

8EHQ-0296-13582



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CHEMICAL MANUFACTURERS ASSOCIATION

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February 2, 1996

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U.S. Environmental Protection Agency
Room E-G99, Mail Code 7407
Office of Pollution Prevention and Toxics
401 M Street, SW
Washington, DC 20460

Attention: TSCA Section 8(e) Coordinator

Contains No CBI

Dear Sir or Madam:

The Cyclohexane Panel of the Chemical Manufacturers Association (CMA) hereby submits to EPA preliminary results of an acute schedule-controlled operant behavior study with cyclohexane. These results are submitted in accordance with Section 8(e) of the Toxic Substances Control Act.

In a Panel sponsored study, schedule-controlled operant methods were used to assess the behavioral effects of acute inhalation exposure to cyclohexane. A food restriction regimen maintained the body weights of adult male rats (10 rats/group) approximately 10% below their *ad libitum* feeding weight. The rats were trained to emit lever-pressing responses in order to obtain food in standard operant behavior test chambers. Operant sessions occurred five days per week for approximately nine weeks prior to cyclohexane inhalation exposure. Daily operant performance on the multiple fixed ratio-fixed interval (FR20-FI120 seconds) schedule of reinforcement was stable from session to session prior to a single 6-hour exposure to cyclohexane by the inhalation route. The measures of operant performance were fixed ratio response rate, fixed ratio pause duration, fixed interval response rate, and fixed interval index of curvature. On the test day, different groups were exposed by inhalation to targeted cyclohexane concentrations of 0 ppm, 500 ppm, 2,000 ppm, or 7,000 ppm, and the operant test session began approximately 30 minutes after removal of the rats from the inhalation chambers.

The characteristic patterns of operant performance were qualitatively similar across groups. There was, however, a statistically significant change in one quantitative measure of operant performance. On the exposure day, the fixed ratio of response for the 7,000 ppm group decreased (11%) from this group's rate on the day prior to exposure. This change in

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performance was greater than the decrease (less than 1%) over the same period for the control group. The other measures of operant performance were not affected by cyclohexane exposure. Exposure to 500 ppm or 2,000 ppm cyclohexane had no detectable effects on any measure.

The effect of 7,000 ppm atmospheric cyclohexane on fixed ratio response rate was transient. No compound-related effects of cyclohexane were detected on the day after exposure, nor were any compound-related effects apparent for up to two weeks following exposure. The transient compound-related effect of 7,000 ppm cyclohexane on fixed ratio response rate might be related to sedation that has been previously reported during exposure of animals to higher concentrations of cyclohexane. Slight reductions in fixed ratio response rate, however, could also be caused by CNS stimulation or be due to other factors that are not directly related to impairment of central nervous system function (e.g., novel environmental stimuli, such as odors, associated with the exposure). Thus, the extent to which the slight reduction in one aspect of schedule-controlled operant performance represents an adverse effect of cyclohexane and the potential impact on human health is not known.

The seven member companies of the CMA Cyclohexane Panel on whose behalf this submission is being made include:

Chevron Chemical Company
1301 McKinney
Room 1016
Houston, TX 77010
Panel Contact: Mr. Mike Liittjohann
Telephone: 713/754-4425

CITGO Refining & Chemicals, Inc.
6100 S. Yale Avenue
Tulsa, OK 74136
Panel Contact: Mr. John Grabowski
Telephone: 918/495-4764

DuPont
Barley Mill Plaza 25-1312
P.O. Box 80025
Wilmington, DE 19880-0025
Panel Contact: Dr. Jorge Olguin
Telephone: 302/992-3826

Huntsman Corporation
3040 Post Oak Blvd.
Houston, TX 77056
Panel Contact: Mr. Gerald Piper
Telephone: 713/235-6100

Koch Industries
4111 E. 37th Street N
P.O. Box 2256
Wichita, KS 67201
Panel Contact: Ms. Carol Komin
Telephone: 316/828-6720

Phillips Petroleum Company
411 S.W. Keeler
12C1 Phillips Building
Bartlesville, OK 74004
Panel Contact: Fred Marashi, Ph.D.
Telephone: 918/661-8153

Sun Company, Inc.
Ten Penn Center, 19th Flr.
1801 Market Street
Philadelphia, PA 19103-1699
Panel Contact: Ms. Joanne Houck
Telephone: 215/977-6182

If you have any questions regarding this letter, please contact Jonathon T. Busch of my staff at 703/741-5633.

