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

007993

JUN 20 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Dithiopyr (MON-15100/MON-7200) -- Company Response to Tox Branch Review
EPA ID# 524-UGN

Chemical (Caswell) No. 717C
RD Record No. 265,818
HED Project No. 0-1408

FROM: Irving Mauer, Ph.D., Geneticist
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06-14-90

TO: Joanne I. Miller, PM 23
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and

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6/19/90

THRU: Karl P. Baetcke, Ph.D., Chief
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Registrant Monsanto Agricultural, St. Louis, MO

Request Appraise registrant's response (Ward to Miller, June 6, 1990), to Tox Branch-I assessment of the following mutagenicity study ("UNACCEPTABLE"):

MON-7200: in vitro Cytogenetic Test, performed at the Institute of Environmental Toxicology, Tokyo (Japan), Study #ET-86-79, Final Report issued August 1, 1986, and catalogued by Monsanto as submission R.D., #900, Volume 13 (EPA MRID No. 410015-12).

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Background:

This study was judged unacceptable due to the following reporting deficiencies ("essential procedural information was not provided"):

(1) Although this single assay was conducted with apparently sufficient procedural controls providing presumptively valid negative results, no information on harvesting techniques and other constrictions, nor on cytological (slide) preparation was provided in the Final Report.

(2) Additionally, some explanation is required as to the discrepancy in the appearance and purity of the lot of MON 7200 used n the Japanese study ("light brown solid," 97.6%) compared to the Dayton batches used in the other (U.S.) studies of this submission ("light yellow powder," 91.5 to 93.7%).

[From DER, attached to memo: Mauer to Miller, dated April 18, 1990 --- Doc. # 007863]

Registrant Response/Agency Appraisal

Item 1: The registrant has provided, by copy of a letter (dated May 1, 1990) from the study director (Dr. Y.F.X. Sasaki) at the performing laboratory (Institute of Environmental Toxicology, Tokyo), full and complete information on the procedural gaps (inadvertently) omitted from the initial Final Report, including harvesting techniques, chromosome (cytological slide) preparation, criteria for validity, inter alia, plus published documentation of same.

This additional information is accepted as satisfying the aforementioned procedural omissions noted in the Agency's initial review.

Item 2: The registrant also has responded to second issue ("discrepancy in appearance and purity of the test samples") by the following clarification:

" The in vitro cytogenetics test was one of the first toxicology studies conducted with dithiopyr; it employed a test sample that came from a relatively small batch synthesized by our research chemists in St. Louis. The remainder of the genotoxicity studies were conducted some months later and employed a test sample that came from a larger batch of dithiopyr prepared at Monsanto's pilot production plant in Dayton, Ohio. The type of equipment used at the pilot production plant is quite different from that used in the research laboratories because it is designed for production of much larger batches of a chemical. The type of differences noted in dithiopyr

color and purity are commonly seen when a production process is "scaled up".
(cited in toto from Monsanto Letter of June 6, 1990)

The Agency also finds this additional information reasonable and accepted as satisfying Item 2 of the Agency's initial judgment.

Tox Branch Conclusion:

Since both additional procedural information and clarification of the apparent deficiencies noted in our initial assessment of this study have been provided, the attached one-liner assessment has been upgraded to ACCEPTABLE.

Dithiopyr/lca