2,2-BIS(BROMOMETHYL)PROPANE-1,3-DIOL

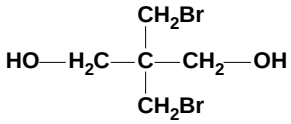
1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 3296-90-0
Chem. Abstr. Name: 2,2-Bis(bromomethyl)propane-1,3-diol
IUPAC Systematic Name: 2,2-Bis(bromomethyl)propane-1,3-diol
Synonyms: 1,3-Dibromo-2,2-dihydroxymethylpropane; 1,3-dibromo-2,2-dimethylolpropane; 2,2-dibromomethyl-1,3-propanediol; dibromoneopentyl glycol; pentaerythritol dibromide; pentaerythritol dibromohydrin

1.1.2 *Structural and molecular formulae and relative molecular mass*



$C_5H_{10}Br_2O_2$ Relative molecular mass: 261.94

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Off-white crystalline powder (Ameribrom, 1996), with a slight, mild, musty odour (National Toxicology Program, 1996)
(*b*) *Boiling-point*: 134 °C at 0.13 kPa (Dead Sea Bromine Group, 1998)
(*c*) *Melting-point*: 109.5 °C (Ameribrom, 1996)
(*d*) *Density:* 2.23 g/cm^3 (Ameribrom, 1996)
(*e*) *Spectroscopy data*: Infrared (prism [48246], grating [35246]), ultraviolet/visible and nuclear magnetic resonance (proton [20723], C-13 [5652]) spectral data have been reported (Sadtler Research Laboratories, 1980)

(*f*) *Solubility*: Soluble in water (20 g/L at 25 °C) and benzene; very soluble in acetone, isopropanol and methanol; slightly soluble in carbon tetrachloride and xylene (Ameribrom, 1996)
(*g*) *Volatility*: Vapour pressure, 1.33 kPa at 178 °C; 3.33 kPa at 200 °C (Dead Sea Bromine Group, 1998)
(*h*) *Octanol/water partition coefficient (P)*: log P, 2.29 (Dead Sea Bromine Group, 1998)
(*i*) *Conversion factor*[1]: $mg/m^3 = 10.71 \times ppm$

1.1.4 *Technical products and impurities*

2,2-Bis(bromomethyl)propane-1,3-diol is currently available with a purity of 98.5% (Ameribrom, 1996; Dead Sea Bromine Group, 1998). 2,2- Bis(bromomethyl)-propane-1,3-diol was available earlier as a technical product with a purity of 79%. Several impurities were identified in the technical product: 2,2-bis(hydroxymethyl)-1-bromo-3-hydroxypropane, 2,2-bis(bromomethyl)-1-bromo-3-hydroxypropane and pentaerythritol (National Toxicology Program, 1996).

Trade names for 2,2-bis(bromomethyl)propane-1,3-diol include: FR-522 and FR-1138.

1.1.5 *Analysis*

No methods have been reported for analysis of 2,2-bis(bromomethyl)propane-1,3-diol in environmental matrices.

1.2 Production

2,2-Bis(bromomethyl)propane-1,3-diol can be produced by replacement of the hydroxyl groups of pentaerythritol with bromide (National Toxicology Program, 1996).

The total world market for flame retardants is estimated at just under 1 million tonnes per year (Roskill Information Services, 1997).

Information available in 1999 indicated that 2,2-bis(bromomethyl)propane-1,3-diol was manufactured by one company each in Israel and Ukraine (Chemical Information Services, 1999).

1.3 Use

2,2-Bis(bromomethyl)propane-1,3-diol is a reactive flame retardant that is used primarily in unsaturated polyester resins for moulded products and in rigid polyurethane

[1] Calculated from: $mg/m^3 = (\text{relative molecular mass}/24.45) \times ppm$, assuming a temperature of 25 °C and a pressure of 101 kPa

foams. It is increasingly used in CFC (chlorofluorocarbon)-free foam products designed to meet more stringent standards of flame retardancy (Ameribrom, 1996; National Toxicology Program, 1996).

1.4 Occurrence

1.4.1 *Natural occurrence*

2,2-Bis(bromomethyl)propane-1,3-diol is not known to occur as a natural product.

1.4.2 *Occupational exposure*

No data were available to the Working Group.

