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TR-2166

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.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.

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.

WDD for LDC 8/16/82

William Dykstra

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