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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Baygon; Metabolism Study

TO: Jay S. Ellenberger (PM 12)
Registration Division (TS-767)

11/29/83

FROM: Robert P. Zendzian Ph. D.
Toxicology Branch
HED (TS-769)

THROUGH: William Butler, Head
Review Section III

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Registration No. 2F1244
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Tox Chem No. 508

Registrant Mobay

O-isopropoxyphenol has been identified as a major metabolite of Baygon (o-isopropoxyphenyl N-methyl carbamate) in the liver and kidney of cows at 0.04 and 0.22 ppm respectively. Based on this observation Toxicology Branch requested a rat metabolism study of Baygon in order to determine if this compound was also a metabolite of Baygon in the rat. If the rat metabolism study shows that o-isopropoxyphenyl and/or its conjugate is a major metabolite of Baygon it is of no toxicological concern since the metabolite would have been tested in the process of toxicology testing of Baygon in the rat.

The registrant has replyed to the Agency's request and has presented its case that sufficient information exists to make the metabolism study unnecessary. The information submitted has been reviewed and it is concluded that the rat metabolism study is not necessary. Further it is concluded that the residues of o-isopropoxyphenyl in the cow liver and kidney are of no toxicological concern.

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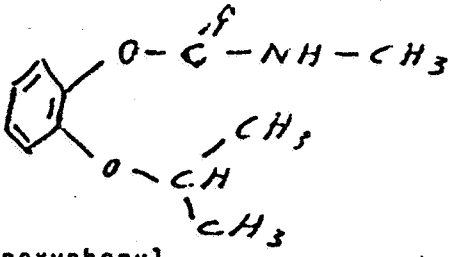
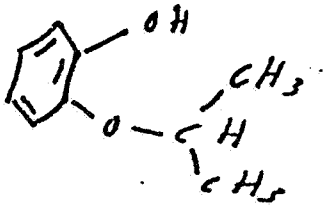
Baygon (o-isopropoxyphenyl N-methyl Carbamate)



O-isopropoxyphenyl



Esterases capable of catalyzing the hydrolytic production of o-isopropoxyphenyl are ubiquitous in vertebrate species. The information from the cow study indicates that the hydrolysis was probably performed in the liver and the metabolite was in the process of being excreted by the kidney probably as a conjugate. Mobay has submitted information showing that this metabolite is produced in man and the rat.

Dawson et. al. (1964) have reported the results of a study to determine human exposure to Baygon by detecting the o-isopropoxyphenyl metabolite in the urine. After developing two methods to detect the metabolite in urine the authors performed two experiments with humans. In the first experiment six male volunteers each took a single dose of the metabolite (92.2mg) orally and 24 hours urine was collected. The urine samples were processed and examined by gas chromotography. O-isopropoxyphenyl was detected in the urine of all individuals. Three subjects took 50mg of Baygon orally and 24 hour urine was collected. O-isopropoxyphenyl was detected in all three urine samples. Recovery was established as 98.5%.

Three studies were submitted showing the production of o-isoproproxyphenyl in the rat. Everett and Gronberg(1971) studied the metabolism of radio labeled Baygon in the rat. The compound was administered orally and 24 hour excreta and expired air were collected. The major urinary metabolites were identified as 2-hydroxyphenyl-N-methylcarbamate and o-isopropoxyphenyl. These represented 60% of the administered compound and were excreted as conjugates.

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Foss and Krechniak (1980) administered propoxur (Baygon) by the intravenous and the oral routes to rats and determined its metabolic fate. Following a single intravenous dose of 5mg/kg, o-isopropoxyphenyl was detected in tissue within ten minutes. Urinary excretion was biphasic with over 95% excreted in the first rapid phase (half-life 7 hours). A single oral dose of 50mg/kg was rapidly absorbed, with the highest blood levels found in fifteen minutes. O-isopropoxyphenyl was found at highest concentrations in tissue 2 to 4 hours after dosing. The majority of the dose was excreted in the urine in the first 12 hours after dosing.

Abd-Elraof et. al. (1981) reported that the metabolism and excretion of propoxur (Baygon) was not effected in Long-Evens rats treated with lead. O-isoproxyphenyl and 2-hydroxy-methyl-phenylcarbamate were the major metabolites.

These studies clearly show that o-isopropoxyphenyl is a major metabolite of Baygon in the rat and that it appears in the tissue shortly after dosing. Thus in any toxicology study of Baygon in the rat one is also studying this metabolite. On this basis one can conclude that the quantity of metabolite found in liver and kidney is of no toxicological concern.

References

Dawson, J.A., D.F. Heath, J.A. Rose, E.M. Thain & J.B. Ward, The Excretion by Humans of the Phenol Derived in vivo from 2-Isopropoxyphenyl-N-Methylcarbamate, Bull. Wld Hlth Org. 1964, 30, 127-134

Everett, L.J. & R.R.Gronberg, The Metabolic Fate of ®Baygon (o-Isopropoxyphenyl methylcarbamate) in the Rat. Chemagro Corporation, Aug 3, 1971

Foss, W. & J. Krechniak,The Fate of Propoxur in the Rat. Arch. Toxicol. Suppl. 4. 346-349 (1980)

Abd-Elraof, T.K., W.C. Dauterman & R.B. Mailman. In Vivo Metabolism and Excretion of Propoxur and Malathion in the Rat: Effect of Lead Treatment. Toxicology and Aplied Pharmacology 59, 324-330 (1981)

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