K Nitschke 26 February 1980

R & D REPORT

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REV 8(E)

CRI NUMBER

LABORATORY REPORT CODE: HET K-1715-(17)

DATE ISSUED: February 8, 1980

DEPARTMENT: Toxicology Research Laboratory

LAB. NO.: 9 1 7 | PROBLEM NO.: 0 0 0 0 0 8 6

TITLE: A THIRTEEN WEEK REPEATED INHALATION STUDY ON ETHYLENE DIBROMIDE (EDB) IN MALE AND FEMALE RATS

56 PAGES IN FULL REPORT

AUTHOR(S): K. D. Nitschke, R. J. Kociba, D. G. Keyes, R. C. Childs, and M. J. McKenna

AUTHOR(S) SIGNATURE(S): 2-8-80 DGKeyes Feb-8, 1980

REVIEWER'S SIGNATURE: J. C. Ramsey

This report is: ☐ INTERIM ☒ FINAL and mainly: ☒ NEW ☐ REVIEW

DATA REFERENCES (book and page):

78-87

(Refer also to earlier related reports and publications.)

PATENT STATUS: ☐ disclosure submitted ☐ case filed ☐ no patent action required

DESCRIPTIVE SUMMARY WITH CONCLUSIONS:

Male and female CDF (F-344) rats were exposed to 0, 3, 10 or 40 ppm ethylene dibromide, 6 hours/day, 5 days/week for 13 weeks for a total of 67-68 exposures in 95-96 days. Scheduled sacrifices occured after 1, 6, and 13 weeks of exposure. Additional rats were held for a recovery period of 88-89 days and subsequently necropsied. Body weight data was obtained throughout the study and the animals were observed daily for signs of toxicity. Hematology, urinalysis and clinical chemistry parameters were measured. Gross and microscopic pathological examinations were conducted on selected tissues of all animals. Weights of various organs were recorded and organ/body weight ratios were calculated.

Rats exposed to 3 ppm EDB showed no consistent effect in any parameter measured. At 10 ppm, EDB caused slight epithelial hyperplasia of the nasal turbinates in animals necropsied after 1, 6 or 13 weeks of exposure; however, 88 days after the last exposure to EDB, no morphological difference from control animals was observed. Rats exposed to 40 ppm EDB showed a definite adverse response characterized by a decrease in body weight gain throughout the 13-week exposure period, an increase in liver and kidney weights after 6 and 13 weeks of exposure, and pathologic effects in the nasal epithelium. At this concentration the nasal turbinates of rats progressed from very slight hyperplasia of the epithelium after 1 week of exposure to EDB to hyperplasia and nonkeratizing squamous metaplasia of the epithelium after 13 weeks of exposure to EDB. After a recovery period of at least 88 days, only a single focus of hyperplasia of the nasal epithelium in one rat and increased relative liver weights were apparent as residual effects from the subchronic exposure. It is believed that these observations would have returned to control limits if allowed a longer recovery period.

Therefore, while this study has shown that repeated subchronic exposure of rats to 10 or 40 ppm EDB induces pathologic changes in the respiratory epithelium of the nasal turbinates, a subsequent post-exposure phase revealed a lack of progression of the lesions, with almost complete reversion toward normal histologic appearance of the nasal turbinates. In view of these findings, and the lack of any lesion subsequent to repeated exposure to 3 ppm EDB, short-term repeated exposure to

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these concentrations of EDB would not be expected to result in any long term irreversible effects upon the nasal turbinates or other tissues of the body.

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pv

LOCATER SHEET

TOXICOLOGY RESEARCH LABORATORY
HEALTH & ENVIRONMENTAL SCIENCES, USA
DOW CHEMICAL U.S.A.
MIDLAND, MICHIGAN 48640

FILE NO. K1715-17

DEAD STORAGE NO. 1634

TITLE OF REPORT: A Thirteen Week Repeated Inhalation Study on Ethylene Dibromide (EDB) in Male and Female Rats

DATE REPORT ISSUED: February 11,1980

AUTHOR(S): K. D. Nitschke, R. J. Kociba, D. G. Keyes, R. C. Childs, and M. J. McKenna

NOTEBOOK(S) - Number and Page(s):

1) 78-87
2) _____
3) _____
4) _____
5) _____
6) _____

SPECIMENS:

1) _____
2) _____
3) _____
4) _____

PATHOLOGY NUMBERS:

Control	79-37–79-76, 79-197–79-216
3 ppm	79-157–79-196, 79-257–79-276
10 ppm	79-117–79-156, 79-237–79-256
40 ppm	79-77–79-116, 79-217–79-236

Slides & Blocks pathology archives

ADDITIONAL DOCUMENTS:

1) _____
2) _____

LOCATION:

_____
_____

ALL DATA ARE SIGNED, DATED, IDENTIFIED BY PROJECT FILE NUMBER, LOGICALLY ORGANIZED, AND ADEQUATELY BOUND IN COMPLIANCE WITH GOOD LABORATORY PRACTICES PROCEDURES.

