CV[b] (%)	Maximum (mg/kg)
Soy sauce and soy sauce-based products		Europe (EC Scoop Task 3.2.9), 2004	0.005-0.15	282	222	0.092	286	1.37
		Hong Kong SAR, 2003	0.0015	84	82	0.001	NA	0.003
		USA, 2000-2002	0.025	39	17	0.621	309	9.84
		Australia, 2001-2002	0.010	39	17	0.070	216	0.60
		Japan, 2005-2006	0.004	40	33	0.005	64	0.02
		All		484	371	0.110	332	9.84
Meat and meat products		Australia, 2001-2002	0.005	99	51	0.019	125	0.11
Fish and sea food		Australia, 2001-2002	0.005	29	26	0.0025	111	0.024
Food ingredients:	Acid HVPs	Japan, 2005-2006	0.002	40	30	0.008	148	0.070
	Malt extract	Europe (EC Scoop task 3.2.9), 2004	0.010	24	21	0.008	104	0.025
		All		56	13	0.008	134	0.070

CV: coefficient of variation; acid-HVP: acid-hydrolysed vegetable protein; LOQ: limit of quantification; NA: not available; SAR: Special Administrative Region of China.

[a] Concentrations of less than the LOD or LOQ were assumed to be half of those limits and the mean was weighted according to the number of samples from countries.

[b] Coefficient of variation (standard deviation divided by mean, %)

Figure 3. Percentage of 1,3-dichloro-2-propanol/3-chloro-1,2-propanediol in different soy sauce and soy sauce-based products and acid-HVP



Acid HVP: acid-hydrolysed vegetable protein.

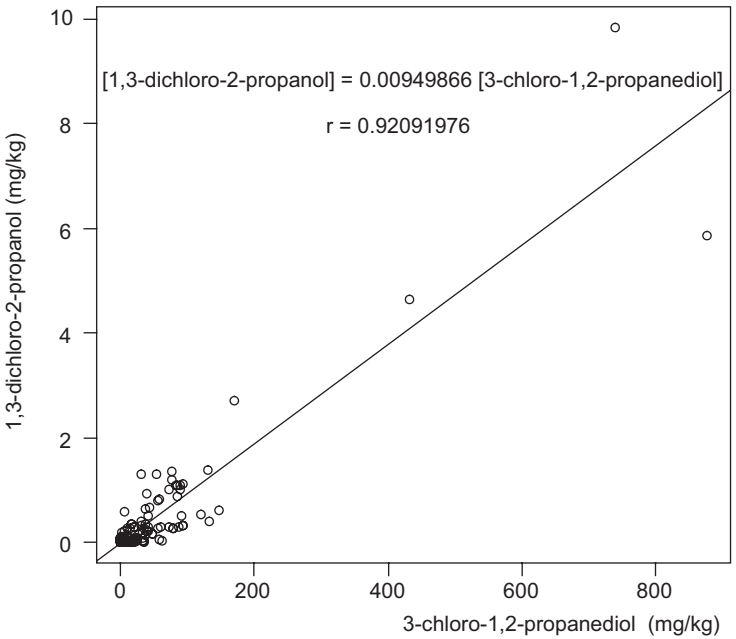
Although to be validated this model needs to be tested with other data sets, it represents at this time the best first approach to considering the relationship between the levels of 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol in the same kinds of product: soy sauce and related sauce-based products.

Moreover, it could be deduced from data on samples containing 3-chloro-1,2-propanediol at concentrations between greater than 0.4 mg/kg and 1000 mg/kg that such samples would contain 1,3-dichloro-2-propanol at a concentration of about 1%. The data also seem to show that samples containing 3-chloro-1,2-propanediol at between less than 0.4 mg/kg and the LOQ would contain a higher proportion of 1,3-dichloro-2-propanol, at around 34% on average (only four samples, not shown in Figure 2), but this is could also be caused by an analytical artefact whereby the measurement of quantifiable levels of a substance at concentrations close to the LOD and LOQ is subject to some uncertainty.

