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Submitting Organization	EASTMAN CHEM CO		
Contractor	EASTMAN CHEM CO		
Document Title	INITIAL SUBMISSION: TSCA HLTH & SFTY STUDY CVR SHT REPORTING PRELIMINARY RESULTS IN 4-WEEK INHALATION TOXICITY STUDY IN RATS OF CYCLOPROPYL METHYL KETONE, DATED 021500		
Chemical Category	CYCLOPROPYL METHYL KETONE		

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EASTMAN

Eastman Chemical Company
P. O. Box 431
Kingsport, Tennessee 37662

February 15, 2000

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Attn: TSCA Section 8(e)
Room G99 East Tower
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
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Washington, DC 20460-0001

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Ladies and Gentlemen:

Eastman Chemical Company submits the following *preliminary information* as required under TSCA §8(e) for your consideration.

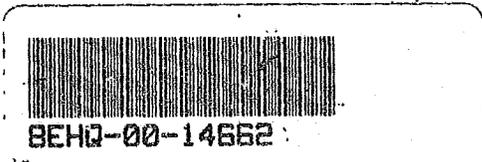
Four-Week Inhalation Toxicity Study in Rats of Cyclopropyl methyl ketone

If you have questions, you may contact me by telephone at (423) 229-2238 or the technical contact, Karen R. Miller, Ph.D., at (423) 229-1654.

Very truly yours,

A. James Cox

A. James Cox
Principal Technical Representative
Product Safety and Stewardship



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cc: 8(e) file

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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: Four-Week Inhalation Study in the Rat of Cyclopropyl Methyl Ketone <input type="checkbox"/> continuation sheet attached		Submission date: February 14, 2000 Docket Number, if any:
2.1 SUMMARY/ABSTRACT ATTACHED <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID 8(e)2000-1	2.3 FOR EPA USE ONLY
3.0 CHEMICAL/TEST SUBSTANCE IDENTITY <input type="checkbox"/> Contains CBI CAS #: 765-43-5 Purity: 100% <input checked="" type="checkbox"/> Single Ingredient <input type="checkbox"/> Commercial/Technical Grade <input type="checkbox"/> Mixture Trade Name: N/A Common Name: Same Reported Chemical Name (specify nomenclature if other than CAS name): Cyclopropyl methyl ketone		
Other chemical(s) present in tested mixture <input type="checkbox"/> continuation sheet attached	CAS Number Name None known	% WEIGHT
4.0 REPORT/STUDY TITLE <input type="checkbox"/> Contains CBI Four-Week Inhalation Toxicity Study in Rats of Cyclopropyl methyl ketone. (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) STUDY TYPE: STOX SUBJECT ORGANISM (HE,EE only): RATS ROUTE OF EXPOSURE (HE only): INHL VEHICLE OF EXPOSURE (HE only): Other: Other: Other: AIR		
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>Marc G. Schurger</u> Title: <u>Director, Product Safety and Regulatory Programs</u> Phone: <u>(423) 229-5921</u> Company Name: <u>Eastman Chemical Company</u> Company Address: <u>P. O. Box 431, Kingsport TN 37662-5280</u> Submitter Address (if different): Technical Contact: <u>Karen R. Miller, Ph.D.</u> Phone: <u>(423) 229-1654</u> <input type="checkbox"/> continuation sheet attached		
8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS <input type="checkbox"/> Contains CBI <input type="checkbox"/> continuation sheet attached		

Submitter Signature: Marc G. Schurger

Date: 2/15/00

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9.0 CONTINUATION SHEET

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8(e)2000-01

Preliminary Results from a 4-Week Inhalation Study of
Cyclopropyl Methyl Ketone (CPMK)

In this study, male and female Sprague-Dawley rats were exposed to nominal concentrations of 0, 0.05, 0.3, or 1.0 mg/l of CPMK for 6 hours per day, 5 days per week excluding holidays for 22 exposures. Animals were observed for clinical signs of toxicity prior to exposure, during and after exposure and once daily on non-exposure days. Body weights and feed consumption were measured weekly.

The following summarizes what we believe are the significant results. Reduced or soft feces were observed in some of the 1.0 mg/L treated groups. Mean red blood cell counts, hemoglobin concentrations, and hematocrit values were higher for the 1.0 mg/L male group, mean white blood cell counts and lymphocyte counts were lower for the 1.0 and 0.3 mg/L female groups, and mean atypical lymphocyte counts were higher for the 0.3 mg/L female groups when compared with the control group. Macrocytosis was observed for male rats from the 1.0 and 0.3 mg/L groups. Evaluation of blood cell morphology did not suggest any other test substance-related effects. Although the hematology changes suggest an effect on the bone marrow, no histopathological changes were observed in the marrow and the marrow was not considered a target organ for toxicity of the test substance. Mean urea nitrogen levels were higher for the 1.0 mg/L male and female groups and the 0.3 mg/L female groups when compared with the control groups. While urea nitrogen has been used as an indicator of kidney function, the mean serum creatinine levels and the mean kidney weights were comparable among the groups and the kidneys from all animals were normal when examined by light microscopy. Therefore, the significance of the elevated serum urea nitrogen levels is unclear. Mean total bilirubin levels were higher for the 1.0 mg/L male group and mean triglyceride levels were higher for the 1.0 mg/L female group when compared with the control group.

The mean relative liver weight was higher for the 1.0 mg/L male group when compared with the control group. A lower mean brain weight for the 1.0 mg/L female group appeared to be related to a low brain weight observed for a single animal from this group. When the brain weights were analyzed statistically with this animal excluded, the mean weights were comparable among the groups. All other terminal body weights and organ weights for rats from all exposure levels were comparable to the control groups.

Test substance-related changes observed at necropsy were limited to pale livers for the 1.0 mg/L male and the 1.0 and 0.3 mg/L female groups, and pale hearts for the 1.0 mg/L male and female groups. No other test substance-related gross lesions were observed on necropsy examinations. Histopathologic examination of tissues indicated test substance-related effects in the heart and liver. Heart effects consisted of myocyte vacuolation for the 1.0 mg/L male group and the 1.0 and 0.3 mg/L female groups, myocardial necrosis for the 1.0 and 0.3 mg/L male and female groups, and myocarditis for all exposed male and female groups. Liver effects consisted of hepatocellular cytoplasmic vacuolation for all male and female test substance exposed groups. However, the changes in the liver were considered to be adaptive changes in metabolism since serum enzymes such as ALT and SDH, which are considered to

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reflect hepatocellular damage, were not altered. No other test substance-related changes were observed. Neither a no-observed-adverse effect concentration (NOAEC) nor a no-observed-effect concentration (NOEC) was identified.