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

SEP 27 1984

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Lindane - Mutagenicity Data in response to PD-4 on Lindane
Accession #254504/EPA Reg. Nos.: 359-686, 359-687, 40083-1 and 21137-3. Caswell No.: 527

TO: G. LaRocca, PM#15
Registration Division (TS-769C)

FROM: Irving Mauer, Ph.D.
Geneticist, Section VI
Toxicology Branch/HED (TS-769C)

THRU: William L. Burnam, Chief
Toxicology Branch/HED (TS-769C)

9-24-84
9/25/84
9/27/84

Registrant: Centre International D'Etude
Du Lindane (C.I.E.L.)
Bruxelles, Belgium

Action Requested: Evaluate the following mutagenicity assay:

"In vivo sister chromatid exchange assay in CF1-mouse bone marrow cells with Lindane", performed by Research and Consulting Company AG (Report #RCC-05705), 4452 Itingen, Schweiz.

TB Evaluation: This study is judged UNACCEPTABLE (see attached DATA REVIEW).

TOXICOLOGY BRANCH: DATA REVIEW

CHEMICAL: Lindane

Caswell: 527
EPA Chem.: #009001

STUDY TYPE: Mutagenicity: Sister-chromatid exchange in mice (in vivo SCE).

CITATION: In vivo sister chromatid exchange assay in CF1-mouse bone marrow cells with LINDANE (Oral Application).

ACCESSION NO./MRID No.: 254504/NA

SPONSOR/TESTING LAB.: Centre International D'Etudes
Du Lindane (C.I.E.L.)
Bruxelles/RCC,
Research & Consulting Company AG
4452 Itingen/Schweiz

STUDY No./DATE: RCC Project 025705/June 20, 1984

TEST MATERIAL: Lindane (technical), batch/lot no. 83/33, 99.8% a.i., suspended in arachis oil for oral administration.

PROCEDURES: A copy of the procedures, performed according to referenced standards, is attached to this review. Briefly, the test article was orally administered to male and female CF-1 mice (10-12 wk old) at single dose levels of, respectively, 2/1.6, 10/8 and 50/40 mg/kg, reportedly 1/75th, 1/15th and 1/3rd the LD_{50}. Cyclophosphamide (CP, 50 mg/kg) served as the positive control.

RESULTS: No toxicity was reported in any treated group, although the high-dose was presumably one-third of the LD_{50}. Sampling of bone marrow cells (30/animal) 22 hr following single doses of test compound revealed a slight but statistically significant increase over oil controls in SCE frequency only in high-dose males, and decreases in high-dose females, but no dose-related trends. The authors consider these findings ".... to be random occurrances not related to treatment with the test article ...," since ".... all values were within the limits of control values; [and] no statistically significant differences [from controls] were observed after the results of males and females had been pooled ..." The positive control group (treated with CP) responded appropriately, with clearly significant increases in SCE (10X oil controls).

CONCLUSIONS: The authors concluded that "... under the experimental conditions reported during this in vivo sister chromatid exchange assay with LINDANE, no chromosome damage was observed in the bone marrow cells of the animals treated at 2/1.6-, 10/8- and 50/40 mg/kg body weight (males/females). Thus, no potential chromosome mutagenic activity was evident in this in vivo test ...."

TB EVALUATION/CORE: UNACCEPTABLE, since: (1) Insufficient dosage was administered, as indicated by the lack of animal and/or cyto-toxicity, i.e., no evidence was presented that the test compound was absorbed in effective concentrations to affect the target tissue, bone marrow. (2) Thirty cells per animal is an insufficient number cells analyzed. (3) A minimum of 7 animals per dose, and analysis of 100 cells per animal, are recommended by the OECD Guidelines cited by the authors (OECD Short-term Toxicology Group, Draft No. 14, U.S. proposal October, 1980).

R C C

RESEARCH & CONSULTING COMPANY AG

M & M ATTACH to REV.

CM CELAMERCK

Document No.

111AC-457-020

PROJECT 025705

IN VIVO SISTER CHROMATID EXCHANGE ASSAY

IN CF1-MOUSE BONE MARROW CELLS

WITH

LINDANE

(ORAL APPLICATION)

REPORT

P.O. Box 4452 Itingen / Switzerland
Phone 061 / 98 52 52 Telex 966 136 RCC CH

Lindane toxicology review

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