(b) Food ingredients

The co-occurrence of 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol in the same food samples was reported in 10 samples of acid-HVP products provided by Japan. In spite of the few data available, the analyses showed a very

Figure 4. Co-occurrence of 1,3-dichloro-2-propanol and 3-chloro-1,2-propanediol at quantifiable concentrations in soy sauce and soy sauce-based products



good Pearson correlation ($r = 0.8736$). As shown by the linear regression obtained from these data, the relationship between 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol is highly statistically significant and a model of linearity could be proposed. The formula given below describes a linear relationship to predict the concentration of 1,3-dichloro-2-propanol from a quantified level of 3-chloro-1,2-propanediol in acid-HVPs as food ingredients:

[1,3-dichloro-2-propanol] = 0.0017738 [3-chloro-1,2-propanediol]

(c) Other food products

Only data from the European Union report and Australia give information on the co-occurrence of 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol in other foods. The levels of 1,3-dichloro-2-propanol in various foods were highly variable and, in main foods, 1,3-dichloro-2-propanol was detected in the absence of detected levels of 3-chloro-1,2-propanediol. 1,3-Dichloro-2-propanol is mainly found at quantifiable level in samples of meat and meat products (50 out of 115 samples) at concentrations that ranged from 0.006 to 0.11 mg/kg. In these products, the concentration of 1,3-dichloro-2-propanol was generally found to be higher than that of 3-chloro-1,2-propanediol. Two samples of fish fillet from the Australia market were found to contain 1,3-dichloro-2-propanol at a concentration of 0.006 and 0.024 mg/kg. 3-Chloro-1,2-propanediol was quantified in 33% of these 50 samples.

Co-occurrence was reported in 16 samples of thick meat sausage (dry-fried), sausage meat (raw or cooked), leg ham and beef (minced cooked), with the average concentration of 1,3-dichloro-2-propanol being 0.034 mg/kg and of 3-chloro-1,2-propanediol being 0.014 mg/kg.

Summary of national occurrence data and co-occurrence of 3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol

Data on 1,3-dichloro-2-propanol analysed in food were obtained from several countries. 1,3-Dichloro-2-propanol was only found at quantified levels in samples of soy sauce, of ingredients such as acid-HVPs and malt products, of minced beef (dry-fried, raw or cooked), pork ham, sausage meat (raw or cooked) and in samples of fish fillet (battered and fried). Average levels in samples of soy sauce-based products ranged from 0.09 mg/kg for soy oyster sauce to 0.6 mg/kg for soy mushroom sauce. Average levels were 0.024 mg/kg in samples of fish product, 0.034 mg/kg in samples of meat products and 0.022 mg/kg in samples of malt products.

1,3-Dichloro-2-propanol was detected only in samples that also contained 3-chloro-1,2-propanediol, except in samples of meat and meat products where 1,3-dichloro-2-propanol was detected in the presence (18 samples) and in the absence (32 samples) of detected levels of 3-chloro-1,2-propanediol. In meat products, the concentrations of 1,3-dichloro-2-propanol were generally higher than those of 3-chloro-1,2-propanediol.

The Committee noted that 1,3-dichloro-2-propanol is found in samples of soy sauce and soy sauce-based products when the concentrations of 3-chloro-1,2-propanediol exceed 0.4 mg/kg. Based on limited data, there appears to be a linear relationship between the concentrations of 1,3-dichloro-2-propanol and 3-chloro-1,2-propanediol, but there was considerable scatter in the data at low concentrations and there was some variation between different types of products. Additional occurrence data would be needed to confirm these relationships, before they could be used to predict the concentrations of 1,3-dichloro-2-propanol based on the concentrations of 3-chloro-1,2-propanediol.

5. ESTIMATED DIETARY INTAKE

5.1 National assessments of intake from diet

Dietary intakes of 1,3-dichloro-2-propanol have been reported for 10 countries (Australia, Denmark, Finland, France, Germany, Ireland, the Netherlands, Sweden, Thailand and the UK). No dietary intakes were available for Latin America and Africa. Mainly, countries have calculated national intake using deterministic modelling by crossing national individual consumption data with national mean occurrence data obtained from surveys conducted in their country.

