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Office of Pollution Prevention & Toxics
U.S. Environmental Protection Agency
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ATTN: FYI Coordinator

Re Bis-2-Propylheptyl Phthalate (CASRN 53306-54-0)

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") has recently received preliminary data from a rat subchronic feeding study being conducted at The Central Toxicology Laboratory (Macclesfield, Cheshire, U.K.). Union Carbide and Kvaerner Process Technology are co-sponsors of this study.

The results are presented below. Their implications with respect to human health or the environment is very uncertain, as are indeed the biological reliability and relevance of the measurements. The information is herewith submitted for the Agency's information.

In this study, groups of rats have received feed containing bis-2-propylheptyl phthalate (CASRN 53306-54-0) at concentrations of 0, 500, 5000 or 12000 ppm over a 14 week period. Animals were sacrificed immediately after dosing was discontinued. Two additional groups which had received the feed containing 0 or 12000 ppm throughout the study period, were held for 4-weeks without further treatment and then sacrificed.

Significant decreases in body weight gain were noted in animals receiving 12000 ppm in feed. By the end of the dosing period, a 23% and 19% decrease in body weight was seen for males and females respectively when compared to the control group. This difference in weight gain was partially resolved by the end of the 4 week recovery period. Body weights in males receiving 5000 ppm in feed were slightly depressed (6% compared to controls). The decreased

weight gain was accompanied by a decrease in food consumption and hematological changes in the 12000 ppm group. The hematological changes appeared to be associated with decreased hemaglobin. Increased liver weights with concurrent increases in peroxisome enzyme levels were noted in all treatment groups. These latter changes were anticipated based on structure activity relationships with other phthalate esters (DEHP, etc.)

In addition to the observations described above, there appeared to be effects on certain selected sperm measurements from the male rats. These effects were related solely to velocity measurements (Table 1) At the end of the 4 week recovery period similar effects were not observed in any of the velocity indices. Other indices of sperm viability were unaffected by treatment including; total sperm, static count, percent motile, motile count, total sperm concentration and sperm/g tissue (Table 2). There were no effects at any of the dose levels on the stages development in epididymal sperm.

The meaning of the findings on sperm analysis is unclear. The effect of nutritional deficits, as evidenced by decreased body weight gain, on indices of sperm motility are not well studied. This is particularly important with respect to measurements made on epididymal sperm which require fructose as a sole energy source. The limited number of animals on which measurements were conducted coupled with the magnitude of variation, both with and between observation periods, complicate the evaluation of the statistical analysis. Finally, the pattern of response is not typical of that expected from materials causing effects on sperm development. The effects appear to be rapidly resolved after dosing is discontinued and as animals resume a more normal growth pattern. This could indicate the importance of the nutritional state of the animal on motility indices. Therefore, the relevance of these data to hazard evaluation is not clear at this time.

A copy of the final study will be submitted to the Agency promptly after it issues, upon request.

Very truly yours,

William C. Kuryla, Ph.D.
Associate Director
Product Safety
(203/794-5230)

Attachments

Table 1: Bis-2-Propylheptyl Phthalate - 90-Day Dietary Feeding Study in Rats
Sperm Velocity Measurements

		Main Study				Recovery	
		Dietary Concentrations of Bis-2-Propylheptyl Phthalate (ppm)					
		0 (Control)	500	5000	12000	0 (Control)	12000
Velocity (VSL)	Mean	61.1	57.6	54.4	46.0**	44.1	37.9
	S.D.	8.3	8.9	10.9	11.1	17.8	18.5
	N	6	6	6	6	9	9
Velocity (VCL)	Mean	231	234	215	202.3*	197.6	187.3
	S.D.	17.7	17.1	25.7	26.6	39.1	38.7
	N	6	6	6	6	9	9
Velocity (VAP)	Mean	101.9	97.5	91.8*	85.7**	83.7	78.8
	S.D.	9.9	6.9	8.9	10.8	16.4	17.3
	N	6	6	6	6	9	9
Sperm Motility (%)	Mean	84	81	81	80	68	71
	SD	3.2	5.5	3.8	7.9	19	11
	N	6	6	6	6	6	6

* P<.05
** P<.01

Table 2: Bis-2-Propylheptyl Phthalate - 90-Day Dietary Feeding Study in Rats
Other Sperm Measurements

		Dietary Concentrations of Bis-2-Propylheptyl Phthalate			
		0 (Control)	500	5000	12000
Total Sperm	Mean	439.0	335.8	376.5	461.2
	S.D.	163.9	97.7	106.0	150.9
	N	6	6	6	6
Static Count	Mean	67.0	62.5	72.0	93.7
	S.D.	18.5	16.3	23.7	64.4
	N	6	6	6	6
Motile Count	Mean	372.0	273.3	304.5	367.5
	S.D.	148.3	91.8	88.9	116.3
	N	6	6	6	6
Total Concentration	Mean	35.5	28.2	32.5	40.1
	S.D.	14.0	8.0	9.0	12.8
	N	6	6	6	6
Sperm/g Tissue	Mean	161.0	132.2	156.7	197.4
	S.D.	69.7	37.2	42.9	71.5
	N		6	6	6