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UNION CARBIDE CORPORATION 39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001

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Office of Pollution Prevention & Toxics
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401 M Street, SW
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Attn: 8(e) Coordinator

Re: **Union Carbide Corporation's TSCA 8(e) Submission [REDACTED]
Concerning Methylmercaptopropionaldehyde (CASRN 3268-49-3)**

Dear Sir or Madam:

As a follow-up to the above-noted submission concerning methylmercaptopropion-aldehyde (MMP; CASRN 3268-49-3), or as a separate submission, Union Carbide Corporation herewith submits the following information. This information concerns a positive in vitro mutagenicity test and a positive in vivo genotoxicity test with an impure sample of MMP. The results of the preliminary (unaudited) findings are described below.

Test Material

MMP was 97.1% pure with the following impurities:

Acetaldehyde	=	0.15%
Methyl mercaptan	=	0.3 %
Acetone	=	0.6 %
Acrolein	=	0.05%
Acetic acid	=	0.25%
Pyridine	=	0.3 %
Hydroquinone	=	0.1 %
Benzene	=	0.0002%

mm
9/7/94

L5178Y/tk⁺ Mouse Lymphoma Cell Forward Mutagenesis Assay

Dimethyl sulfoxide was used as solvent and diluent. Studies were conducted in the presence and absence of metabolic activation (S9 liver homogenate from Arochlor 1254-induced male Sprague-Dawley rats). A preliminary range-finding assay was conducted up to 10 $\mu\text{l ml}^{-1}$ in the presence and absence of metabolic activation; and based on the findings the highest concentration of MMP selected for testing was 1.0 $\mu\text{l ml}^{-1}$.

In a first mutagenesis assay, with test concentrations of 0.0001-0.0562 $\mu\text{l ml}^{-1}$ without metabolic activation and 0.0562-0.562 $\mu\text{l ml}^{-1}$ with metabolic activation, no concentrations tested yielded survival in the range 10-20%. Therefore a second assay was conducted using MMP concentrations of 0.001-0.04 $\mu\text{l ml}^{-1}$ without S9 and 0.01-0.25 $\mu\text{l ml}^{-1}$ with S9. Clear concentration-related increases in mutation frequencies were obtained both with and without S9 (see attached Table 1). Colony size analysis (attached Table 2) showed concentration-related increases in σ mutants in the presence and absence of S9, and slight increases in λ mutants only at the highest concentrations tested. Thus MMP induced both gene and chromosomal mutations, but primarily chromosomal mutations, at the tk focus in L5178Y mouse lymphoma cells.

Mouse Bone Marrow Micronucleus Test

Based on a probe study, male and female CD1 mice were exposed nose-only for one hour on each of ten successive days to 37.4, 68.5 and 155.6 ppm MMP vapor. Bone marrow was collected 24-hr after the second exposure. An air exposed group served as a control. There were five males and five females for each exposure group. A positive control group received an intraperitoneal injection of triethylene melamine (0.4 mg kg⁻¹). Results are shown in appended Tables 3 (male mice) and 4 (female mice).

For the air and MMP groups there was no effect on the proportionate ratio of polychromatophilic to normochromic erythrocytes, indicating an absence of bone marrow toxicity. For male mice there was a statistically significant increase in the number of micronucleated polychromatophils (expressed as a proportion of total polychromatophils) at all exposure concentrations. For female mice, the number of micronucleated polychromatophils was increased at all exposure concentrations, but without statistical significance. Clear positive results were obtained with the positive control material (triethylene melamine).

In Summary

An impure sample of MMP produced positive results with an *in vitro* L5178Y/tk⁺ mouse lymphoma cell mutagenesis assay both in the presence and absence of metabolic activation. Exposure of mice to MMP vapor produced a clear increase in bone marrow micronucleated polychromatophils in males, but an equivocal result in females. The mouse micronucleus test accords with the primarily σ colony response in the L5178Y lymphoma assay. In a *Salmonella typhimurium* reverse mutation assay, conducted in both the presence and absence of S9, no mutagenic response was seen in strains TA98, TA100, TA1535, TA1537, and TA1538.

Copies of the final (audited) reports will be sent to the Agency promptly after they issue.
Please contact the undersigned with questions, if any, at 203/794-5230.