Consistent with their national food consumption data, all countries except Germany calculated estimates for the adult population and children. Mean occurrence data used in the calculation are those reported in the preceding section

on country occurrence data, where all values classified as being less than the LOQ were assumed to have 1,3-dichloro-2-propanol at a concentration of half the LOQ, except for Thailand where no information was available concerning the treatment of data below the quantification limit. Intake estimates were calculated on a per-kilogram of body weight basis. Estimates reported by each country are described according to the two following variables of intake distribution (mean and high-percentile dietary exposures):

- Average estimates: combination of the average food consumption and mean occurrence data for food consumed
- P95: 95th percentile of the intake distribution

Table 7 summarizes national estimated dietary intakes of 1,3-dichloro-2-propanol from various food sources, including soy sauce and soy sauce-based products.

Table 8 summarizes national estimated consumption of soy sauce and soy sauce-based products by consumers only from various countries, and the corresponding estimated dietary intakes of 1,3-dichloro-2-propanol.

(a) Australia

Australia submitted the results of dietary exposure assessment for chloropropanols (FSANZ, 2003). Intake calculations were obtained in a deterministic way using a dietary modelling computer program (Dietary Modelling of Nutritional Data, DIAMOND) crossing mean concentration of 1,3-dichloro-2-propanol in a wide range of foods, including soy sauce and soy sauce-based products consumed by each individual reported in the 1995 National Nutrition Survey based on 24 h-recall methodology. To provide a more refined estimate of dietary exposure, values for concentrations that were below the limit of reporting (LOR = 78%) were assigned a concentration equal to the LOR.

Dietary exposure was conducted using food groupings based on the Codex GSFA classification system for food additives. Foods are classified according to major food types, as raw and processed foods, to which reported analytical concentrations are assigned. Calculations are made in assigning concentrations of 1,3-dichloro-2-propanol to food groups for food eaten “as is”, as well as for food used as ingredients in mixed foods. Where a single food from a food group was analysed, the concentration of 1,3-dichloro-2-propanol was assigned to the whole group, assuming that like foods would contain 1,3-dichloro-2-propanol at a similar concentration. This is likely to result in an overestimation of dietary, but assumes a worst-case scenario.

Table 7 shows that the intake estimates for whole population aged more than 2 years ranged from 0.041 µg/kg bw per day on average to 0.105 µg/kg bw per day for consumers at the 95th percentile. Children aged between 2 and 12 years had exposures that ranged from 0.051 µg/kg bw per day on average to 0.136 µg/kg bw per day for consumers at the 95th percentile. Children aged between 13 and 19 years had exposures that ranged from 0.035 µg/kg bw per day on average to 0.094 µg/kg bw per day for consumers at the 95th percentile. Adults aged 20 years

and older had exposures that ranged from 0.039 µg/kg bw per day on average to 0.101 µg/kg bw per day for consumers at the 95th percentile.

Major contributors to estimated dietary exposures to 1,3-dichloro-2-propanol for all groups were minced meat (45%), sausages (25%), bread (10%) soy and oyster sauce (7%), and ham and bacon (6%).

(b) European Union

No national estimates of dietary intake of 1,3-dichloro-2-propanol were available from the European Commission report (European Union, 2004).

As a first approach to estimating exposure to 1,3-dichloro-2-propanol among the European Member States involved in the Scientific Cooperation on levels of 3-chloro-1,2-propanediol and related substances in foodstuffs (European Union, 2004), an assessment of estimated intake was made by the Committee at its present meeting. This assessment was based on data on occurrence and food consumption available for food sources found to contain 1,3-dichloro-2-propanol, which were published in the European Commission report and the Australian report.