Sincerely,

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

Langley A. Spurlock, Ph.D., CAE
Vice President, CHEMSTAR

cc: Cyclohexane Panel
Cyclohexane Toxicology Research Task Group
John Harris, EPA
Director, Office of Compliance Monitoring

Triage of 8(e) Submissions

Date sent to triage: _____

NON-CAP

CAP

Submission number: 13582A

TSCA Inventory: **(Y)** N D

Study type (circle appropriate):

Group 1 - Gordon Cash (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX SEN **(w/NEUR)**

Group 3 -HERD (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

- This is the **original 8(e)** submission; refile after triage evaluation.
- This **original** submission has been **split**; rejoin after triage evaluation.
- Other:

Photocopies Needed for Triage Evaluation

entire document:	(0)	1	2	3
front section and CECATS:	(0)	1	2	3
Initials: <u>JW</u>	Date: <u>6/26/96</u>			

CECATS TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # 8E110: 0296-13582 SEQ A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: Chemical Manufacturers Association

INFORMATION REQUESTED: FLWP DATE: _____

0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

0639 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

0401 NO ACTION REPORTED

0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 02/02/96 OTS DATE: 02/05/96 CSRAD DATE: 02/26/96

CHEMICAL NAME: _____ CAS# 110-82-7

INFORMATION TYPE:	P	F	C	INFORMATION TYPE:	P	F	C
0201 ONCO (HUMAN)	01	02	04	0216 EPI/CLIN	01	02	04
0202 ONCO (ANIMAL)	01	02	04	0217 HUMAN EXPOS (PROD CONTAM)	01	02	04
0203 CELL TRANS (IN VITRO)	01	02	04	0218 HUMAN EXPOS (ACCIDENTAL)	01	02	04
0204 MUTA (IN VITRO)	01	02	04	0219 HUMAN EXPOS (MONITORING)	01	02	04
0205 MUTA (IN VIVO)	01	02	04	0220 ECO/AQUA TOX	01	02	04
0206 REPRO/TERATO (HUMAN)	01	02	04	0221 ENV. OCCUREL/FATE	01	02	04
0207 REPRO/TERATO (ANIMAL)	01	02	04	0222 EMER INCI OF ENV CONTAM	01	02	04
0208 NEURO (HUMAN)	01	02	04	0223 RESPONSE REQUEST DELAY	01	02	04
0209 NEURO (ANIMAL)	01	02	04	0224 PROD/COMP/CHEM ID	01	02	04
0210 ACUTE TOX. (HUMAN)	01	02	04	0225 REPORTING RATIONALE	01	02	04
0211 CHR. TOX. (HUMAN)	01	02	04	0226 CONFIDENTIAL	01	02	04
0212 ACUTE TOX. (ANIMAL)	01	02	04	0227 ALLERG (HUMAN)	01	02	04
0213 SUB ACUTE TOX (ANIMAL)	01	02	04	0228 ALLERG (ANIMAL)	01	02	04
0214 SUB CHRONIC TOX (ANIMAL)	01	02	04	0239 METAB/PHARMACO (ANIMAL)	01	02	04
0215 CHRONIC TOX (ANIMAL)	01	02	04	0240 METAB/PHARMACO (HUMAN)	01	02	04
				0241 IMMUNO (ANIMAL)	01	02	04
				0242 IMMUNO (HUMAN)	01	02	04
				0243 CHEM/PHYS PROP	01	02	04
				0244 CLASTO (IN VITRO)	01	02	04
				0245 CLASTO (ANIMAL)	01	02	04
				0246 CLASTO (HUMAN)	01	02	04
				0247 DNA DAM/REPAIR	01	02	04
				0248 PROD/USE/PROC	01	02	04
				0251 MSDS	01	02	04
				0299 OTHER	01	02	04

TRIAJE DATA: NON-CBI INVENTORY YES (CONTINUE) NO (DROP) DETERMINE

ONGOING REVIEW: YES (DROP/REFER) NO (CONTINUE) REFER:

SPECIES: RAT TOXICOLOGICAL CONCERN: LOW Ac. inh MED HIGH

USE: _____ PRODUCTION: _____

COMMENTS:

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L

Acute inhalation toxicity in the rat is of low concern. Operant-behavior trained male rats (10/concentration) were exposed for 6 hours to concentrations of 0, 500, 2000, or 7000 ppm. Thirty minutes after exposure, rats were tested to determine their operant performance (lever-pressing response to obtain food). No changes from pre-exposure operant performance were noted at the two lower concentration; however, at 7000 ppm, rats showed an 11% decrease in performance. The day after exposure, performance had returned to normal.