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

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FEB 10 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Evaluation of Benzyl Benzoate for Chromosomal Aberrations in Human Lymphocytes Submitted Under MRID 420231-02

Tox Chem No.	082
Submission No.	S436234, S436240
DP Barcode No.	D193385, D193384
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The data evaluation record for the chromosome aberration assay in human lymphocytes in vitro with benzyl benzoate, submitted by Fisons Corporation toward satisfying the mutagenicity Registration Guideline Series 84-2 testing requirement, is herewith submitted to Registration Division. The study is Acceptable. For further details see the data evaluation review. Under the conditions of the study, the test material did not induce structural chromosome damage in human lymphocytes exposed in vitro.

Reviewed by: Irving Mauer, Ph.D., Geneticist
Toxicology Branch-I, HED (H7509C)
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09-27-93
9/29/93

DATA EVALUATION RECORD

MRID NUMBER No.: 420231-02
PC No.: 009501
RD Record No.: S-436240, S 436234
EPA ID No.: 059820-E
Tox Chem. No.: 082
Project No.: D193384
D193385

I. SUMMARY

STUDY TYPE: (84-2) Mutagenicity---Chromosome damage in vitro (HLC)

CHEMICAL: Benzyl Benzoate

SYNONYMNS: Acarosan®

SPONSOR: Fison Corporation

TESTING FACILITY: Cytotest Cell Research (CCR), Rossdorf (FRG)

TITLE OF REPORT: Chromosome Aberration Assay in Human Lymphocytes in vitro with Benzyl Benzoate

AUTHOR(S): A. Heidemann

STUDY NUMBER: 203411

DATE ISSUED: May 16, 1991

CONCLUSIONS: Negative for inducing structural chromosome damage in human lymphocytes exposed in vitro with/without metabolic activaton to cytotoxic (250 ug/mL/-S9)or precipitating (500 ug/mL/+S9) concentrations.

TB-I EVALUATION: ACCEPTABLE

II. DETAILED REVIEW

A. TEST MATERIAL: Benzyl Benzoate

Description: Colorless liquid
Batches (Lots): 18504
Purity (%): 99
Solvent/carrier/diluent: Ethanol

B. TEST ORGANISM: Primary mammalian cell cultures

Species: Human lymphocytes (from blood donor)
Source: Female, 41 years (not on medication)

C. STUDY DESIGN (PROTOCOL): This study was designed to assess the clastogenic potential of the test article when administered in vitro to human lymphocyte cultures, according to established (published) procedures and FIFRA Test Guidelines.

A Statement of Quality Assurance measures (inspections/audits) was provided.

A Statement of adherence to Good Laboratory Practice (GLP) was provided.

D. PROCEDURES/METHODS OF ANALYSIS: Following preliminary cytotoxicity testing, lymphocytes, separated from blood drawn from a 41-year old healthy female, were established in duplicate culture for 48 hours under phytohemmaglutinin stimulation, then exposed for four hours to solvent or graded concentrations of test article in the absence or presence of mammalian metabolic (S9) activation. Twenty-four and 48 hours later, the cultures were harvested, and the cells prepared for microscopy on glass slides by conventional cytological procedures, including staining by Giemsa. The mutagenic clastogens ethylmethansulfonate (EMS, 0.72 mg/mL) and cyclophosphamide (CPA, 60 ug/mL) served as positive control for, respectively, the non-activated (-S9) and activated (+S9) portions of the assay.

The slide preparations were examined under oil immersion optics (1000X), and 100 metaphases per culture scored for the conventional array of structural chromosome aberrations. In addition, cytotoxicity was ascertained by mitotic index, and polyploid cells were also enumerated.

Standard criteria for assay acceptability and evaluation of results (including chi-square analysis) were applied.

E. RESULTS: In preliminary cytotoxicity tests (Report Tables 1a, 1b), the test article was moderately to severely toxic in non-activated cultures at 250 ug/mL and 500 ug/mL (25% relative survival), but minimally to not-at-all with S9 activation at the HDT, 500 ug/L; however, concentrations above 500 ug/mL precipitated. Hence, the dose levels chosen for the main assay were:

S9	24 Hr. (ug/mL)	48 Hr. (ug/mL)
Without	10, 100, 250	250
With	30, 250, 500	500

In the main assay (individual culture results were included as Report Tables 3 thru 18), no increased chromosomal damage was evident at any concentration, with/without S9 activation (Summary Report Tables 19 and 20, attached here), nor in incidence of polyploidy (Report Table 2). By contrast, both positive controls induced highly significant increases in structural aberrations. The author concluded that Benzyl Benzoate was not clastogenic in this assay.

F. TB EVALUATON: ACCEPTABLE

ATTACHMENT: (Summary) Data Tables

Disk 8:D193384.DER:MB:9/24/93

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BENZYL BENZOATE

Page_____ is not included in this copy.

Pages 6 through 7 are not included.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

X FIFRA registration data.

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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.