This assessment took into account the weighted average concentration of 1,3-dichloro-2-propanol reported in Table 6 for the following food sources: soy sauce products (0.092 mg/kg), meat and meat products (0.019 mg/kg, corresponding to the weighted mean from Australia) and fish products (0.0025 mg/kg, corresponding to the weighted mean from Australia). Average food consumption and consumption at the 95th percentile for these products reported by member states in the EC report was used. Estimated dietary intakes were assessed for eight members of the European community (Denmark, Finland, France, Germany, Ireland, the Netherlands, Sweden and UK) according a mean body weight of 65 kg for adults, 30 kg for children and 15 kg for young children. Owing to differences in the consumption data reported by countries (whole-population, consumers only) and the mode of calculation of intake, estimates of dietary exposure to 1,3-dichloro-2-propanol made by the Committee at its present meeting are likely to be overestimated, as high-percentile (95th) intakes of different products have been summed and it is improbable that a consumer will have a high consumption of all products. Table 6 summarizes estimated intakes for mean and high-percentile consumption from various food sources.

- Estmates of average intake from all sources ranged from 0.008 to 0.048 µg/kg bw per day for the adult population and from 0.011 to 0.035 µg/kg bw per day for children. For consumers at a high percentile (95th), including young children, estimated intakes ranged from 0.025 to 0.133 µg/kg bw per day.
- Estimated intakes from meat and meat products ranged from 0.007 µg/kg bw per day on average to 0.069 µg/kg bw per day for adults at the 95th percentile of consumption. Children have exposures that ranged from 0.009 µg/kg bw per day on average to 0.075 µg/kg bw per day at the 95th percentile of consumption.
- Estimated intakes from soy sauce and related products ranged from 0.001 µg/kg bw per day on average to 0.023 µg/kg bw per day at the 95th percentile for adults. Exposures for children ranged from 0.002 µg/kg bw per day on average to 0.055 µg/kg bw per day at the 95th percentile (Table 8).

Meat and meat products made the greatest contribution to total exposure to 1,3-dichloro-2-propanol in all groups and countries when compared with soy sauce and soy sauce-based products, from 72% to 99% versus <1% to 28%, respectively.

Consumption of soy sauce and soy sauce-based products by consumers only from various countries and estimated dietary exposure to 1,3-dichloro-2-propanol

Table 8 summarizes consumption and estimated dietary intakes of 1,3-dichloro-2-propanol from soy sauce and soy sauce-based products in consumers only from various countries. The percentage of consumers of soy sauce and soy sauce-based products was reported to range from 1.4% to 8% in the adult population and from 1% to 8.7% in children. Consumption ranged from 1 to 30 g/day, for various countries, in adults and from 0.6 to 16 g/day in children. An estimate of dietary intakes of 1,3-dichloro-2-propanol was obtained using consumption of soy sauce by consumers only in each country and a fixed weighted concentration of 1,3-dichloro-2-propanol in soy sauce as described in reports by countries (Australia, 0.069 mg/kg; and European countries, 0.092 mg/kg). A standard average body weight of 65 kg for adults, 30 kg for children and 15 kg for young children was used.

For adults, average intakes ranged from 0.001 to 0.011 µg/kg bw per day and intakes at the 95th percentile ranged from 0.006 to 0.032 µg/kg bw per day. In children, average intakes ranged from 0.002 to 0.012 µg/kg bw per day, and intakes at the 95th percentile ranged from 0.007 to 0.055 µg/kg bw per day.

Summary of national intake estimates

National estimates of dietary intake of 1,3-dichloro-2-propanol provided by Australia and estimates for European Union member states were assessed by the Committee based on available occurrence data provided both by member states and Australia. Intakes were calculated by linking individual consumption data with mean occurrence data, using the actual body weight of the consumer as reported in consumption surveys.

At the national level, intake estimates from various food sources including soy sauce and soy-sauce products ranged from 0.008 to 0.051 µg/kg bw per day for the average in the general population. For consumers at a high percentile (95th), including young children, intake estimates ranged from 0.025 to 0.136 µg/kg bw per day.

Meat products are the main contributor to intake in all national estimates, ranging from 45% to 99% depending on the country diet. Soy sauce and soy sauce-based products contributed up to 30% in all national estimates. Other food groups contributed up to 10% of the total intake.

