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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

FAP#5H5071/PP#5F1571: Monitor in rats - reject letter of 8/8/75, T.A. Gardner, PM # 15.

DATE: SEP 18 1975

TB

T.A. Gardner, PM # 15
and Chemistry Branch

Chevron Chemical Co.
Richmond Calif.

Related Petitions	
0F0956	2G1248 (orthene)
4E1424	3F1375 (orthene)

Subject letter stated that the proposed tolerances of 2 ppm in cauliflower, tomatoes and lettuce and 5 ppm in tomato paste was in excess of the established NEL for ChE inhibition of 1 ppm. This information was included in my review of 1/15/75 in which I also stated that "No new toxicity data accompany the petition". This was true at the time of my review, however, petitioner had submitted toxicity data but it had not reached us. We herewith review these data.

1. 90 day dog feeding study (IBT # c8128, 7/28/70)

Test material (70% AI) was administered once daily to 4 groups of 3 males and 3 females each at levels of 0, 0.025, 0.075 and 0.25 mg/kg BW in gelatin capsules. Blood samples were examined at -14, -7, 0,1,3,6,9,15,28,49,63,77, and 90 days (final day of treatment).

- The dogs were returned to normal diets and an additional sample was obtained at 120 days. The blood was examined for plasma and RBC ChE activity.

- Body weights, food consumption, behavior and general appearance were recorded at suitable intervals.

Results:

Males receiving 0.25 mg/kg BW showed a net loss in body weight for the 90 day period of 0.6 kg compared to a net gain of about 1 kg for the middle, low and control groups.

A well defined RBC-ChE inhibition occurred in the males and females receiving 0.25 mg/kg. Lower doses yielded responses similar to that of the controls.

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Conclusions:

This 90 day oral ingestion study demonstrated a NEL of 0.075 mg/kg/day in dogs equivalent to 3 ppm in the diet.

2. Dog ChE study (IBT# 17081)

This study utilizes a multiple commulative dosing schedule which is not acceptable for tolerance purposes because a single no-effect level can not be determined.

3. 3 Month dog feeding study (FFB Bayer AG # 2164, 6/26/70)

Methods:

4 groups of 2 males and 2 females each were offered diets containing 0, 1.5, 5 or 10 ppm monitor for ninety days. Body weights were recorded weekly and blood and urine samples were a obtained initially, at 1 month and at termination. Clinical examinations were done:

Hb, RBC, WBC, differentials, sed rate, Hct, prothrombin times; ALP, GPT, GOT, Sorbitol DH, LDH, OCT, bilirubin, total protein, BUN and creatinine.

Urinalyses: sugar, protein, blood, sediment, bile salts and PAH-IAH renal clearance data.

ChE activity determination initially and at 1, 4, 8 and 13 weeks by a hydroxamate method.

Organ weights were obtained at termination (no histopathological examinations).

Results:

There were no treatment-related deviations from control values in any of the parameters tested except for ChE activity where the 5 and 15 ppm groups showed significant decrease in activity for the females and the 15 ppm group showed significant decrease for the males.

Conclusion:

The 3 month feeding NEL for monitor in the dog monitor in the dog is at least 1.5 ppm but less than 5 ppm.

4. 90 day rat ChE inhibition (FFBayer AG #2165, 6/29/70).

Levels tested: 0,2, 6, 20 and 60 ppm in the diet
Measurements: Body weight and food consumption weekly;
Hematology (Hb, Hct, RBCs, WBCs, MCH, MCV, differentials and prothrombin times); Clinical chemistry (glucose, cholesterol, ALP, GOT, GPT, OCT, bilirubin and total protein, BUN and creatinine).

Urinalysis (sugar, blood, protein, bile salts and sediments).

ChE activity in plasma and rbcs at 8 days and at 4, 8 and 13 weeks.

Organ weights were obtained at termination.

Results:

Body weights and food intake - 60 ppm males and females showed less weight gain that did others.

Hematology, clinical chemistry, urinalysis and post-mortem findings revealed no noteworthy differences between control and treated groups.

RBC ChE activity - significant loss of activity in 6, 20 and 60 ppm groups.

Conclusions:

The demonstrated NEL for RBC-ChE inhibition in rats is 2 ppm monitor in the diet for 90 days.

Discussion:

In light of this additional information TB can now conclude that the ChE NEL is 2 ppm in ninety day studies based on the most recent rat findings (Bayer AG # 2165). The original 1 ppm NEL was derived from the initial study (IBT # C6484) reviewed by Dr. Quaife in PP#OF0956, review of 10/28/70, which had the next higher "effect level" of 3 ppm.
(All the submitted dog studies had demonstrated ChE NEL of 3 ppm.)

Recommendation:

On the basis of relevant toxicity data, TB can now recommend CB considerations permitting, that the tolerances proposed for residues of the insecticide, Monitor; O,S-dimethyl phosphoramidothioate, at 2 ppm in cauliflower, lettuce and tomatoes be established. We also recommend that the tolerance of 3 ppm in non-human food item,

cottonseed hulls be established.

We cannot recommend favorably for the tomato pomace tolerance of 5 ppm since this is a human food item and this level exceeds 2 ppm.

David L. Ritter 9/15/75

David L. Ritter, Toxicologist
Toxicology Branch
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cc: Branch Reading File FAP#5H5071/PP#5F1571

Initial: O.E. Paynter

DLRitter:gac 9/12/75