1.4.3 *Environmental occurrence*

2,2-Bis(bromomethyl)propane-1,3-diol may enter the environment as fugitive dust, through wastewater and through disposal of resins and foams which may contain the compound as an impurity. 2,2-Bis(bromomethyl)propane-1,3-diol may be persistent in water (Environmental Protection Agency, 1983; Elwell *et al*., 1989; Dunnick *et al*., 1997). No data were available to the Working Group on levels of 2,2-bis(bromomethyl)propane-1,3-diol in the environment.

1.5 Regulations and guidelines

No occupational exposure limit or guideline has been established for 2,2-bis-(bromoethyl)propane-1,3-diol.

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

3.1 Oral administration

3.1.1 *Mouse*

Groups of 60 male and 60 female B6C3F$_1$ mice, six weeks of age, were fed diets containing 0, 312, 625 or 1250 mg/kg diet (ppm) 2,2-bis(bromomethyl)propane-1,3-diol (technical grade FR-1138®; with a composition of 78.6% 2,2-bis(bromomethyl)-

propane-1,3-diol, 6.6% 2,2-bis(hydroxymethyl)-1-bromo-3-hydroxypropane, 6.9% 2,2-bis(bromomethyl)-1-bromo-3-hydroxypropane, 0.2% pentaerythritol and 7.7% dimers and structural isomers) for 104–105 weeks. Average daily doses were 0, 35, 70 or 149 mg/kg bw for male mice and 0, 40, 80 or 170 mg/kg bw for female mice. Survival in both males and females treated with 1250 ppm was significantly lower than that of controls and this decrease in survival was associated with development of treatment-related tumours. Mean body weights of exposed male and female mice were similar to those of controls throughout the study. As shown in Table 1, male mice treated for two years had significantly increased incidences of Harderian gland, lung and forestomach tumours. In females, increased incidences of Harderian gland, lung, subcutaneous and forestomach tumours were observed. A marginal increase in the incidence of haemangiomas/haemangiosarcomas was observed in females (National Toxicology Program, 1996; Dunnick *et al*., 1997).

3.1.2 *Rat*

Groups of 49–50 male and 49–50 female Sprague-Dawley rats, eight to nine weeks of age, were fed diets containing FR-1138® (with a composition of 80% 2,2-bis(bromomethyl)propane-1,3-diol, 8% 2,2′-bis(bromomethyl)-1-bromo-3-hydroxypropane and 6% 2,2-bis(hydroxymethyl)-1-bromo-3-hydroxypropane) at doses of 0, 5 or 100 mg/kg bw per day for two years. Slight reductions in body weight were observed in treated males. Survival was not significantly different among the groups; most rats died or were killed at between 17 and 24 months. No treatment-related effects on tumour incidence were noted (Keyes *et al*., 1980).

Groups of 60 male and 60 female Fischer 344/N rats, six weeks of age, were fed diets containing FR-1138® (as used in the mouse study) at concentrations of 0, 2500, 5000 or 10 000 ppm for 104–105 weeks. A stop-exposure group of 60 male rats received 20 000 ppm in the diet for three months, after which animals received control diet for the remainder of the two-year study. Average daily doses were 0, 100, 200 or 430 mg/kg bw for males and 0, 115, 230 or 460 mg/kg bw for females. Stop-exposure male rats received an average daily dose of 800 mg/kg bw. Survival at two years of male and female rats exposed continuously to 5000 and 10 000 ppm and of the 20 000-ppm stop-exposure male rats was significantly lower than that of controls. Mean body weights of the 10 000-ppm male rats and 20 000-ppm stop-exposure male rats were lower than those of controls. Body weights of the other treated groups were in general similar to those of controls. Male rats in the stop-exposure group began to die of treatment-related tumours (particularly intestinal tumours) by one year of age. As shown in Table 2, significantly increased incidences of neoplasms in various organs of both male and female rats were observed, with males exhibiting a wider range of affected organs than females. In male rats that received 20 000 ppm for three months, then standard diet for the remainder of the study, essentially the same pattern of proliferative changes and tumours occurred as in male rats fed the agent continuously.

