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(A)

January 25, 1995

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Document Processing Center (TS-790)
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street SW
Washington, DC 20460

COMPANY SANITIZED

Dear 8(e) Coordinator:

BENZOHETEROCYCLE

This letter is to inform you of the results of an approximate lethal dose (ALD) study in mice and a mini-metabolism study in rats. In the ALD study, the test material was administered once by gavage to male mice at dose levels of 12 to 670 mg/kg. Deaths occurred in mice dosed at 26 mg/kg and higher except at 200 mg/kg. Clinical signs, including incoordination, low or high carriage, low or high posture, lethargy, barrel-rolling, or splayed rear legs, were observed in mice dosed at 26, 40, 90, 130, 200, 300, 500 or 670 mg/kg and are detailed in the enclosed report. The test material appears to have an approximate lethal dose of 26 mg/kg.

In the mini-metabolism study, the test material was administered as a single dose of 25 mg/kg by gavage to ten male rats. No deaths were observed. Clinical signs, including abnormal gait, prostrate posture, spread limbs, and leaning to the right side, were observed at 1.5-2 hours and 6 hours post dose. At 48 hours post dose, all animals appeared normal. No formal report will be written for this study.

Under these experimental conditions, the clinical signs described above would appear to be reportable, based upon EPA guidance regarding the reportability of such data under TSCA Sect. 8(e) criteria.

A copy of the final report for the ALD study is enclosed.

Sincerely,

mm
2/1/95

Oral Approximate Lethal Dose (ALD) Study with

The oral approximate lethal dose study with was conducted in male mice. The study was conducted according to Standard Operating Procedure No. SE113-P-001,

The test substance was suspended in Mazola® corn oil/acetone (85:15) and administered by oral gavage to one male mouse each at dosages of 12, 17, 26, 40, 60, 90, 130, 200, 300, 500, or 670 mg/kg. Experimental details of the study are archived in Quality Assurance and in laboratory notebook

Death occurred in mice dosed at 26, 40, 60, 90, 130, 300, 500, and 670 mg/kg. No clinical signs of toxicity were observed in the mouse dosed at 12 mg/kg. The mouse dosed at 17 mg/kg had weight loss of approximately 7% of initial body weight by the day after dosing. Incoordination, lethargy, low posture, low carriage, or ruffled fur was observed up to 3 days after dosing in the mouse dosed at 26 mg/kg. This mouse had weight loss of approximately 22% of initial body weight by 3 days after dosing and was found dead 4 days after dosing. The mouse dosed at 40 mg/kg exhibited incoordination, splayed rear legs, low or high posture, low or high carriage, or lethargy up to 6 days after dosing. This mouse had weight loss of approximately 27% of initial body weight by 6 days after dosing and was found dead 7 days after dosing.

The mouse dosed at 60 mg/kg was found dead the day after dosing before clinical signs of toxicity were apparent. Incoordination, barrel-rolling, low posture, low carriage, or lethargy was observed up to 4 days after dosing in the mice dosed at 90 or 130 mg/kg. The mouse dosed at 90 mg/kg also exhibited ruffled fur during the study. Weight loss of approximately 31 or 33% of initial body weight occurred by 4 days after dosing the mice dosed at 90 or 130 mg/kg, respectively. These mice were found dead 5 days after dosing.

The mouse dosed at 200 mg/kg had weight loss of approximately 7% of initial body weight by 2 days after dosing and exhibited incoordination up to 3 days after dosing. The survival of this mouse cannot be explained. Incoordination, splayed rear legs, low posture, low carriage, or red-stained fur was observed up to 8 days after dosing in the mouse dosed at 300 mg/kg. This mouse had weight loss of approximately 29% of initial body weight by 8 days after dosing and was found dead 9 days after dosing.

[]

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CBI Substantiation

Support for [] claim of confidential business information for the information claimed as CBI is provided.

1. Confidential treatment should be afforded for ten years. Information should remain confidential until that time [].

2. No.

3. [] identity and the chemical identity [] are only disclosed to a second party [] under a nondisclosure (secrecy) agreement. [] has not otherwise disclosed the information claimed as CBI to other parties.

4. All documents relating to [] are stored in locked, limited-access facilities and designated as proprietary, trade secret or confidential. [] having access to the information are contractually prohibited from disclosing [] proprietary/confidential information outside the [].

