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Data Evaluation Record

Study Type: Gene mutation in mouse lymphoma (L5178Y) cells.

004586

Study Identification: "An Evaluation of Mutagenic Potential of MON 097 Employing the L5178Y TK+/- Mouse Lymphoma Assay."

Lab. performing study: SRI International
Menlo Park, CA 94025

Sponsor: Monsanto Agricultural Products Co.
St. Louis, MO. 63167

Study no.: SR 81-150

Project no.: LSC-2575 (SRI)

Accession no.: 071970

Report date: August, 1982

Submitted to EPA: 9/22/83

Study director: Ann D. Mitchell, Ph.D.

Reviewed By: D. Stephen Saunders Jr., Ph.D.
Toxicologist, Section V
TOX/HED (TS-769)

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

DSD 8/2/85
J. Mauer
8/2/85

Conclusions: Positive for gene mutations in mouse lymphoma cells (L5178Y) only in the presence of metabolic activation. Negative for gene mutations in the absence of metabolic activation. The purity of the test substance was not stated, therefore it was not clear whether the technical grade of active ingredient was tested in this assay.

Classification: Acceptable

Materials

- 1) Test chemicals: Acetochlor (MON 097), a "plum-colored liquid"; lot NBP 1924845; % a.i. not stated.

Positive controls: Ethyl methanesulfonate (EMS)- no metabolic activation
3-methylcholanthrene (3-MC)- with metabolic activation

Metabolic activation: S-9 fraction (9,000 x g supernatant) from Arochlor 1254-induced rat liver (male Fischer-344 rats).

- 2) Doses tested: Acetochlor- 20, 30, 45, 60, 76, 100 and 400 ul/l without S-9.
5, 15, 20, 30, 40, 50, 100 and 250 ul/l with S-9.

vehicle control- 1% DMSO.

positive control- 500 ug/ml EMS without S-9
6 ug/ml 3-MC with S-9

- 3) Test system: Mouse lymphoma L5178Y cells, heterozygous for thymidine kinase.

Methods

A photocopy of the submitted methods is appended. The methods were reviewed and the following point(s) are noted:

None.

Results/Discussion

The selection of doses tested in the presence or absence of metabolic activation (S-9) were based on the results of a range-finding assay. Doses of acetochlor of ≥ 100 μ l/l were cytotoxic as evidenced by relative suspension growth of less than 5% of the solvent control group in the range finding assay.

In the primary study, incubation of mouse lymphoma cells with acetochlor in the absence of S-9 did not produce any effect on mutation frequency at any of the tested doses (data not shown). Doses of 100 μ l/l resulted in average relative suspension growth of about 10% of control, and were therefore cytotoxic. The positive control without S-9, EMS, induced an increase in mutation frequency of about 5.6x control values, demonstrating that the test system could respond appropriately to a direct-acting mutagen.

Incubation of lymphoma cells with acetochlor in the presence of S-9 produced an apparent dose-related increase in mutation frequency (Table 1). Doses of 40 μ l/l and above were apparently cytotoxic as evidenced by dose-dependent decreases in relative suspension growth and relative cloning efficiency. The positive control with S-9, 3-MC, caused an average increase in mutation frequency of 5.4x control values, demonstrating that the test system could respond appropriately to a mutagen requiring metabolic activation.

Table 1. Effect of Acetochlor and S-9 on Mutation Frequency^a

<u>Test Material</u>	<u>Dose</u>	<u>Relative Suspension Growth (%)^b</u>	<u>Relative Cloning Efficiency (%)^c</u>	<u>Mutation Frequency (% control)</u>
DMSO	1%	100.0	100.1	-
3-MC	6 μ g/ml	47.7	35.6	538.8
MON 097	5 μ l/l	82.9	97.8	102.0
MON 097	15 μ l/l	89.1	85.4	150.3
MON 097	20 μ l/l	82.2	77.8	155.9
MON 097	30 μ l/l	45.3	70.6	220.3
MON 097	40 μ l/l	12.6	36.1	427.1
MON 097	50 μ l/l	7.9	17.2	523.2
MON 097	100 μ l/l	3.2	NC	-
MON 097	250 μ l/l	3.3	NC	-

^adata excerpted from submitted study.

Classification: Acceptable

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