2,4-D/TOX (9)

November 22, 1971

2,4-D - Dimethylamine Salt of 2,4 dichlorophenoxy acetic acid

Releasable

Mr. Drew M. Baker, Chief
Pesticides Control Branch/PTD

Pesticide Petition No. 1E1046

Dept. of the Army
Corps of Engineers

Request for the following tolerances:

1 ppm in or on fish
1 ppm in or on crops (corn, soybeans, sugar beets, etc.)
0.1 ppm in water

There are several previous petitions (by other petitioners) on 2,4-D and the toxicological evaluation shows consistently a very low toxicity of the compound. For example: PP 7F0589 (memo May 1, 1967 by Dr. H. Quaife) PP 414 (memo Dec. 20, 1965 by Dr. G. E. Whitmore) and PP 272 (memo Dec. 5, 1963 by Dr. G. E. Whitmore).

The present petition does not contain any original toxicity data. The data for this review are derived from a comprehensive FDA study by M. M. Hansen et al (Tox. Appl. Phar. 20, 122 (1971)). Two year rat and dog feeding studies showed no significant effects at 1250 ppm for the rat and at 500 ppm for the dog. Both levels were the highest ones fed to the respective animals. A 3-generation rat reproduction study showed no deleterious effects at a level of 500 ppm (25 mg/kg/day); at 1500 ppm the number of pups surviving to weaning was sharply reduced. The paper makes reference to tumor and/or carcinoma production in rats fed 2,4-D. The data however are not very convincing since statistical analysis was inconsistent. A critical evaluation (memo Oct. 23, 1970 by Dr. H. A. Weinberger) also points out that there is no support of a positive carcinogenic effect of 2,4-D.

Condensation products of some chlorophenoxy acids, the dioxins, have been shown to be highly teratogenic in amounts as low as 0.5 µg/kg/day administered during the organogenic phase of gestation. The teratogenic effect, is dependent on the degree of chlorination of the dibenzo dioxins. The 2,7 dichlorobenzo-p-dioxin which is the expected condensation product of 2,4-D has been shown not to produce terata when fed at a quantity as high as 2 mg/kg/day during the gestation period of the golden hamster. Furthermore at a massive dose of 100 mg/kg/day the technical 2,4-D (Dow Chemical) was not embryotoxic in rats and hamsters.

From the proposed use one can estimate that man's total intake of 2,4-D could not be more than 0.023 mg/kg/day. The feeding and reproduction studies described above show that this level would leave a large margin of safety (500X). Based on the data available, it also can be ruled out that 2,4-D or its possible by-product 2,7 dichlore dibenzo-p-dioxin is producing cancer or terata.

Recommendations

1. Chemistry Branch's considerations permitting, the toxicity data support the safety of the requested tolerances of 2,4-D in or on fish and the raw agricultural crops in question. The requested tolerance of 0.1 ppm in water can be classified as a negligible residue.

2. Some data submitted with the petition however seem to indicate that at least temporarily the 2,4-D concentration in water may be 2 ppm and in fish as high as 39 ppm.

These inconsistencies should be referred to the Chemistry Branch.

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Division Reading File
Branch Reading File
PP #1E1046

NEngler/ccw 11/22/71
Init: GEWhitmore
Init: CWilliams