The Committee concluded that based on national estimates, an intake of 0.051 µg/kg bw per day of 1,3-dichloro-2-propanol could be taken to represent the average for the general population and that an intake of 1,3-dichloro-2-propanol of 0.136 µg/kg bw per day could be taken to represent consumers with a high intake. In these intake estimates for average to high intake, young children are also included.

Table 7. Estimated dietary intake of 1,3-dichloro-2-propanol from various food sources including soy sauce and soy sauce-based products

Country	Population group	Intake of 1,3-dichloro-2-propanol (μg/kg bw per day)[a]	
		Mean	95th Percentile[b]
Australia	All (≥ 2 years)	0.041	0.105
	2–12 years	0.051	0.136
	13–19 years	0.035	0.094
	≥ 20 years	0.039	0.101
Denmark	Adult	0.040	—
Finland	Adult	0.010	—
France	≥ 18 years	0.018	0.038
	3–14 years	0.031	0.064
Germany[c]	Adult	0.008	0.026
	14 years	0.011	0.036
Ireland	Adult	0.048	0.077
Netherlands	Adult	0.021	0.053
	Children	0.036	0.099
Sweden	Adult	0.011	0.025
United Kingdom[c]	≥ 18 years	0.016	0.041
	1.5–4.5 years	0.035	0.133

[a] Only 5% of consumers had exposures above this level.

[b] Estimated dietary intakes of 1,3-dichloro-2-propanol for European countries were assessed by the Committee based on available food consumption data and a fixed weighted concentration of 1,3-dichloro-2-propanol for food categories found to contain 1,3-dichloro-2-propanol in the European Union report (European Union, 2004) (soy sauce and soy sauce-based products) and in the Australian report for the other foods group (meat and fish products). Standard average body weights of 65 kg for adults, 30 kg for children and 15 kg for young children were used.

[c] Consumers only

5.2 International estimates of intake from GEMS/Food Consumption Cluster Diets

The new descriptions of the GEMS/Food Consumption Cluster Diets allow a better refinement of intake assessments for chloropropanolsl, e.g. information is provided on soy sauce consumed as is and oil of soya bean for other uses, cheese processed, which makes the diets more relevant than those used for the previous evaluation by the Committee.

Table 8. Consumption of soy sauce and soy sauce-based products by consumers only from various countries and estimated dietary exposure to 1,3-dichloro-2-propanol

Country	Population group	No of consumers (%)	Consumption (g/day)		Intake of 1,3-dichloro-2-propanol (µg/kg bw per day) [a]	
			Mean	P95[b]	Mean	P95
Australia	All (≥ 2 years)	13 858 (7.6)	9.3	27.9	—	—
	2–12 years	2 079 (4.9)	4.8	16.2	0.011	0.037
	13–19 years	1 063 (8.7)	9.3	25.4	—	—
	≥ 20 years	10 716 (8.1)	10.1	30.3	0.011	0.032
France	≥ 18 years	1 474 (2.4)	3.6	5.8	0.005	0.008
	3–14 years	1 014 (1)	3.4	5.6	0.010	0.017
Germany	Adult	25 000 (5.5)	0.9	4.3	0.001	0.006
	4–14 years	2 614 (6.6)	0.6	2.2	0.002	0.007
Ireland	Adult	958 (1.9)	1.9	4.1	0.003	0.006
Netherlands	Adult	4 711 (3.7)	6.1	16.0	0.009	0.023
	Children	1 383 (7.5)	4.0	14.5	0.012	0.044
Sweden	Adult	1 212 (1.4)	2.3	4.8	0.003	0.007
United Kingdom	Adult	2 197 (8.7)	4.0	9.0	0.006	0.013
	1–4 years	1 675 (2.4)	4	9.0	0.006	0.055

[a] Estimated dietary intakes of 1,3-dichloro-2-propanol were obtained using consumption of soy sauce by consumers only in each country and a fixed weighted concentration of 1,3-dichloro-2-propanol in soy sauce as described in reports (Australia, 0.069 mg/kg; and European countries, 0.092 mg/kg). Standard average body weights of 65 kg for adults, 30 kg for children and 15 kg for young children were used.