Table 1. Neoplastic lesions in mice treated with 2,2-bis(bromomethyl)-propane-1,3-diol in the diet

Tumour site/type	Number of animals with tumours			
Dose (mg/kg diet):	0	312	625	1250
Males				
Harderian gland				
Adenomas	3/50	6/51	12/50**	18/49**
Carcinomas	1/50	1/51	4/50	4/49
Adenomas and carcinomas combined	4/50	7/51	16/50**	22/49**
Lung (alveolar/bronchiolar)				
Adenomas	12/50	4/51	12/50	21/49**
Carcinomas	3/50	7/51	8/50	11/49**
Adenomas and carcinomas combined	15/50	11/51	16/50	25/49**
Forestomach				
Squamous-cell papillomas	0/50	3/51	2/50	2/49
Squamous-cell carcinomas	0/50	0/51	1/50	2/49
Papillomas and carcinomas combined	0/50	3/51	3/50	4/49*
Females				
Harderian gland				
Adenomas	2/52	6/50	8/51*	15/50**
Carcinomas	1/52	6/50	5/51	7/50*
Adenomas and carcinomas combined	3/52	12/50**	13/51**	19/50**
Lung (alveolar/bronchiolar)				
Adenomas	3/52	3/50	9/51*	17/50**
Carcinomas	2/52	2/50	6/51	5/50
Adenomas and carcinomas combined	5/52	5/50	15/51*	19/50**
Skin, subcutaneous				
Fibrosarcomas/sarcomas	0/52	1/50	4/51	12/50**
Forestomach				
Squamous-cell papillomas	0/52	1/50	5/51*	3/50
Circulatory system				
Haemangioma/haemangiosarcomas	1/52	2/50	0/51	5/50*

From National Toxicology Program (1996); Dunnick *et al*. (1997)
* $p < 0.05$, logistic regression test
** $p \leq 0.01$, logistic regression test

Significantly increased incidences of neoplasms of the skin, subcutaneous tissue, mammary gland, Zymbal gland, oral cavity, oesophagus, forestomach, small and large intestines, peritoneum, lung and thyroid were observed in males. Increased incidences of neoplasms of the mammary gland, oesophagus and thyroid were observed in female rats (National Toxicology Program, 1996; Dunnick *et al*., 1997).

Table 2. Neoplastic and related lesions in rats treated with 2,2-bis(bromomethyl)propane-1,3-diol in the diet for three months (stop-exposure) or two years

Tumour site/type	Number of animals with tumours				
Dose (mg/kg diet):	0	2500	5000	10 000	20 000 stop-exposure
Males					
Skin					
All skin tumours (benign and malignant)	4/51	6/53	14/51**	24/55**	21/59**
Subcutaneous tissue					
Fibroma	2/51	8/53*	11/51**	15/55**	7/60
Fibrosarcomas/sarcomas	0/51	1/53	2/51	3/55	3/60
Fibromas and sarcomas combined	2/51	9/53*	13/51**	16/55**	10/59**
Mammary gland					
Fibroadenomas	0/51	4/53*	6/51**	6/55**	5/60**
Zymbal gland					
Adenomas	0/51	0/53	1/51	3/55	2/60
Carcinomas	2/51	1/53	3/51	2/55	15/60**
Adenomas and carcinomas combined	2/51	1/53	4/51	5/55	15/60**
Oral cavity					
Squamous-cell papilloma	0/51	4/53*	8/51**	10/55**	12/60**
Oesophagus					
Squamous-cell papilloma	0/51	0/53	1/51	5/55*	0/60
Forestomach					
Squamous-cell papilloma	0/51	0/53	0/51	1/55	5/60**
Small intestine					
Adenomas	0/51	0/53	0/51	0/55	1/60
Carcinomas	0/51	0/53	0/51	2/55	4/60
Adenomas and carcinomas combined	0/51	0/53	0/51	2/55	5/60*
Large intestine					
Adenomas	0/51	0/53	3/51	4/55	10/59*
Carcinomas	0/51	0/53	0/51	0/55	2/59
Adenomas and carcinomas combined	0/51	0/53	3/51	4/55	11/59**
Peritoneum					
Malignant mesotheliomas	0/51	3/53	8/51**	9/55**	26/60**
Lung					
Alveolar/bronchiolar adenomas	1/51	0/53	3/51	1/55	4/60
Alveolar/bronchiolar carcinomas	0/51	1/53	0/51	3/55*	3/60
Alveolar/bronchiolar adenomas and carcinomas combined	1/51	1/53	3/51	4/55**	7/60**
Thyroid					
Follicular-cell adenomas	0/51	1/53	2/51	2/55	7/59*
Follicular-cell carcinomas	0/51	1/53	4/51*	1/55	2/59
Adenomas and carcinomas combined	0/51	2/53	6/51*	3/55	9/59**

