March 17, 1972

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

Pesticide Petition No. 77249

Union Carbide Corporation
800 Hyatt Building
Washington, D.C. 20225

Request for the following tolerance:

1.5 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, 1972 by Dr. C.E. Whitmore
(DHA 302). Most species tested that did produce terata did so at high
level of intake which were sometimes close to the LD50. The dog on the
other hand is a very sensitive animal and for it the no-effect level for
lactation is 3 mg/kg/day during the gestation period. Species
tested which were not affected are: hamsters, rats, rabbits, gerbils and
two strains of mice. Species affected were: dog, some strains of mice,
poles pigs and possibly sheep.

A recent study was initiated by FDA Contract 17-22 but the results were
requisite because of small numbers of animals and some concerns concerning
the controls used. There was, however, a suspicion of an increased abortion
rate in certain studies caused by carbaryl.

In a conference of June 2, 1971 between Dr. Hall (Helon Institute), repre-
sentatives of Union Carbide and the Division of Pesticides Tolerances, it
was concluded that in order to further consider carbaryl petitions the
original gestation study must be repeated. Only then could a conclusion
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 in animals are hydrolysis
to 1-Naphthol(1) and hydroxylation to 4-hydroxy carbaryl(2). These meta-
bolites 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; men 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 has 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 (66))

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
NCERL Committee as far as carcinogenicity is concerned, since acceptable
data and adequate testing has been provided using at least two species.
(NCERL committee report p. 409; 1969)

Recommendation

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

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Branch Reading File
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