[b] 95th percentile: only 5% of consumers had exposures above this level.

Data on distribution contamination from aggregate food items taking into account the weighting of samples from submitted and published results have been described according to the GEMS/Food categorization of 13 cluster diets (WHO, 2006). Table 6 shows the summary of the distribution-weighted concentration of 1,3-dichloro-2-propanol in soya sauce and soy sauce-based products, in other foods and in food ingredients from various countries from 2001 to 2006 reported as the best available occurrence data.

In general, the food items analysed were well characterized and it was possible to match sources, contamination and consumption to the new GEMS/Food cluster diets. Occurrence data were multiplied by the total mean consumption of the corresponding food category or subcategory reported, to derive mean total intakes

per cluster diet of 1,3-dichloro-2-propanol from all food sources. A summary of the international dietary intake estimates expressed in µg/kg bw per day is presented in Table 9.

International mean intakes from all sources were estimated to range from 0.008 to 0.090 µg/kg bw per day for the 13 GEMS/Food cluster diets, assuming a body weight of 60 kg.

Meat and meat products made the greatest contribution to total exposure in all cluster diets except for clusters C, G, K and L and ranged from 54% to 72%. Soya sauce and oil of soya beans contributed more than 10% of the total exposure in all cluster diets (range, 24–68%; Table 9). Fish products contributed less than 5% of the total exposure in all cluster diets, except clusters A and J.

Table 9 Summary of estimates of international dietary intake of 1,3-dichloro-2-propanol from all food sources (in µg/kg bw per day) for the 13 GEMS/Food Consumption Cluster Diets

Diet	Food category						Total
	Soya [a]		Meat[b]		Fish[c]		
	Intake[d]	% Total intake	Intake[a]	% Total intake	Intake[a]	% Total intake	Intake
A	0.003	31	0.006	63	0.001	6	0.009
B	0.012	26	0.034	72	0.001	2	0.047
C	0.011	57	0.008	40	0.001	3	0.019
D	0.007	30	0.016	66	0.001	4	0.024
E	0.012	30	0.026	67	0.001	2	0.039
F	0.013	24	0.040	72	0.002	3	0.055
G	0.020	55	0.015	42	0.001	3	0.036
H	0.019	41	0.027	58	0.001	1	0.047
I	0.004	31	0.008	65	0.000	4	0.012
J	0.003	30	0.005	62	0.001	8	0.008
K	0.036	58	0.025	41	0.000	1	0.062
L	0.042	68	0.017	28	0.002	4	0.062
M	0.041	46	0.048	54	0.001	1	0.090

GEMS/Food: Global Environment Monitoring System—Food Contamination Monitoring and Assessment Programme

[a] Soya sauce and oil of soya beans.

[b] Meat from cattle, pigs and sheep

[c] Fish, marine and freshwater.

[d] Weighted average concentration as reported in Table 8 for the food category or subcategory considered and food consumption in new 13 GEMS/Food Consumption Cluster Diets.

6. COMMENTS

Toxicological data

At its present meeting, the Committee reviewed two new studies of genotoxicity, a test for micronucleus formation in rat bone marrow in vivo and an assay for unscheduled DNA synthesis in rat hepatocytes in vivo/in vitro, which met appropriate standards for study protocol and conduct. In those assays, 1,3-dichloro-2-propanol yielded negative results in the tissues assessed. However, toxicity was not demonstrated in the tissues and hence the level of exposure is unclear. No other new data were available.

