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

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JUL 8 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Trichlorfon --- Company Response to Mutagenicity Review.
Submitted under ACCESSION No. 262090.

ID # 3125-9. Caswell 385

TO: Wm. Miller/G. Otakie, PM 16
Registration Division (TS-767)

FROM: Irving Mauer, Ph. D.
Toxicology Branch
Hazard Evaluation Division (TS-769)

07-01-86

THRU: Jane E. Harris, Ph.D., Head
Section VI, Toxicology Branch
Hazard Evaluation Division (TS-769)

Registrant: Mobay Chemical Corporation

Action Requested: (660) Appraise registrant's response of March 17, 1986, to the following mutagenicity study, classified UNACCEPTABLE. (TB Doc. # 004561):

"Mobay Report No. 68925 - Dominant Lethal Study on Male Mouse to Test for Mutagenic Effects. (Performed by B. Herbold, Bayer Institut für Toxikologie, Report # 8745, November 15, 1979)"

TB Conclusions: In our previous review of this study (attached to this memo as APPENDIX I), TB judged it unacceptable for the reasons stated therein. With its response of March 17, 1986, Mobay submitted addtional copies of the original report of this study (Bayer Institut für Toxikologie No. 8745), stated to now include an "addendum." This addendum is a letter from Dr. Herbold of Bayer's Institute for Toxicology (dated December 3, 1985) to Mobay's Dr. L. Machemer, re-iterating that the single dose of 250 mg/kg trichlorfon administered to the main test group of animals was selected on the basis of the pilot study at doses of 750 and 500 mg/kg. Further, it is stated:

"... Since I had to use one dose due to the methodology established in the Institute, I regard 250 mg/kg body weight as the highest possible dose for this study. This is true especially since all treated animals had to be capable of inseminating the females, as well as to impregnate them." (as translated from the Ger man by Mobay).

5 pages

The justification provided in this letter addendum, however, does not address the deficiencies stated in our original review, and thus this study remains UNACCEPTABLE as a comprehensive evaluation of the potential for trichlorfon to induce dominant lethality in mice.

06/30/86

APPENDIX - I

004561

TOXICOLOGY BRANCH: DATA REVIEW

CHEMICAL: Trichlorfon

Caswell: 385
EPA Chem. No: 057901

STUDY TYPE: Mutagenicity - chromosome aberrations (dominant lethal test) in mice

CITATION: "Dominant Lethal Study on Male Mouse to Test for Mutagenic Effects."

ACCESSION NO./MRID NO.: 257819/na

SPONSOR/TESTING LAB.: Mobay/Bayer AG Institut fur Toxikologie

STUDY NO./DATE: Mobay No. 68925 (Bayer No. 8745)/November 15, 1979

TEST MATERIAL: L13/59 (technical trichlorfon), Batch No. 809831030 (98.4% ai)

Procedure:

Two groups of 50 male NMRI mice (supplied by S. Ivanovas GmbH, Kisslegg/Algau) were given either a single oral dose of 250 mg/kg test substance by intubation (suspended in 0.5% Cremophor EL) or the emulsifier alone, immediately following each was caged serially to single untreated females for a total of 12 matings of 4 days duration each. The single test dose was chosen on the basis of a preliminary acute test in females treated orally at 750 and 500 mg/kg, both of which "induced symptoms." Uteri were examined 14 days after mating to determine preimplantation and post-implantation losses, based upon counts of total, viable, and dead (deciduoma + resorptions + dead embryos) implants and corpora lutea. Implant data for dose and time periods were analyzed after transformation by ANOVA ($p < 0.05$) and F-tests, and frequency distributions between test and control groups compared by a non-parametric test.

Results:

Other than "mild drowsiness" one hour after trichlorfon administration (in an unstated number of animals), no clinically adverse effects were reported in treated males. Analysis of individual data for all mated females (in 12 Appendices to the

Report) revealed no differences between treated and control groups in fertilization ratio, pre-implantation loss, total implants, dead and/or viable implantations, or post-implantation loss (deciduomata + resorptions + dead embryos).

Conclusions:

The author concluded that 250 mg/kg trichlorfon had no adverse effects on treated males, their fertility, or on parameters of dominant lethality.

TB Evaluation:

This study is UNACCEPTABLE as a mutagenic evaluation of dominant lethals, since:

1. Only one dose was used, and that is considered insufficient to affect treated animals or reproductive processes.

2. No positive controls were run concurrently to determine transport to germ cells, or sensitivity of the animals to respond.

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004561

JUL 16 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Trichlorfon RS - Studies submitted to Satisfy Data Requirements. Accession No. 257819.
ID No. 3125-9

Caswell No. 385
Chemical No. 057901

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch
Hazard Evaluation Division (TS-769)

TO: William Miller/G. Otakie, PM-16
Registration Division (TS-767)

THRU: Jane E. Harris, Ph.D., Head
Section VI
Toxicology Branch
Hazard Evaluation Division (TS-769)

Registrant: Mobay Chemical, Kansas City, Missouri

Action Requested: Review the following studies on DYLOX, submitted April 22, 1985, to satisfy data requirements for the TRICHLORFON REGISTRATION STANDARD, Toxicology (technical, Table A):

1. Mobay Report No. 68783 - "Micronucleus Test on Mouse to Evaluate L 13/59 for Potential Mutagenic Effects." (Performed by B. Herbold, Bayer AG Institut fur Toxikologie, Report #8505, July 18, 1979.)

2. Mobay Report No. 68925 - "Dominant Lethal Study on Male Mouse to Test for Mutagenic Effects." (Performed by B. Herbold; Bayer AG Institut fur Toxikologie, Report #8745, November 15, 1979).

3. Mobay Report No. 69298 - "Studies of Embryotoxic and Teratogenic Effects on Rats Following Oral Administration." (Performed by L. Machemer, Bayer AG Institut fur Toxikologie, Report #8400, May 29, 1979.)