Very truly yours,

A handwritten signature in black ink, appearing to read 'W. Kuryla', written in a cursive style.

William C. Kuryla, Ph.D.
Associate Director
Product Safety

WCK/cr

TABLE 1. Results from definitive L5178Y/tk⁺ mouse lymphoma forward cell mutagenesis assay with methylmercaptopropionaldehyde in the presence (+) and absence (-) of metabolic activation.^a

Chemical	+/- S9	Conc./ml	RSG(%)	RTG (%)	MF x 10 ⁻⁶	IMF x 10 ⁻⁶	Notes
DMSO	-	10.0 µl	101.96	105.21	70		
DMSO	-	10.0 µl	98.04	94.91	58		
MTP	-	0.001 µl	89.70	100.95	56	-	
MTP	-	0.010 µl	80.96	106.50	77	13	
MTP	-	0.015 µl	60.95	70.95	94	30	
MTP	-	0.020 µl	57.89	47.70	117	53	
MTP	-	0.025 µl	44.96	35.18	144	80	♦
MTP	-	0.030 µl	27.99	17.37	174	110	♦♦
MTP	-	0.035 µl	17.74	7.98	281	217	♦♦
MTP	-	0.040 µl	7.68	2.40	545	482	♦♦
Hycanthone	-	7.5 µg	46.05	33.30	296	233	♦♦
Hycanthone	-	10.0 µg	50.40	27.01	289	225	♦♦
DMSO	+	10.0 µl	88.23	97.23	43		
DMSO	+	10.0 µl	111.77	100.36	47		
MTP	+	0.01 µl	99.92	91.41	41	-	
MTP	+	0.05 µl	89.20	81.89	26	-	
MTP	+	0.10 µl	68.39	48.32	67	23	
MTP	+	0.15 µl	45.91	27.00	85	40	
MTP	+	0.20 µl	23.51	11.46	228	184	♦♦
MTP	+	0.25 µl	10.24	2.35	647	602	♦♦
Cyclophosphamide	+	2.5 µg	97.71	40.20	221	176	♦♦
Cyclophosphamide	+	3.0 µg	61.07	14.47	317	272	♦♦

^aRSG = Relative suspension growth

RTG = Percent relative total growth

MF = Mutant frequency

IMF = Induced mutant frequency

Notes: • IMF ≥ 70 × 10⁻⁶

• IMF ≥ 100 × 10⁻⁶

• DMSO = dimethyl sulfoxide

• MTP = methylmercaptopropionaldehyde

TABLE 2. Differential and total colony mutation frequencies in a definitive L5178Y/tk^{-/-} mouse lymphoma forward mutagenesis assay with methylmercaptopropionaldehyde in the presence (+) and absence (-) of metabolic activation.^a

Chemical	+/- S9	Concentration of chemical/ml	σ MF x 10 ⁻⁶	λ MF x 10 ⁻⁶	Total MF x 10 ⁻⁶
DMSO	-	10.0 μ l	31	34	70
DMSO	-	10.0 μ l	28	30	58
MTP	-	0.001 μ l	24	39	56
MTP	-	0.010 μ l	43	34	77
MTP	-	0.015 μ l	69	25	94
MTP	-	0.020 μ l	86	30	117
MTP	-	0.025 μ l	118	26	144
MTP	-	0.030 μ l	115	51	174
MTP	-	0.035 μ l [*]	217	64	281
MTP	-	0.040 μ l [*]	427	115	545
Hycanthone	-	7.5 μ g	203	93	296
Hycanthone	-	10.0 μ g	211	78	298
DMSO	+	10.0 μ l	22	20	43
DMSO	+	10.0 μ l	22	24	47
MTP	+	0.01 μ l	15	26	41
MTP	+	0.05 μ l	16	10	26
MTP	+	0.10 μ l	52	15	67
MTP	+	0.15 μ l	59	26	85
MTP	+	0.20 μ l	194	35	228
MTP	+	0.25 μ l [*]	538	109	647
Cyclophosphamide	+	2.5 μ g	177	44	221
Cyclophosphamide	+	3.0 μ g	269	48	317

^aMF = Mutation frequency

DMSO = dimethyl sulfoxide

MTP = methylmercaptopropionaldehyde

TABLE 3. Results of mouse bone marrow micronucleus assay with methylmercapto-propionaldehyde with male mice.^a

