Dr. Parkin

ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

003693

Date: August 9, 1972

Reply to Attn of:

Subject: Addendum to memorandum of July 10, 1972 for o-isopropoxyphenyl methylcarbamate (Baygon, Bay 39007) in or on various raw agricultural commodities.

To: Mr. Drew M. Baker, Jr., Chief
Petitions Control Branch
Pesticides Tolerances Division

Pesticide Petition No. 2F1244

Chemagro Corporation
P. O. Box 4913
Kansas City, Missouri 64120

TOXICOLOGICAL EVALUATION

The following studies which are pertinent to our toxicologic requirements were incorporated into Section D of the petition and were not considered in our original evaluation of toxicity data in Section C.

I. The Metabolic Fate of Baygon in the Rat (Chemagro Corp.; 28797).

A. Procedure

1. Individual rats were administered 8 mg/kg of isopropoxy-1,3-14_C or carbonyl-14_C labelled Baygon by intubation. Sodium hydroxide traps for expired gases were sampled at one hour, three hours, at 3 hour intervals thereafter through 54 hours, and at 72 hours. Toluene traps were changed at 12, 24, 48, and 72 hours. Urine and feces samples were collected every 12 hours until sacrifice at 72 hours.

2. A female rat was intubated with 10 mg/kg of labelled Baygon (isopropoxy-1,3-3_H and carbonyl-14_C in a 3_H/14_C ratio of 15:1). Ethanolamine traps for expired gases were sampled each hour for 9 hours and then at 12, 18, and 24 hours. The urine and feces were collected at 6, 12, and 24 hours.

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3. A rat was treated orally with 5 mg/kg of isopropoxy-1,3-14_C labelled Baygon. The expired gases were collected in sodium hydroxide traps for 24 hours after treatment.

B. Results

Rats orally treated with BAYCON eliminated 85% of the administered dose within 16 hours of administration, 20-25% as volatile compounds (CO_2, acetone), and 60% in the urine as conjugates, the remainder in the feces. The major route of metabolism in rats is depropylation to 0-hydroxyphenyl N-methylcarbamates, or hydrolysis of the carbamate linkage to give isopropyl phenol. The minor metabolic pathway is believed to be ring hydroxylation at either the 5 or 6 position with secondary hydroxylation of the α-carbon of the isopropoxy group. An additional metabolic pathway can be drawn from the N-hydroxy methyl metabolite. Metabolites which are ring hydroxylated in the 2 or 6 position form N-conjugates while the others form 0-conjugates.

II. The Acute Oral Toxicity of o-Hydroxyphenyl N-Methylcarbamate to Rats (18608).

Adult female rats were administered this Baygon metabolite suspended in 0.2% aqueous carboxymethylcellulose via stomach tube. Toxic doses produced tremors within one hour and death was preceded by convulsions. Death or apparent complete recovery occurred within a day of treatment. The approximate LD_{50} was 1100 mg/kg.

III. Plant Metabolism of Baygon (Chemagro Corp.; 21746).

Following foliar application of carbonyl and isopropoxy labelled Baygon C^{14} to growing plants (bean and corn) large quantities of Baygon were volatilized from the leaf surface. Baygon comprised 69-98% of the residue remaining after 5 days and 36% of the residue at 14 days. Metabolites tentatively identified were β-glucosides of o-hydroxyphenol N-methylcarbamate and o-isopropoxyphenyl N-hydroxymethylcarbamate and the corresponding unconjugated forms.

IV. Metabolism of Baygon in Corn Plants (Chemagro Corp,; 29233).

Baygon accounted for 50% of the residue at the 14-day sampling interval. β-glucosides of o-hydroxyphenyl-N-methylcarbamate

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and o-isopropoxyphenyl-N-hydroxymethylcarbamate accounted for 19.2 and 3.5% of the remaining activity. Most of the 9.6% unidentified activity was associated with solids and 17.6% was lost probably due to hydrolysis of the carbamate moiety.

DISCUSSION

The petitioner has fulfilled requirement #3 of Dr. M.L. Quaife in her review of PP# 9C0765 (April 7, 1969) with the above data. The metabolic pathways of Baygon on treated commodities and in the rat appear to be very similar. The major metabolites are identical in beans, corn, and the rat.

The principal metabolite, o-hydroxyphenyl N-methylcarbamate, is approximately 10-fold less toxic than the parent compound in the female rat.

Technical Baygon	LD_{50} 87-110 mg/kg
o-Hydroxyphenyl N-methylcarbamate	LD_{50} 1100 mg/kg

RECOMMENDATION

Toxicology Branch considers the metabolism requirement (#3) to now be fulfilled. The present petition is still considered deficient until requirements #2,4, and 5 (memo of July 10, 1972) are met.

William E. Parkin, D.V.M., D.P.H.
Toxicology Branch
Pesticides Tolerances Division

cc: JCCummings
PRD/EPA
Atlanta Branch (CLewis)
Perrine Branch
Division Reading File
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