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

SYSTEMS INTEGRATION GROUP, INC. 006563

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Registration No. 3125-319; Bayleton - Accession No. 260443

Caswell No.: 862AA

FROM: George Z. Ghali, Ph.D.
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THRU: Reto Engler, Ph.D., Chief
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Registrant: Mobay Chemical Corporation
Kansas City, MO 64120

1/28/88

Action Requested

Evaluation of miscellaneous toxicology data including:

Report No. 80264	Acute Oral Toxicity of BAYLETON 50% Wettable Powder in Dogs
Report No. 86728	MEB 6447 (Triadimefon) Two-Generation Study with Rats
Report No. 86793	MEB 6447, Triadimefon - Pol Test on E. Coli to Evaluate for Potential DNA damage

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Report No. 90106 — Dermal Absorption of ^{14}C-BAYLETON Applied as a 50% Wettable Powder in Rabbits

Report No. 90297 — Triadimefon - (Interaction of Triadimefon with Liver Microsomes) Studies on Rat and Mouse In Vivo and In Vitro

Conclusions and Recommendations

For Conclusions, Recommendations, and Core Classification of each study in this report, please see the Data Evaluation Records (DERs) for individual studies.

The following is a brief summary on each study.

1. Acute Oral Toxicity of Bayleton 50% W.P. in Dogs, Mobay's Report No. 80264.

   According to the author, "administration of a solution of the 50% WP approximately 2.5 times more concentrated than the strongest finished spray (about 200 mg/kg) resulted in no toxicity, while solutions approximately 12.5 times more concentrated than the strongest finished spray (about 1000 mg/kg) resulted in toxicity in one of the two dogs of each sex."

   The study was classified as Supplemental information.

2. Two-Generation Study in Rats, Mobay's Report No. 86728.

   Bayleton was tested in Wistar rats at levels of 0, 50, or 1800 ppm for 100 days. There were no malformations in the pups. The duration of gestation and the number of still-births were similar in all groups.

   In the low-dose group (50 ppm), reproductive parameters were not affected in all generations. The F1 rats demonstrated a statistically significant reduction ($p < 0.01$) in body weight for gestation days 1, 6, and 15. At autopsy, statistically significant ($p < 0.05$) increases in the absolute and relative ovary weights of F0 rats were also observed at this dose level.

   In the high-dose group (1800 ppm), the growth of F0 and F1 parents and of F1 and F2 pups, as well as their birth weights, were statistically reduced. In the F1

and F2 pups, viability was statistically reduced. In the F2 and F3 pups, the litter sizes were statistically reduced. The fertility, insemination, and gestation indices did not vary between the F0 rats treated with 1800 ppm and the control group. The statistically significant reduction in the number of fertilized females in the F1 1800 ppm group was attributed to the males' greatly reduced willingness to mate. It was shown that the F1 males that did not mate were also the most growth retarded. The F1 males in the 1800 ppm group had approximately 100 percent higher testosterone serum levels than those of the controls; however, no correlation was found between the males' unwillingness to mate and individual testosterone levels.

At autopsy, the 1800 ppm rats demonstrated many variations in organ weights, which were statistically significant. The absolute and/or relative liver weights, which were significantly higher in the males (F0 and F1) and females (F0), are definitely treatment related. This was confirmed by a histologically diagnosed increase of liver hypertrophy in the F1 males of this treatment group.

From the data available, under the conditions of this study, it is concluded that no systemic no-observed-effect level (NOEL) can be set. The systemic lowest-observed-effect level (LOEL) is 50 ppm (low dose) in diet, based on statistically significant reductions in body weights of the F1 females in the 50 ppm treatment group on gestation days 1, 6, and 15. Statistically significant increases in absolute and relative ovary weights in the F0 generation support the selection of this LOEL. The reproductive NOEL is 50 ppm in diet and the reproductive LOEL is 1800 ppm, based on statistically significant reductions in the 1800 ppm F1 pups' mean birth weight, lactational weights and viability for days 0 to 5, and viability for days 5 to 28. Statistically significant differences found in the F2 pups of this high-dose group included reduced litter size, reduced viability on days 5 and 28, and reduced birth and lactational weights. No effects that could be related to treatment were observed in any of the 50 ppm treatment group pups.

The study was classified as Core Supplementary and may be upgraded to Core Minimum upon the receipt of data on food consumption, clinical observations, organ data for the 50 ppm group of the F1 generation, and individual birth weights of pups.

3. Evaluation of Potential DNA Damage in E. Coli, Mobay's Report No. 86793.

The data presented do not support the author's conclusion. The data presented in this report showed no inhibition zones for bacterial growth for the two E. coli strains employed. This may be interpreted as a solvent diffusion problem. If the solvent cannot penetrate the agar layer, it would be impossible to influence the bacterial growth. The study was classified as Unacceptable for possible technical problems in the conduct of the test.

4. Mutagenicity Test on Bacterial System, Mobay's Report No. 89028.

This report included data on 1) recombination assay in B. subtilis, and 2) reverse mutation in S. typhimurium.

The data presented on the recombination assay are insufficient for making an adequate conclusion. The data indicated technical problems in the conduct of the test as reflected by the complete absence of inhibition of bacterial growth in both strains of E. coli. The absence of inhibition zones may be attributed to the inability of the solvent to penetrate the agar layer. The study was therefore classified as Unacceptable.

The data submitted on the reverse mutation assay were inadequate to make a meaningful evaluation and conclusion. The data were presented as summary tables and it was not clear how many replicates were used or whether the data presented were in fact an average of these replicates. No standard deviations were included to assess the variation of these replicates. In addition, the experimental details were lacking in this report.

The study was therefore classified as Unacceptable.

5. Dermal Absorption of ^{14}C-Bayleton Applied as a 50% Wettable Powder in Rabbits, Mobay's Report No. 90106.

The raw data, including radioactivity counting, counting efficiency, levels of radioactivity in the skin wash, blood, and urine at different time intervals, in addition to radioactivity level in the carcass, were not provided in this report. Without these data, a meaningful conclusion cannot be made. The study was therefore classified as Unacceptable.

6. Interaction of Triadimefon With Liver Microsomes: In Vivo and In Vitro Studies on Rat and Mouse, Mobay's Report No. 90297.

The interaction of triadimefon with cytochron P-450 reflects the strong affinity of triadimefon to binding to the microsomal cytochrom. The binding spectra with a maximum absorption peak of 430 nu and a trough at 390 mu in the differential spectrum indicates a typical type II substrate binding spectrum.

Triadimefon is also capable of inducing monooxygenese activity. Female rats are more responsive to induction than males. In mice, at a reasonable nontoxic dose (50 mg/kg), the response in both males and females was quantitatively equal. However, at higher doses (100 mg/kg), the induction was not increased in males, but increased significantly in females. The study was classified as Supplemental information.