5. No.

6. Yes. [] Disclosure of the CBI information would permit a competitor to specifically know and understand [] efforts and to forego the necessary time and expense to identify/ develop this compound, thus capitalizing on []. [] believes that a competitor's knowledge of the chemical identity [] interest in this compound would give a competitor several years advantage [] and would allow it to forego much of the R&D costs that it would otherwise have to bear. [].

7. a. No.

b. Yes. The chemical identity [] would, potentially, disclose proprietary mixture [].

c. Yes. Disclosure of [] would reveal the identity and source of the [].

The mouse dosed at 500 mg/kg had weight loss of approximately 20% of initial body weight by 2 days after dosing and exhibited incoordination, barrel-rolling, or hyperactivity up to 3 days after dosing. This mouse was found dead 4 days after dosing. The mouse dosed at 670 mg/kg exhibited incoordination, barrel-rolling, lethargy, and yellow-stained perineum and had weight loss of approximately 22% of initial body weight by 3 days after dosing. This mouse was found dead 4 days after dosing.

Under the conditions of this test, an approximate lethal dose for was 26 mg/kg. This substance is considered to be highly toxic (ALD 5-49 mg/kg) when administered as a single oral dose to male mice.

Issue date: 1/5/95

Triage of 8(e) Submissions

Date sent to triage: APR 19 1995

NON-CAP

CAP

Submission number: 133/4A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (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; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only	
entire document: <u>0</u> 1 2 pages <u> </u>	pages <u>1, 3, 4</u>
Notes:	
Contractor reviewer: <u>POB</u>	Date: <u>3/21/95</u>

CECATS TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # BEHQ: 0195-13314 3 SEQ. A
 TYPE: INT. SUPP FLWP
 SUBMITTER NAME: Confidential

INFORMATION REQUESTED: FLWP DATE: _____
 0501 NO INFO REQUESTED
 0502 INFO REQUESTED (TECH)
 0503 INFO REQUESTED (VOL ACTIONS)
 0504 INFO REQUESTED (REPORTING RATIONALE)
 DISPOSITION:
0679 REFER TO CHEMICAL SCREENING
 0678 CAP NOTICE

0401 NO ACTION REPORTED
 0402 STUDIES PLANNED/IN PROGRESS
 0403 NOTIFICATION OF WORKING RATIONALE
 0404 LABEL/MSDS CHANGES
 0405 PROCESSING/CHANGING CHANGES
 0406 APP/USE DISCONTINUED
 0407 PRODUCTION DISCONTINUED
 0408 CONFIDENTIAL

SUB. DATE: 01/25/95 OTS DATE: 01/27/95 CSRAD DATE: 02/01/95

CHEMICAL NAME: Benzo[h]heterocycle
 CAS# Confidential

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	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. OCCURREL/FATE	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04
<u>0209</u> NEURO (HUMAN)	01 02 04	<u>0223</u> RESPONSE REQUEST DELAY	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	<u>0224</u> PROD/COMP/CHEM ID	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04
<u>0212</u> ACUTE TOX. (ANIMAL)	01 02 04	0226 CONFIDENTIAL	01 02 04
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04
0215 CHRONIC TOX (ANIMAL)	01 02 04	0239 METAB/PHARMACO (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 NO
 CAS SR NO
 Ongoing Review YES (DROP/REFER) NO (CONTINUE)
 Species MOS RAT
 Toxicological Concern: LOW MED HIGH
 Production: CONFIDENTIAL
 Status: IN TRIAGE Non-CBI

8(E) -13314A

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ACUTE ORAL TOXICITY IN MALE MICE IS OF HIGH CONCERN BASED ON AN LD50 LESS THAN 26 MG/KG. DOSAGES (GAVAGE) AND MORTALITY DATA ARE AS FOLLOWS: 0 MG/KG (0/1); 12 MG/KG (0/1); 17 MG/KG (0/1); 26 MG/KG (1/1); 40 MG/KG (1/1); 60 MG/KG (1/1); 90 MG/KG (1/1); 130 MG/KG (1/1); 200 MG/KG (0/1); 300 MG/KG (1/1); 500 MG/KG (1/1); AND 670 MG/KG (1/1). CLINICAL SIGNS OF TOXICITY AT DOSES ABOVE 12 MG/KG INCLUDED WEIGHT LOSS, INCOORDINATION, LETHARGY, LOW OR HIGH POSTURE, LOW OR HIGH CARRIAGE, RUFFLED FUR, AND BARREL-ROLLING.