Table 2 (contd)

Tumour site/type	Number of animals with tumours				
Dose (mg/kg diet):	0	2500	5000	10 000	20 000 stop-exposure
Females					
Mammary gland					
Fibroadenomas	25/50	45/51**	46/53**	45/52**	
Oesophagus					
Squamous-cell papilloma	0/50	0/51	1/53	10/52**	
Thyroid					
Follicular-cell adenomas	0/50	0/51	2/53	3/52	
Follicular-cell carcinomas	0/50	0/51	0/53	1/52	
Adenomas and carcinomas combined	0/50	0/51	2/53	4/52**	

From National Toxicology Program (1996); Dunnick *et al*. (1997)
* $p < 0.05$, logistic regression test
** $p < 0.01$, logistic regression test

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

No data were available to the Working Group.

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

The acute oral LD_{50} of 2,2-bis(bromomethyl)propane-1,3-diol in male rats was reported to be 3458 mg/kg bw (95% CI, 2810–4257 mg/kg) (Keyes *et al*., 1980).

Thirteen-week toxicity studies of 2,2-bis(bromomethyl)propane-1,3-diol were conducted in male and female Fischer 344/N rats and B6C3F_1 mice to determine target organ toxicity. 2,2-Bis(bromomethyl)propane-1,3-diol (technical grade, 78.6% pure) was administered by gavage in corn oil for five days per week to rats, 6–7 weeks of age, at doses of 0, 50, 100, 200, 400 or 800 mg/kg bw and to mice, 6–9 weeks of age,

at doses of 0, 25, 50, 100, 200 or 400 mg/kg bw, or in the feed at concentrations of 0, 1250, 2500, 5000, 10 000 or 20 000 ppm for rats and 0, 625, 1250, 2500, 5000 or 10 000 ppm for mice. In both studies, the kidney (papillary degeneration and necrosis) and urinary bladder (hyperplasia of the transitional-cell epithelium) were target organs, with mice being more sensitive than rats. Male rats and mice were more sensitive than females to the development of renal papillary degeneration or necrosis. At similar dose levels, on a mg/kg bw basis, treatment-related lesions in rats were similar in the gavage and feed studies. Lesions developed at a slightly lower dose level in mice treated by gavage than in those given the chemical in the diet (Elwell *et al.*, 1989; National Toxicology Program, 1996).

In a two-year study, male and female Fischer 344/N rats and B6C3F_1 mice received 0, 2500, 5000 or 10 000 ppm [average daily doses, 0, 100, 200 and 430 mg/kg bw for males and 115, 230 or 460 mg/kg bw for females] and 0, 312, 625 or 1250 ppm [average daily doses, 0, 35, 70 or 140 mg/kg bw for males and 40, 80 or 170 mg/kg bw for females] 2,2-bis(bromomethyl)propane-1,3-diol (purity, 78.6%; FR-1138®) in the diet, respectively. Non-neoplastic effects observed in the kidney of rats included papillary degeneration, increases in the incidences of hyperplasia of the renal papilla epithelium, hyperplasia of the transitional epithelium lining the renal pelvis and focal renal tubule atrophy in male rats. In male rats, transitional-cell hyperplasia of the urinary bladder was also present. In female mice, the incidence of alveolar epithelial hyperplasia was greater than in the control group (National Toxicology Program, 1996).

Groups of male and female Sprague-Dawley SPF-derived rats, seven to eight weeks of age, were placed on a lifetime diet supplying 0, 5 or 100 mg/kg bw per day FR-1138® (containing 80% 2,2-bis(bromomethyl)propane-1,3-diol). No changes in haematological parameters, urinary parameters or blood urea nitrogen, serum glutamic pyruvic transaminase and serum alkaline phosphatase levels were observed. Rats ingesting the dietary level of 5 mg/kg FR-1138 per day had no adverse effects related to the treatment. At the higher dose, evidence of toxicity included degenerative changes in the liver (increased centrilobular homogeneity of the hepatocellular cytoplasm), eye (bilateral diffuse opacity of the lenses) and increased incidence of thyroid retention cyst formation (Keyes *et al.*, 1980).

