7/18/85

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

004580

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Naled RS - Data submitted May 9, 1985, in Response to DCI (21-day Rat Inhalation) under Accession No. 257963. EPA Registration No. 239-1633

Caswell No. 586

FROM: Irving Mauer Ph.D.
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TO: William Miller/G. Otakie, PM-16
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THRU: Jane E. Harris, Ph.D., Section Head
Section VI
Toxicology Branch
Hazard Evaluation Division (TS-769)

Registrant

Chevron Chemical, Richmond CA.

Action Requested

Review and evaluate the following study, submitted May 9, 1985:

Three-Week Aerosol Inhalation Toxicity Study of Chevron Naled Technical in Rats--Preliminary Data Release: SOCAL 2334, March 7, 1985, S-2457, performed at the Chevron Environmental Health and Toxicology Center, Richmond CA.

TB Conclusion

Core Supplementary Data. (See below, and attached TOXICOLOGY BRANCH: DATA REVIEW.)

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Background

These preliminary data were submitted as a range-finding study in order to select dose levels to be used in a 90-day subchronic inhalation study to be scheduled at a later date. According to the registrant, the purpose of this submission was ". . . to present data on the cholinesterase effects and chamber concentrations. [Further] A report summarizing the other data collected during this study will be issued at a later date." (from Section II of Report S-2457).

It should be noted that both an acute inhalation LC_{50} study in the rat as well as a 90-day inhalation study are required to be submitted under FIFRA section 3(c)(2)(B) [NALED Pesticide Registration Standard, issued June 1983 - Table A, Section 158.135 Toxicology]. The present report satisfies neither of these data requirements.

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TOXICOLOGY BRANCH DATA REVIEW

CHEMICAL: Naled

Caswell: 586
EPA Chem.#: 034401

STUDY TYPE: Subchronic (21-day Range-Finding) Inhalation - Rat

CITATION: "Three-week Aerosol Inhalation Toxicity Study of Chevron Naled Technical in Rats - Preliminary Data Release Socal 2334."

ACCESSION No./MRID No.: 257963/NA

SPONSOR/TESTING LAB: Chevron/Environmental Health and Toxicology (Chevron)

STUDY NO./DATE: S-2457/March 7, 1985

TEST MATERIAL: Naled technical, SX-1554 (89.3% ai), a pale yellow viscous liquid

PROCEDURES:

Four groups of young adult (60-day old) male and female Fischer-344:CDF (F-344)/Crl Br rats were exposed to an aerosol of undiluted test material at nominal concentrations of 0 (filtered air only), 4, 8, and 16 ug/L for 6 hours/day for a total of 15 exposures over a 21-day period. Actual chamber concentrations of naled and bromodichloroacetaldehyde (BDCA, a hydrolysis product of naled) were determined hourly throughout the exposure period, while dichlorovos (DDVP), a minor constituent of technical naled, was determined once a week. Particle size was monitored weekly. Red blood cell and plasma cholinesterase activities were determined after the fifth exposure (orbital sinus samples) and at sacrifice (15 exposures), at which time half-brains were also analyzed for cholinesterase activity. At necropsy, selected organs were weighed (lungs, liver, kidneys, adrenals, and brain) and a roster of 27 organs and tissues as well as any gross lesions examined for pathological changes; nasal passages, trachea, lungs, and testicles were submitted for histopathological examination.

RESULTS:

The overall mean chamber concentrations based on chemical analysis of the chamber atmosphere during the course of the 3+ week exposures were given as 3.4, 7.2, and 12.1 ug/L (table 1 of

report). Significant dose-related depressions of circulating (greater after 15 exposures) as well as brain cholinesterase activities were noted at all concentrations of naled in both males and females (tables 2 through 5 of report). Compared to control values, mean percent inhibition of RBC-AChE after five exposures ranged from 26 percent (low-dose females) to 84 percent (high-dose females), while mean plasma ChE inhibition ranged from 33 percent (low-dose males) to 89 percent (high-dose females). At termination (15 exposures), low-dose male and female RCB-AChE registered 58 percent and 43 percent inhibition, respectively, while high-dose values were 94 pertent and 93 percent; plasma values did not change at any dose level. Brain cholinesterase activity was significantly depressed ($p \leq 0.01$) at all doses in both sexes, ranging from 23 to 28 percent at the LDT to over 60 percent in high-dose animals. The authors noted that the animals may have been exposed dermally as well as orally (due to whole body exposure), but could not estimate the amount of test substance absorbed by these routes. [Clinical observations, body weights, food consumption, hematology serum chemistry, organ weights, and pathology are to be submitted later in the final report.]

TB EVALUATION : NOEL for cholinesterase inhibition is less than 3.4 ug/L (actual)

CORE SUPPLEMENTARY DATA.

NOTE: According to test data gaps defined in the Naled Registration Standard, both acute LC_{50} and 90-day inhalation NOEL values are required to be submitted.

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