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

001598

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

DATE: March 29, 1982

SUBJECT: Supona; Re-Evaluation of Mutagenicity Studies (Caswell No. 187, Acc. No's. 232132 and 243716, EPA Reg. No. 59-Q).

FROM: George Z. Ghali, Ph.D.
Review Section IV
Toxicology Branch, HED (TS-769)
G. Ghali 3/29/82

TO: George T. La Rocca
Product Manager (15)
Registration Division (TS-769)

THRU: Christine F. Chaisson, Ph.D. C.F. Chaisson 3/30/82
Review Section IV
Toxicology Branch, HED (TS-769)

Registrant: Burroughs Welcome
Cornwallis Road
R.T.P., N. C. 27709

Action Requested:

Re-evaluation of the following mutagenicity studies:

1. DNA Repair in E. Coli.
2. L5178Y/TK$^{+/-}$ Mouse Lymphoma Cells.

Conclusions and Recommendations:

1. Supona is mutagenic in the Ames/Salmonella test (TA 98 and TA 100).

2. No evidence of DNA damaging potential was detected in E. Coli except for a marginal and equivocal response obtained with strain WP 100. This in fact agrees entirely with our previous conclusion.

3. Re-evaluation of the mutagenicity data in the mouse lymphoma cells L5178Y/TK$^{+/-}$ indicated that the test chemical caused an appreciable increase in the number of mutant cells over the background. More reliable data could have been obtained if the doses tested were more closely situated on the dose-response curve. Furthermore, major deficiencies were observed, these deficiencies may raise questions as for the validity of the study and hence the reliability of data. The results of this test were submitted in a summary form with no individual replicates. For further consideration and more defenitive conclusion the raw data have to be submitted for review, and until then this test should be considered positive.

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Background Information:

In a review by Van Ormer, dated 10/9/78, Supona was reported to be mutagenic in the mouse lymphoma cells L5178Y/TK $^{+/-}$.

In a subsequent review by George Ghali, dated 6/18/81, Supona was reported to be mutagenic in Salmonella typhimurium TA 100 and TA 98. The report also indicated that marginal and equivocal response was obtained for DNA damage in E. Coli (WP 100).

As a result of a meeting with the registrant on 10/2/82, a re-evaluation of these studies was suggested.

Re-evaluation Results:

The test chemical is mutagenic in the Salmonella typhimurium TA 100 with and without metabolic activation and in TA 98 without metabolic activation. The average increase in the number of revertant colonies was 2-4 fold of the spontaneous reversion background. Metabolic activation decreased the mutagenic effect.

When Supona was tested in the E. coli DNA repair assay, a marginal and equivocal response was obtained with strain WP 100. No evidence of DNA damaging potential was detected with other strains both in the presence and absence of the activating system.

Re-evaluation of the mutagenicity study in the mouse lymphoma cells L5178Y/TK^{+-} indicated that the test chemical caused an appreciable increase in the number of mutant cells over the background. This increase ranged from 1.25 to 1.6 fold with and without activation. The data further indicated that a dose-response curve and a higher mutation rate (at a higher survival rate) could have been obtained if the change in the concentration was in smaller increments and the doses tested were more closely situated. Furthermore, major deficiencies with respect to the response to positive controls, the range of S-9 tested, the number of replicates and the reproducibility of the test were observed. These deficiencies may raise questions as for the validity of the test and hence the reliability of the data.

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