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

JUN 7 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of "Justification for Dose Selection in New Methanearsonic Acid (MAA) Mouse Oncogenicity Study (April 28, 1988) EPA ID # 013802. Caswell ~~CAS~~ No. 582 & 549A

TO: Dr. Gerry Werdig
Data Call-In Program
RD (TS-767)

FROM: William L. Burnam
Deputy Chief
Toxicology Branch/HED (TS-769)

WLB 6/2/88

Background

Roger Gardner in his 2/24/87 memo to you had previously agreed with the registrant that the mouse study should be terminated due to increased mortality in many dose groups. I have reviewed Fermenta's new proposals for dose selection in a new mouse onco study. These had been sent to Barbara Briscoe in April but my copies were hand-delivered by Mr. Jerry Lucietta (Fermenta). ~~and have no bean sheet.~~

Discussion

The results of the terminated 42 week study indicate the following:

1. MAA - related mortality in males at doses $\geq$ 1100 ppm and females $\geq$ 2500/1800 ppm

2. Body weight gain was decreased in males at dose $\geq$ 2500/1800 at 13 week into the 42 week study but at 42 weeks, gain was down even in the lowest dose of 300 ppm (23%).

   In females, the lower doses of 300 agnd 1100 ppm had some decrease at 13 weeks whereas at week 42, even the lowest dose of 300 ppm had a 15% decrease.

3. At terminal necropsy, there were dose related changes in the caecum contents even at 00 ppm. In both females and males, there were increasing incidents of metaplasia in the caecum, colon and rectum at all doses.

4. The summary of the 90 day feeding study using doses of 0, 10, 100, 50 and 1250 ppm showed no adverse on any parameter e.g., body weight gain, food intake, signs of toxicity, pathology.

Conclusion

There seems to be cummulative effects of MAA which manifest themselves after 13 weeks and before 42 weeks. It is unknown what happens after 42 weeks and if this toxicity continues to accumulate.

Based on all toxicity seen in the 90 day and the 42 week study, I would recommend doses slightly higher than 300 ppm as the highest dose tested e.g., 400 ppm with the next dose 200 ppm. I agree that two additional lower doses should be used.

cc: Frank Sanders
Judy Hauswirth
Roger Gardner

ccm #23