STUDY DIRECTOR: Kenneth D Nitschke DATE: 5 March 80

27 February 1979

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BIOCHEMICAL RESEARCH LAB. MIDLAND, MICHIGAN 48640

TOX. NO. K 1715-17

FILE NO. K-1715-(17)

REQUEST FOR TOXICOLOGICAL STUDIES

1803 BLDG. HET

NAME OF MATERIAL TO BE TESTED: Ethylene Dibromide

SUBMITTED BY (Signature)	(Date)	(Building)	(Phone)
Doug Rausch	26 Dec 78	768	

SUPERVISOR (Signature)	(Date and Building)	PROJECT SAFETY COORDINATOR	(Date)
K Dnitschke			

ESTIMATED COST	ACCOUNT NUMBER	LEDGER	LOCATION GROUP / FUNCTION	SECTION / SUB. FUNC	SUFFIX	PROBLEM NO. TO BE USED BY TOXICOLOGY	PROBLEM INDEX NO. LAB.	PROBLEM
$88,000							9	17000008 6

DO NOT WRITE BELOW THIS LINE — COMPLETE ALL INFORMATION ON REVERSE

ROUTE OF ADMINISTRATION: Inhalation

LENGTH OF TREATMENT: 90 day

SPECIES:

RAT	☒M ☒F	RABBIT	☐M ☐F	GUINEA PIG	☐M ☐F
DOG	☐M ☐F	MONKEY	☐M ☐F	HAMSTER	☐M ☐F

OTHER

DOSES

CHECK POINT	DATE
SAMPLE RECEIVED TOXICOLOGY	12 Dec 78
ESTIMATED STARTING TIME	15 Jan 79
ESTIMATED REPORTED DATE	Sept 79
REVISED ESTIMATE REPORTED	
REPORT DRAFTED	
REPORT ISSUED	

FATE OF SAMPLE	DATE
☐ RETURNED	
☐ DESTROYED	
☐ REFERENCE SAMPLE STORED	
☐ REFERENCE SAMPLE TO K STORAGE	

NOTES

DATE PROJECT COMPLETED

NOTES, CHANGES, ADVERSE EFFECTS NOTED

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SAMPLE INFORMATION

NAME

1,2 Dibromoethane

MOLECULAR FORMULA	MOLECULAR WEIGHT	SAMPLE REFERENCE, SOURCE AND/OR IDENTIFICATION
$C_2H_4Br_2$	187.88	

SYNONYMS

ethylene dibromide, ethylene bromide

STRUCTURAL FORMULA OR COMPOSITION

PHYSICAL AND CHEMICAL PROPERTIES

ESTIMATED PURITY OF SAMPLE	SAMPLE ANALYSIS	RESULTS
99.84%	☐ YES ☐ NO	

BOILING POINT	EXPLOSIVE LIMITS (% BY VOLUME IN AIR)	FLASH POINT	IGNITION TEMP.	MELTING POINT	VAPOR PRESSURE
°C mmHG		°F	°C	°C	mmHG 25°C

CORROSIVENESS (to common metals)	PHYSICAL STATE	COLOR

CHEMICAL REACTIVITY	ODOR (include concentration in air)

STABILITY (to pH change, heat, light)

EDB is sensitive to light & will breakdown

Why are toxicological studies needed? Include stage of development, proposed use, method of handling, and amount handled. Do you know of any adverse effects from human exposure?

	DATE		DATE		DATE
☐ PROTOCOL COMPLETED		☐ STATISTICS DONE		☐ SLIDES TO BE READY	
☐ ANIMALS ORDERED		☐ CLINICAL TESTS REPORTED		☐ SLIDES READ	
☐ ANIMALS STARTED ON TEST		☐ HEMATOLOGY TESTS REPORTED		☐ HISTOPATH REPORTED	
☐ NECROPSY DONE		☐ SLIDES STARTED		☐ WORK ALL DONE, READY TO WRITE	

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