Chemical	Average Dose	Animal #	PCE Ratio ^a	MN/PCE (%)	MN/NCE (%)	Notes
Air	N/A	1	17.81	0.00	0.50	
		2	14.89	0.00	0.50	
		3	10.96	2.50	0.00	
		4	11.96	2.50	0.00	
		5	16.95	2.50	0.00	
		Ratios/Dose:	14.40	1.50	0.20	
MTP	374 ppm	1	11.92	0.00	0.00	
		2	24.58	10.00	0.00	
		3	15.89	0.00	2.02	
		4	16.83	0.00	1.01	
		5	9.95	10.00	0.00	
		Ratios/Dose:	15.85	4.00	0.60	◆
MTP	88.5 ppm	1	16.86	7.50	1.01	
		2	10.92	2.50	0.50	
		3	17.38	10.00	1.01	
		4	10.45	10.00	0.50	
		5	10.95	0.00	0.00	
		Ratios/Dose:	13.32	6.00	0.60	◆◆◆
MTP	155.6 ppm	1	17.86	10.00	0.00	
		2	12.92	15.00	0.00	
		3	11.92	0.00	2.01	
		4	12.95	5.00	3.03	
		5	12.94	0.00	1.01	
		Ratios/Dose:	13.72	6.00	1.21	◆◆
TEM	04 mg/kg	1	7.98	20.00	3.02	
		2	4.99	15.00	1.00	
		3	1.00	10.00	0.00	
		4	7.98	30.00	0.00	
		5	10.96	15.00	0.00	
		Ratios/Dose:	6.59	18.00	0.80	◆◆◆◆

^aPCE ratio = ratio of polychromatophilic erythrocytes/normochromic erythrocytes
 MN/PCE = ratio of micronucleated polychromatophils/polychromatophilic erythrocytes
 MN/NCE = ratio of micronucleated polychromatophils/normochromic erythrocytes
 MTP = methylmercaptpropionaldehyde
 TEM = triethylene melamine (positive control)
 Statistical significance: 0 = p<0.05; 00 = p<0.02; 000 p = <0.01; 0000 p = <0.001

TABLE 4. Results of mouse bone marrow micronucleus assay with methylmercapto-propionaldehyde with female mice.^a

Chemical	Average Dose	Animal #	PCE Ratio^b	MN/PCE (%)	MN/NCE (%)	Notes
Air	N/A	1	12.86	0.00	0.00	
		2	23.67	0.00	2.02	
		3	14.88	0.00	2.01	
		4	6.98	0.00	0.00	
		5	6.98	0.00	2.01	
		Ratios/Dose:	13.10	0.00	1.21	
MTP	374 ppm	1	12.91	0.00	0.00	
		2	16.77	0.00	0.00	
		3	9.93	0.00	0.00	
		4	19.72	0.00	2.01	
		5	28.43	0.00	3.03	
		Ratios/Dose:	17.58	0.00	1.01	
MTP	885 ppm	1	19.72	5.00	1.01	
		2	13.93	0.00	0.00	
		3	16.88	0.00	2.02	
		4	34.35	0.00	2.03	
		5	14.90	5.00	0.00	
		Ratios/Dose:	19.99	2.00	1.01	
MTP	155.6 ppm	1	22.62	0.00	1.01	
		2	14.88	5.00	3.01	
		3	14.91	0.00	0.00	
		4	16.88	5.00	1.01	
		5	23.88	0.00	2.04	
		Ratios/Dose:	18.64	2.00	1.21	
TEM	04 mg/kg	1	10.92	35.00	0.00	
		2	9.96	30.00	1.01	
		3	3.00	15.00	2.01	
		4	9.94	0.00	0.00	
		5	5.98	5.00	0.00	
		Ratios/Dose:	7.97	17.00	0.60	◆◆◆◆

^aPCE ratio = ratio of polychromatophilic erythrocytes/normochromic erythrocytes
 MN/PCE = ratio of micronucleated polychromatophils/polychromatophilic erythrocytes
 MN/NCE = ratio of micronucleated polychromatophils/normochromic erythrocytes
 MTP = methylmercaptopropionaldehyde
 TEM = triethylene melamine (positive control)
 Statistical significance: 0000 = p < 0.0001