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

Treinen *et al.* (1989) investigated 2,2-bis(bromomethyl)propane-1,3-diol (purity, 87.3%) in a continuous breeding study by administration in the feed to Swiss CD-1 mice at levels of 0, 0.1, 0.2 and 0.4% (daily doses estimated to be 0, 141, 174 and 589 mg/kg

bw, respectively) to 20 male/female pairs per group. A control group of 40 breeding pairs was included. Dosing started seven days before and continued during a 98-day cohabitation period. At the end of the 98-day cohabitation period, the males were removed, allowing the dams to deliver and rear the final litter, while dosing continued. From weaning at postnatal day 21, these F_1 litters received 2,2-bis(bromomethyl)propane-1,3-diol at parental doses until mated with similarly treated non-siblings at 74 ± 10 days of age (20 breeding pairs per group). In addition, cross-over mating was performed on the parental (F_0) animals from the 0.4% dose level (20 breeding pairs per group). During the cohabitation period, postpartum body weights of the dams as well as weight gain in both males and females were significantly reduced at the two highest dose levels. In the same groups, a dose-dependent decrease in live pup weight, adjusted for average litter size, was observed. In the 0.4% dose group, the number of litters per pair and the number of live pups born per litter were reduced. In the F_1 generation, weight gain was significantly reduced at the two highest dose levels in males and at the highest dose level in females. Also, the number of live pups born per litter and adjusted live pup weight was significantly decreased in the high-dose group compared with controls. Cross-breeding of the F_0 exposed (0.4%) males and females with F_0 controls after 11 weeks of dosing resulted in a reduction of the number of live pups per litter and of pup weight only when exposed females (0.4%) were mated with control males. In addition, fertility was lower in exposed females, a parameter not affected in other parts of the study. The reduction in body weights of high-dose males was paralleled by reduction of the weight of reproductive organs, with spermatozoal parameters showing no sign of toxicity (Morrissey *et al*., 1989; Treinen *et al*., 1989). Differential counting of follicles was performed in ovaries originating from the cross-bred F_0 females (controls and 0.4%) and the F_1 females (all dose levels) (ovaries from 10 mice per group). Numbers of follicles were reduced in females exposed to 0.2 or 0.4% 2,2-bis(bromomethyl)-1,3-propanediol (Bolon *et al*., 1997).

Effects on the weight of male reproductive organs, epididymal spermatozoal parameters and estrous cyclicity were addressed after dietary administration of 2,2-bis-(bromomethyl)propane-1,3-diol for 13 weeks to groups of 10 males and 10 females per dose level. Dose levels were 0, 2500, 5000 and 10 000 ppm in $B6C3F_1$ mice (corresponding to estimated daily doses in males of 0, 500, 1300 and 3000 mg/kg bw and 0, 600, 1200 and 2900 mg/kg bw in females). In Fischer 344/N rats, doses were 0, 5000, 10 000 and 20 000 ppm (corresponding to estimated daily doses in males of 0, 400, 800 and 1700 mg/kg bw and 0, 400, 800 and 1630 mg/kg bw in females). In both species, mean body weight was depressed at doses of 5000 ppm and above, and was parallelled by reduced weight of the male reproductive organs, to a greater extent in mice than in rats (National Toxicology Program, 1996). In several studies, as in the National Toxicology Program continuous breeding study, no depression of reproductive organ weight was observed without concurrent reduction of body weight in mice and rats. Estrous cyclicity and spermatozoal parameters were not affected (Morrissey *et al*., 1989; Treinen *et al*., 1989; National Toxicology Program, 1996).

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 3 for references)

While two studies of the bacterial mutagenicity of 2,2-bis(bromomethyl)propane-1,3-diol gave negative results, a positive result was obtained in *Salmonella typhimurium* TA100 when liver S9 from Aroclor-induced male Syrian hamsters was used at a concentration of 30% (v/v). In other strains of *S. typhimurium* and in experiments with rat liver S9, no mutagenic activity was detected.

2,2-Bis(bromomethyl)propane-1,3-diol caused a dose-related increase in chromosomal aberrations in Chinese hamster ovary cells, but only at doses that caused significant cytotoxicity; a majority of the breaks were located in the heterochromatic region of the long arm of chromosome X, but the reasons for this are unclear. Induction of sister chromatid exchanges in Chinese hamster ovary cells was judged to be equivocal.

2,2-Bis(bromomethyl)propane-1,3-diol caused significant increases in micronucleated normochromatic erythrocytes in peripheral blood samples from male and female mice exposed for 13 weeks via the diet, whereas in tests for micronucleus formation in mouse bone marrow, results were positive for females but inconsistent for males [routes of administration were different].

