

8EHQ-0601-14946

MR 48493

TSCA HEALTH & SAFETY STUDY COVER SHEET - revised 6/25/96

TSCA CBI STATUS:

☐ CHECK IF THIS PAGE CONTAINS CONFIDENTIAL BUSINESS INFORMATION (CBI)

Clearly mark the confidential information with bracketing and check the box in the appropriate section (☐ Contains CBI). Submit a sanitized cover sheet with CBI deleted. Mark the sanitized copy, "Public Display Copy" in the heading.

{PRIVATE } 1.0 SUBMISSION TYPE <input type="checkbox"/> Contains CBI <input type="checkbox"/> 8(d) <input checked="" type="checkbox"/> 8(e) <input type="checkbox"/> FYI <input type="checkbox"/> 4 <input type="checkbox"/> Other: specify <input checked="" type="checkbox"/> Initial submission <input type="checkbox"/> Follow-up submission <input type="checkbox"/> Final report submission Previous EPA Submission or Title if Update or Follow-up: _____ Docket Number, if any: _____ <input type="checkbox"/> continuation sheet attached		Submission date: May 31, 2001								
2.1 SUMMARY/ABSTRACT ATTACHED <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID 8(e)2001-2800	2.3 FOR EPA USE ONLY Contain NO CBI								
3.0 CHEMICAL/TEST SUBSTANCE IDENTITY <input type="checkbox"/> Contains CBI <i>Reported Chemical Name (specify nomenclature if other than CAS name):</i> CAS #: 6846-50-0 2-Methylpropanoic acid 2,2-dimethyl-1-(1-methylethyl)-1,3-propanediyl ester Purity: 99.0% <input checked="" type="checkbox"/> Single Ingredient <input type="checkbox"/> Commercial/Technical Grade <input type="checkbox"/> Mixture Trade Name: _____ Common Name: 2,2,4-Trimethyl-1,3-pentanediol Diisobutyrate										
Other chemical(s) present in tested mixture <input type="checkbox"/> continuation sheet attached <table border="1"> <thead> <tr> <th>CAS Number</th> <th>Nam</th> <th>% WEIGHT</th> </tr> </thead> <tbody> <tr> <td> </td> <td> </td> <td> </td> </tr> </tbody> </table>			CAS Number	Nam	% WEIGHT					
CAS Number	Nam	% WEIGHT								
4.0 REPORT/STUDY TITLE <input type="checkbox"/> Contains CBI REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN THE RAT (Preliminary Results) <input type="checkbox"/> continuation sheet attached										
5.1 STUDY/TSCATS INDEXING TERMS [CHECK ONE] HEALTH EFFECTS (HE): <input checked="" type="checkbox"/> ENVIRONMENTAL EFFECTS (EE): _____ ENVIRONMENTAL FATE (EF): _____										
5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4-digit codes) <table border="1"> <thead> <tr> <th>STUDY TYPE: RTOX</th> <th>SUBJECT ORGANISM (HE,EE only): RATS</th> <th>ROUTE OF EXPOSURE (HE only): ORAL</th> <th>VEHICLE OF EXPOSURE (HE only): FOOD</th> </tr> </thead> <tbody> <tr> <td>Other: _____</td> <td>Other: _____</td> <td>Other: _____</td> <td>Other: _____</td> </tr> </tbody> </table>			STUDY TYPE: RTOX	SUBJECT ORGANISM (HE,EE only): RATS	ROUTE OF EXPOSURE (HE only): ORAL	VEHICLE OF EXPOSURE (HE only): FOOD	Other: _____	Other: _____	Other: _____	Other: _____
STUDY TYPE: RTOX	SUBJECT ORGANISM (HE,EE only): RATS	ROUTE OF EXPOSURE (HE only): ORAL	VEHICLE OF EXPOSURE (HE only): FOOD							
Other: _____	Other: _____	Other: _____	Other: _____							
6.0 REPORT/STUDY INFORMATION <input type="checkbox"/> Contains CBI <input checked="" type="checkbox"/> Study is GLP Laboratory: <u>Health and Environment Laboratories, Eastman Kodak Company</u> <u>1100 Ridgeway Avenue, Rochester, NY 14652</u> Source of Data/Study Sponsor (if different than submitter) _____ <input type="checkbox"/> continuation sheet attached Report/Study Date: <u>Not yet available</u> Number of Pages: <u>Not yet known</u>										
7.0 SUBMITTER INFORMATION <input type="checkbox"/> Contains CBI Submitter: <u>Karen R. Miller, Ph.D.</u> Title: <u>Principal Technical Representative</u> Phone: <u>(423) 229-1654</u> Company Name: <u>Eastman Chemical Company</u> Company Address: <u>P. O. Box 511, Kingsport TN 37662-5054</u> Submitter Address (if different): _____ Technical Contact: _____ Phone: _____ <input type="checkbox"/> continuation sheet attached										
8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS <input type="checkbox"/> Contains CBI <input type="checkbox"/> continuation sheet attached										

