

US EPA ARCHIVE DOCUMENT

BB-12/13
T12-2166



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

MEMORANDUM

9/2/82

002166

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Oxyfluorfen; EPA Reg.#707-145; Mutagenic Assay
CASWELL#188AAA Accession#247909

Recommendations:

The mammalian cell point mutation assay is unacceptable. To be considered acceptable, the following questions are required to be addressed:

- a) There was no NOEL established in the activation assay.
- b) The test material was not tested in the non-activation segment below the level of precipitation.
- c) Untreated mutation frequencies were not run.
- d) The mutant frequencies of the solvent controls are very erratic.

Review:

Mutagenicity Evaluation of RH-2915 Technical in the Mouse Lymphoma Forward Mutation Assay (LBI Project No. 20989; June, 1982)

RH-2915 technical (72.5% a.i., TD 81-306, Lot No. 2-3985) was tested for mutagenic activity at the thymidine kinase (TK) locus in the Mouse Lymphoma L5178Y (TK+/-) cells both with and without Aroclor 1254-induced 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 or 3 days and then cloned into agar containing 5-bromo-2'-deoxyuridine or trifluoro thymidine to select for TK locus mutants. After incubation for approximately 10 days, the mutant colonies were counted and compared to the results of simultaneous solvent controls.

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Results:

Without activation, concentration of 62.5 to 1000 ug/ml, which yielded 75.2 to 7.6% relative growth, resulted in mutant frequencies similar to negative control values. Cultures treated with concentrations of 62.5 ug/ml and higher appeared cloudy and contained precipitate.

With a metabolic activating system (9000 xg supernatant from Aroclor 1254-induced rat livers), the mutant frequency was significantly increased 1.9 to 3.5 times background) after treatment at all doses. These increases in mutant frequency were sporadic but were confirmed in 4 of 5 independent trials of the assay and occurred most consistently at high toxicities (10 out of 13 treatments with less than 20% relative growth; 9 out of 32 treatments with 20 to 50% relative growth).

Conclusion:

RH-2915 technical is mutagenic in the presence of an activation system.

Classification: Unacceptable

To be considered acceptable, the following questions are required to be addressed:

- a) There was no NOEL established in the activation assay.
- b) The test material was not tested in the non-activation segment below the level of precipitation.
- c) Untreated mutation frequencies were not run.
- d) The mutant frequencies of the solvent controls are very erratic.

WJD for LDC 8/16/82

William Dykstra
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