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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: December 14, 1981
SUBJECT: Effect of oryzalin on DNA repair, TB/HED comment on.
TO: PM Mr. R. Taylor
Registration Division (TS-767)
FROM: Mary L. Quaife, Ph.D.
Toxicology Branch/HED (TS-769)

EPA #'s 1471-96, 102, and 112, and 100
Caswell No. 623A

E. Lilly & Co.
Greenfield, Indiana

Conclusion: Oryzalin tech. did not induce DNA repair synthesis in cultured rat hepatocytes. Thus, it was negative for mutagenicity in this test.

Comment: Study is judged to be a valid one.

Test material: Oryzalin tech., from Sodeyco, Charlotte, N.C., Lot X28607. Appendix A (copy attached - 3 pp.) gives analytical characterization of it.

Procedure: To primary cultures of adult rat hepatocytes - from liver of a M Fischer 344 rat - were added tritiated thymidine and appropriate dilutions of solvent, test compound, or positive controls. Cultures were incubated, 20 hrs, and media were removed. Cultures were washed and fixed; stained with 1% aceto-orcein; and air-dried. Air-dried, stained slides were dipped into liquid photographic emulsion; developed; and fixed. Unscheduled DNA synthesis was quantified by counting, under oil-immersion, light microscopy, silver grains in cell nuclei less those in cytoplasm (background). Such counts were made for test compounds at the highest concentration that did not produce pronounced cytotoxicity and at lower concentrations.

Results: Cytotoxicity resulted from exposure to 500 or 1,000 nmoles/ml of N-methyl-N'-nitro-N-nitrosoguanidine or to 10 to 1,000 nmoles/ml, inclusive, of 2-acetylaminofluorene, respectively, ultimate and pro-carcinogen positive controls. No effects were seen in dimethylsulfoxide (solvent) negative control cultures. Cytotoxicity occurred at 500 or 1,000 nmoles/ml of oryzalin. Neither cytotoxicity nor induction of unscheduled DNA synthesis was observed in cultures treated with 0.5 to 100 nmoles/ml, inclusive, of oryzalin.

Introduction: Unsolicited study, "The Effect of Oryzalin on the Induction of DNA Repair Synthesis in Primary Cultures of Adult Rat Hepatocytes," #810217-337-UDS, by G. S. Probst, L. E. Hill, and W. H. Jordan, E. Lilly & Co., Greenfield, Indiana, June, 1981, Acc. No. 246259, is reviewed above, requested by PM.

Oryzalin toxicology review

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Pages 2 through 4 are not included in this copy.

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