In the light of the limitations of the negative results for genotoxicity in vivo, the Committee reconsidered the results from the long-term study of carcinogenicity previously evaluated at its fifty-seventh meeting (Annex 1, reference *154*). In that study, rats were given drinking-water containing 1,3-dichloro-2-propanol at a dose of 0, 2.1, 6.3, or 19 mg/kg bw per day in males and 0, 3.4, 9.6, or 30 mg/kg bw per day in females for 104 weeks. Increased incidences of tumours were demonstrated in both sexes at the two higher doses tested. No increase in tumour incidence was seen at the lowest doses tested, 2.1 and 3.4 mg/kg bw per day for male and female rats, respectively. Treatment-related increases in tumour incidence (adenomas and carcinomas) occurred in liver, kidney (males only), the tongue, and thyroid gland. Certain of the tumours (i.e. liver and kidney) might have arisen by non-genotoxic processes, but no clear mode of action was established. Moreover no mode of action was evident for the increased incidence of tongue papillomas and carcinomas in both sexes of rats at the highest dose. In spite of the negative results for genotoxicity in vivo in the tissues assessed (i.e. bone marrow and liver), the Committee could not exclude a genotoxic basis for the neoplastic findings, because of the absence of persuasive negative genotoxicity data in the target organs for carcinogenicity, and the findings that 1,3-dichloro-2-propanol caused point mutations in bacteria and mammalian cells in culture and caused multi-organ carcinogenicity in both sexes. The Committee therefore confirmed that 1,3-dichloro-2-propanol should be regarded as a genotoxic and carcinogenic compound and performed dose–response modelling of the carcinogenicity data from the long-term study in rats to calculate the margin of exposure, according to the recommendations of the Committee at its sixty-first meeting (Annex 1, reference *166*).

The Committee calculated benchmark doses for 10% extra risk of tumours and 95% lower confidence limit for the benchmark dose ($BMDL_{10}$) values for the incidences of treatment-related tumours at each site for each sex. Extra risk is defined as the additional incidence divided by the tumour-free fraction of the population in the controls. Also, because of the presumed common genotoxic mode of action, the incidences of animals with treatment-related tumours were modelled for each sex. Consistent results were obtained from use of several models for all datasets modelled. The $BMDL_{10}$ values for the individual treatment-related tumours ranged from 7.2 to 19.1 mg/kg bw per day and for the incidence data for tumour-bearing animals from 3.3 to 7.7 mg/kg bw per day, as shown in Table 10.

Occurrence

Data on 1,3-dichloro-2-propanol analysed in food were obtained from several countries. 1,3-Dichloro-2-propanol was only found at quantifiable levels in samples of soy sauce, in samples of ingredients such as acid-HVPs and malt products, in samples of minced beef (dry-fried, raw or cooked), pork ham, sausage meat (raw or cooked) and in samples of fish fillet (battered and fried).

Average concentrations in samples of soy sauce-based products ranged from 0.09 mg/kg in soy oyster sauce to 0.6 mg/kg in soy mushroom sauce. Average concentrations were 0.024 mg/kg in samples of fish product, 0.034 mg/kg in samples of meat products and 0.022 mg/kg in samples of malt products.

1,3-Dichloro-2-propanol was detected only in samples that also contained 3-chloro-1,2-propanediol, except in samples of meat and meat products where 1,3-dichloro-2-propanol was detected in the presence (18 samples) and in the absence (32 samples) of detected levels of 3-chloro-1,2-propanediol. In meat products, the concentrations of 1,3-dichloro-2-propanol were generally higher than those of 3-chloro-1,2-propanediol.

The Committee noted that 1,3-dichloro-2-propanol is found in samples of soy sauce and soy sauce-based products when the concentrations of 3-chloro-1,2-propanediol exceed 0.4 mg/kg.

Based on limited data, there appears to be a linear relationship between the concentrations of 1,3-dichloro-2-propanol and 3-chloro-1,2-propanediol, but there was considerable scatter in the data at low concentrations and there was some variation between different types of products. Additional occurrence data would be needed to confirm the relationships before they could be used to predict the concentrations of 1,3-dichloro-2-propanol based on the concentrations of 3-chloro-1,2-propanediol.

Dietary exposure assessment

National estimates of dietary intake of 1,3-dichloro-2-propanol were provided by Australia, and estimates for European Union member states were assessed by the Committee based on available occurrence data provided both by European Union member states and Australia. Intakes were calculated by linking individual consumption data with mean occurrence data, using the actual body weight of the consumer as reported in consumption surveys.

