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

001854

5/10/82

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: Richard Mountfort (23)
Registration Division (TS-767)

SUBJECT: Goal 2E Herbicide; EPA Reg.#707-145; Addendum to Registration File; Mutagenicity Studies
CASWELL#188AAA Accession Nos: 247206, 246780

Recommendations:

1. The submitted mutagenicity studies are acceptable with the exception of the Mouse Lymphoma Assay on RH-2915 technical.

2. A full report of the Mammalian Cell Point (Mouse Lymphoma) Assay on RH-2915 technical is required to be submitted.

Review:

1. Goal Technical Cytogenetic Study in Rats (Rohm and Haas Report#81R-261; 3/10/82)

Test Material: Goal technical; (TD 81-306; 72.5% a.i., Lot No. 2-3985)

The test material was administered orally in corn oil acutely or subacutely (5 days) to groups of 8 male Sprague-Dawley rats at dosages of 0 (vehicle), 0.12, 0.48 and 1.19 grams/kg. A positive control group received a single intraperitoneal dose of 0.3 mg/kg of triethylenemelamine. Animals were killed and bone marrow slides prepared at approximately 6, 24, and 48 hours after the acute dose, 24-hours after the positive control dose, and 6-hours after the final subacute dose.

Results: Three rats died in the 1.19 g/kg subacute group. The test material did not produce chromosomal aberrations in the bone marrow cells of rats under the conditions of the assay.

Classification: Acceptable

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2. Abstract Taken From the Submission

Mammalian Cell Point Mutation Assay on RH-2915 Technical - Preliminary results; final report not available at this time; tested by Litton Bionetics, Kensington, MD 1981.

RH-2915 technical (72.5% a.i., TD 81-306; Lot 2-3985) was tested for mutagenic activity at the thymidine kinase (TK) locus in the Mouse Lymphoma L5178Y (TK $^{+/-}$) cells both with and without rat liver S-9 metabolic activation. Cells were exposed to the test compound dissolved in dimethyl sulfoxide for 4 hours at 37°C in Fisher's mouse leukemia medium supplemented with L-glutamine, sodium pyruvate, and 10% horse serum. After treatment, cells were grown for 2 days and then cloned into agar containing 5-bromo-2'-deoxyuridine to select for TK locus mutants. After incubation for approximately 10 days, the mutant colonies were counted and compared to the results of simultaneous negative controls.

Without activation, concentrations of 62.5 to 1000 g/ml (approximately 75 to 8% relative growth, respectively) resulted in mutant frequencies similar to negative control values. With a metabolic activating system (9000 xg supernatant from Arochlor-induced rat livers), the mutant frequency was significantly increased (2.6 to 4.1 times background) after treatment with 15.6 and 31.3 g/ml which yielded approximately 34 to 19% relative growth, respectively. Therefore, Rh-2915 technical is mutagenic in the Mouse Lymphoma Assay, in the presence of an activation system.

Classification: Unacceptable

(a) Full report not provided.

3. Mammalian Cell Point Mutation Assay (LBI Project No. 20989; February, 1982)

Test Material: RH-2915; (99.7% a.i., TD 81-308; Lot LN-0453)

The test material was tested for mutagenic activity at the thymidine kinase locus in the mouse lymphoma L5178Y (TK $^{+/-}$) cells both with and without S-9 metabolic activation.

Results: Pure RH-2915 was not mutagenic in the mouse lymphoma assay both in the absence and presence of an activation system.

Classification: Acceptable

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4. Goal Technical: Microbial Mutagen Test Results (Rohm and Haas Report No. 80R-247; February 3, 1982)

Test Material: RH-2915; (72.5% a.i., TD#80-179, Lot#2-3985)

The test material was tested at concentrations ranging from 1.0 to 7,500 ug/plate both with and without S-9 metabolic activation in Salmonella typhimurium strains TA1537, TA1535, TA100, and TA98.

Results: Statistically significant positive results were obtained on the following strains at the following concentrations: TA1537 at 2500 ug/plate and above with activation and 6000 ug/plate and above without activation; TA98 at 500 ug/plate and above with activation and 1000 ug/plate and above without activation; and TA100 at 250 ug/plate and above with activation and 2500 ug/plate and above without activation.

Classification: Acceptable

5. Goal Technical, purified: Microbial Mutagen Test Results (Rohm and Haas Report#80P-384; August 26, 1981)

Test Material: RH-2915, purified, (99.7% a.i., TD#80-180, Lot#TTF068)

The test material was tested at concentrations ranging from 1.0 to 7,500 ug/plate both with and without S-9 metabolic activation in Salmonella typhimurium strains TA1537, TA1535, TA100, and TA98.

Results: The test material was not mutagenic in this assay.

Classification: Acceptable

6. Goal (polar fraction): Microbial Mutagen Assay (Rohm and Haas Report#82R-80; March 31, 1982)

Test Material: Goal (Lot#WJZ1861, polar fraction from Lot#2-3985; TD#81-59B)

The test material was tested in concentrations ranging from 50 to 7,500 ug/plate both with and without S-9 metabolic activation in Salmonella typhimurium strain TA98.

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Results: The polar fraction was mutagenic both with and without metabolic activation at 50 ug/plate and above.

Classification: Acceptable

7. RH-2915 Technical: Unscheduled DNA Synthesis Assay in Primary Rat Hepatocytes (LBI Project#20991; March, 1982)

Test Material: RH-2915; (73% a.i., TD#81-561; Lot#7530)

UDS was assayed at eight concentrations ranging from 0.1 to 25 ug/ml.

Results: Cell survival ranged from 0 to 99.5%. Net nuclear grain counts at all test levels were comparable to controls.

The test material is negative in this assay.

Classification: Acceptable

8. Polar Fraction from RH-2915: Unscheduled DNA Synthesis Assay in Primary Rat Hepatocytes (LBI Project#20991; March 1, 1982)

Test Material: Polar fraction from RH-2915; (Lot#2-3985)

UDS was assayed at seven concentrations of the polar fraction ranging from 0.1 to 10 ug/ml.

Results: Cell survival ranged from 64 to 103%. At 25 ug/ml, cell survival was zero and could not be assayed. Net nuclear grain counts at all test levels were comparable to controls. The test material is negative in this assay.

Classification: Acceptable

William Dykstra, Ph.D WHD SDC 5/18/82
Toxicology Branch
Hazard Evalution Division (TS-769)

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