4.5 Mechanistic considerations

The in-vitro mutagenicity of 2,2-bis(bromomethyl)propane-1,3-diol was dependent on the presence of a metabolic activation system.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

2,2-Bis(bromomethyl)propane-1,3-diol is a flame retardant used in polyester resins and polyurethane foams. No data on human exposure to this substance were available.

5.2 Human carcinogenicity data

No data were available to the Working Group.

Table 3. Genetic and related effects of 2,2-bis(bromomethyl)propane-1,3-diol

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
Salmonella typhimurium TA100, TA1535, TA1537, TA98, reverse mutation	–	–[c]	10 000 µg/plate	Mortelmans *et al.* (1986)
Salmonella typhimurium TA100, reverse mutation	–	+[d]	1000 µg/plate	Zeiger *et al.* (1992)
Salmonella typhimurium TA98, reverse mutation	–	–	6666 µg/plate	Zeiger *et al.* (1992)
Sister chromatid exchange, Chinese hamster ovary cells *in vitro*	–	?	1200	Galloway *et al.* (1987)
Chromosomal aberrations, Chinese hamster ovary cells *in vitro*	–	+	800	Galloway *et al.* (1987)
Micronucleus formation, male B6C3F$_1$ mouse bone-marrow cells *in vivo*	?		400 po × 1	National Toxicology Program (1996)
Micronucleus formation, male and female B6C3F$_1$ mouse bone-marrow cells *in vivo*	+		150 ip × 1	National Toxicology Program (1996)
Micronucleus formation, male and female B6C3F$_1$ mouse peripheral blood erythrocytes *in vivo*	+		2500 ppm feed; 13 w	National Toxicology Program (1996)

[a] +, positive; (+), weak positive; –, negative; ?, inconclusive

[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, µg/mL; in-vivo tests, mg/kg bw/day; po, oral; ip, intraperitoneal; w, week

[c] Aroclor-induced S9 (10%), male Sprague-Dawley rat or male Syrian hamster

[d] Aroclor-induced S9 (30%), male Syrian hamster; negative with 30% S9 from rat liver

5.3 Animal carcinogenicity data

2,2-Bis(bromomethyl)propane-1,3-diol was tested for carcinogenicity as a commercial mixture (FR-1138®) containing 80% of the parent compound in one experiment in mice and in two experiments in rats by oral administration in the diet. In mice, it increased the incidence of tumours of the Harderian gland, forestomach and lung in both males and females and of subcutaneous sarcomas in females. In one study in male rats, it increased the incidences of tumours of the skin, subcutaneous tissue, mammary gland, Zymbal gland, oral cavity, oesophagus, forestomach, small and large intestine, peritoneum, lung and thyroid. In female rats the incidences of oesophageal, mammary gland and thyroid follicular tumours were increased.

5.4 Other relevant data

No data on the metabolism of 2,2-bis(bromomethyl)propane-1,3-diol were available.

Histopathological changes were observed in the kidney and the urinary bladder of rats and mice administered 2,2-bis(bromomethyl)propane-1,3-diol for 13 weeks.

No data on reproductive and developmental effects in humans were available.

No effects were observed, after 13 weeks' exposure, on sperm parameters or vaginal cytology in mice or rats. However, in a mouse continuous breeding study, exposure to 2,2-bis(bromomethyl)propane-1,3-diol in feed caused a female-specific decrease in reproductive capacity.

2,2-Bis(bromomethyl)propane-1,3-diol was mutagenic in only one of several bacterial strains tested, and only with metabolic activation. In cultured mammalian cells, it was only weakly active in tests for chromosomal aberrations and sister chromatid exchanges. Micronucleus formation, indicative of chromosomal damage, was induced in cells from mice exposed to 2,2-bis(bromomethyl)propane-1,3-diol *in vivo*.

5.5 Evaluation

No epidemiological data relevant to the carcinogenicity of 2,2-bis(bromomethyl)-propane-1,3-diol were available.

There is *sufficient evidence* in experimental animals for the carcinogenicity of 2,2-bis(bromomethyl)propane-1,3-diol.

Overall evaluation

2,2-Bis(bromomethyl)propane-1,3-diol is *possibly carcinogenic to humans (Group 2B)*.

6. References

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Dead Sea Bromine Group (1998) *Material Safety Data Sheet: FR-522 (Dibromoneopentyl glycol)*, Beer Sheva, Israel

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