Intake estimates from various food sources including soy sauce and soy-sauce products at the national level ranged from 0.008 to 0.051 µg/kg bw per day for the average in the general population. For consumers at a high percentile (95th), including young children, intake estimates ranged from 0.025 to 0.136 µg/kg bw per day.

Meat products were the main contributor to intake in all national estimates, ranging from 45% to 99% depending on the country diet. Soy sauce and soy sauce-based products contributed up to 30% in all national estimates. Other food groups contributed up to 10% of the total intake.

Table 10. BMD_{10}[a] and $BMDL_{10}$[b] values obtained from fitting models to incidence data for all treatment-related tumours and for individual tumour locations in male and female rats given drinking water containing 1,3-dichloro-2-propanol for 2 years

Treatment-affected sites and tumour types	Range of BMD_{10} values (mg/kg bw per day)	Range of $BMDL_{10}$ values (mg/kg bw per day)
Males		
Tumour-bearing animals/all treatment-associated sites	5.4–7.5	3.3–6.1
Renal adenoma and carcinoma	11.1–12.2	7.2–7.7
Hepatocellular adenoma and carcinoma	14.4–16.0	10.3–12.3
Tongue papilloma and carcinoma	12.4–17.9	8.7–11.6
Females		
Tumour-bearing animals/all treatment-associated sites	8.5–10.3	6.6–7.7
Hepatocellular adenoma and carcinoma	11.2–14.6	9.1–10.1
Tongue papilloma and carcinoma	17.1–22.8	11.5–19.1

[a]BMD_{10}: benchmark dose for 10% extra risk of tumours.

[b]$BMDL_{10}$: 95% lower confidence limit for the benchmark dose. Extra risk is defined as the additional incidence divided by the tumour-free fraction of the population in the controls.

The Committee concluded that based on national estimates, an intake of 0.051 µg/kg bw per day of 1,3-dichloro-2-propanol could be taken to represent the average for the general population and that an intake of 1,3-dichloro-2-propanol of 0.136 µg/kg bw per day could be taken to represent high consumers. In the intake estimates for average to high intake, young children are also included.

7. EVALUATION

The available evidence suggests that 1,3-dichloro-2-propanol occurs at lower concentrations than 3-chloro-1,2-propanediol in soy sauce and related products, and also in food ingredients containing acid-HVP. However, in meat products the concentrations of 1,3-dichloro-2-propanol are generally higher than those of 3-chloro-1,2-propanediol.

The Committee concluded that the critical effect of 1,3-dichloro-2-propanol is carcinogenicity. The substance yielded negative results in two new studies of genotoxicity, a test for micronucleus formation in bone marrow in vivo and an assay for unscheduled DNA synthesis in vivo/in vitro in rat hepatocytes, but limitations in those studies and positive findings in tests for genotoxicity in vitro as well as lack of

knowledge on the modes of action operative at the various tumour locations led the Committee to the conclusion that a genotoxic mode of action could not be excluded. Accordingly, the cancer dose–response data were analysed by dose–response modelling, and the Committee used eight different models to calculate BMD_{10} and $BMDL_{10}$ values. $BMDL_{10}$ values for the individual tumours ranged from 7.2 to 19.1 mg/kg bw per day and for incidence data on tumour-bearing animals for all treatment-affected locations from 3.3 to 7.7 mg/kg bw per day.

The Committee concluded that a representative mean intake for the general population of 1,3-dichloro-2-propanol of 0.051 µg/kg bw per day and an estimated high-level intake (young children included) of 0.136 µg/kg bw per day could be used in the evaluation. Comparison of the mean and high-levels intakes with the lowest $BMDL_{10}$ of 3.3 mg/kg bw per day, which was the $BMDL_{10}$ for incidence data on tumour-bearing animals for all treatment-affected locations, indicates margins of exposure of approximately 65 000 and 24 000, respectively. Based on those margins of exposure, the Committee concluded that the estimated intakes of 1,3-dichloro-2-propanol were of low concern for human health.

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