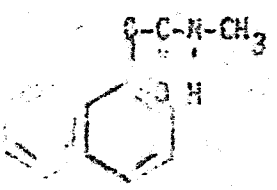
March 17, 1972

Carbaryl, Sevin®, 1-Naphtyl-N-Methyl Carbamate



Dr. Drew A. Baker, Chief
Petitions Control Branch
Pesticides Tolerances Division

File: PP# 2F1220

Pesticide Petition No. 2F1220

Union Carbide Corporation
600 Watt Building
Washington, D.C. 20005

Request for the following tolerance:

5.0 ppm in or on potatoes

Carbaryl has been used extensively for many years and its systemic toxicity is very low. Over the past several years, however, it became apparent that carbaryl is a teratogen depending on the exposure and animal species. The results are summarized in a memo dated Feb. 15, 1970 by Dr. G.E. Whitmore (PP# 9G2). Most species tested that did produce terata did so only at high levels of intake which were sometimes close to the LD_{50}. The dog on the other hand is a very sensitive animal and for it the No-effect level for fetal production is 3 mg/kg/day during the gestation period. Species tested which were not affected are: hamsters, rats, rabbits, gerbils and some strains of mice. Species affected were: dog, some strains of mice, guinea pigs and possibly Sheep.

A primate study was initiated by FDA Contract 67-39 but the results were equivalent because of small numbers of animals and some questions concerning the controls used. There was, however, a suspicion of an increased abortion rate in Cynous monkeys caused by carbaryl.

In a conference of June 2, 1971 between Dr. Weil (Union Institute), representatives of Union Carbide and the Division of Pesticides Tolerances, it was concluded that in order to further consider carbaryl petitions the primate gestation study must be repeated. Only then could a conclusion

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be reached on how much weight should be given to the dog teratogenicity study. Dogs have a different metabolic pathway for carbaryl than rats and other animals.

The two basic pathways of metabolism of carbaryl(c) in animals are hydrolysis to 1-Naphthol(1) and hydroxylation to 4-hydroxy carbaryl(2). These metabolites are then excreted in the urine either directly or as conjugates of glucuronic acid. Monkeys and pigs excrete c and 1; ewes conjugates of c, 1 and 2; man and rat conjugates of 1 and 2. Dogs apparently cannot hydrolyze nor hydroxylate carbaryl even though they can excrete 1-Naphthol *per se* as a glucuronide. It was postulated that dogs must excrete all carbaryl unchanged. (Knaak et. al. J. Agr. Food Chem. 13:537 (65); ibid. 16:1125 (67); ibid. 16:465 (68))

It also should be noted that Carbaryl, on the other hand, is one of the few chemicals which was listed in the definitely "Not Positive" group by the Mrak Committee as far as carcinogenicity is concerned, since acceptable data and adequate testing has been provided using at least two species. (Mrak Committee Report p. 469; 1969)

Recommendation

Since the petition does not contain the requested new primate gestation study the proposed tolerance cannot be supported.

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PM/EP?
Atlanta Branch (CLewis)
Perrine Branch
Division Reading File
Branch Reading File
PP 2F1229

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