RECEIVED
 TSCA HEALTH
 SAFETY
 DIVISION
 JUN 29 11:08 AM '01
 RECEIVED
 TSCA HEALTH
 SAFETY
 DIVISION
 JUN 29 8:27 AM '01

Submitter Signature: Karen R. Miller

Date: 5/31/01



BEHQ-01-14946



88010000157

9.0 CONTINUATION SHEET

TSCA CBI STATUS:

 CHECK IF THIS PAGE CONTAINS CONFIDENTIAL BUSINESS INFORMATION (CBI)

Clearly mark the confidential information with bracketing and check the box in the appropriate section (*Contains CBI*).
Submit a sanitized cover sheet with CBI deleted. Mark the sanitized copy, "Public Display Copy" in the heading.

Submitter Tracking Number/Internal ID

{PRIVATE }8(e)2001-2800

Preliminary Results from a Reproduction/Developmental Toxicity Screening Test in Rats

In a Reproductive/Developmental Toxicity Screening study of 2,2,4-Trimethyl-1,3-pentanediol Diisobutyrate, male and female Sprague-Dawley rats were exposed to 0, 0.15, 0.45, or 1.5% of the test article in the diet during pre-mating, mating, gestation, and lactation phases of reproduction. Mean intake levels of the test substance were 0, 91, 276, and 905 mg/kg/day for males and 0, 115, 346, and 1123 mg/kg/d for females (gestation).

Mean body weight for males and females was significantly lower for the high-dose group during the first week of the study, and for females at the end of gestation. Fertility and fecundity indices were unaffected by treatment. The number of implants for the high dose group was significantly lower than control. This was correlated with a lower trend in the number of corpora lutea although statistical significance was not observed. There was no difference in pre- or post-implantation loss, or litter size on PND0. Although mean litter weight for the high-dose group was significantly lower than for the controls, the mean pup weight was comparable indicating the total litter weight change was a function of the number of pups. By PND4, the litter size and total litter weight for the high-dose group were significantly lower than controls, but all other parameters were comparable. Thus, any apparent reproductive/developmental toxicity seems to be a function of the fewer pups per litter. This occurred in 3 cases (1 animal in the mid-dose group and 2 animals in the high-dose group). Omitting these animals from the analysis results in no significant differences among groups, indicating that the statistical significance is not reflective of the entire group. Thus, the toxicological significance of the lower litter size is unclear. The sperm counts of males that sired litters for the females having fewer pups showed no apparent correlation between sperm count and litter size for these animals implying that the lower litter size was a random phenomenon.

Histopathology did not reveal any significant effect on reproductive organs. No treatment-related changes in sperm motility were observed. Testicular sperm counts for the low- and high-dose group, and epididymal sperm counts for all treated groups were significantly lower than for the controls. When adjusted for epididymal weight, the differences from the control group were no longer statistically significant. Although lower than the control group, the sperm counts in the treated groups were comparable to each other and were not reduced in a clear, dose-dependent manner. Therefore, the apparent reductions may be related to slightly higher control group values rather than a treatment-related effect. This possibility is supported by the lack of a treatment-related effect on fertility in the study, and the lack of lesions observed microscopically in the testes.

A copy of the final report will be provided when it is completed.