

PESTICIDE BRANCH

Division of Pharmacology, Toxicology Branch

Evaluation of pharmacological data presented in support of residue tolerances for Sevin requested for poultry meat and various vegetables.

Pesticide Petition Nos. 311 and 318

Union Carbide Chemicals Co.
New York 17, New York
(AP 15-522)

In P.P.311 the petitioners request a tolerance of 5 ppm in poultry meat as a result of treatment of poultry with dust containing Sevin. In P.P.318 the petitioner requests a tolerance of 10 ppm Sevin on cabbage, broccoli, cauliflower, brussels sprouts, kohlrabi, melons, pumpkins, winter squash and carrots.

The following toxicity data have been presented in previous petitions for Sevin. No new data were presented in these petitions.

Acute Toxicity

The mean oral LD₅₀ for rats is 0.54 gm/kg; for guinea pigs 0.28 gm/kg; and for rabbits 0.71 gm/kg.

Although Sevin has a potential for producing weakness and paralysis of the leg muscles, its effect is only about 1/8 of that produced by a similar dosage of triorthocresyl phosphate. However, dosage levels of 1 gm/kg Sevin did not produce this effect. Skin absorption studies in rabbits show that though Sevin is absorbed, it is difficult to give a lethal dose in this manner.

In rats a substantial portion of oral Sevin appears in the urine as alpha naphthol (some free and some conjugated); 10-45% was excreted within 48 hours.

Atropine sulfate was found to control the poisoning effects very well.

Dogs receiving an oral dose of 0.375 gm/kg of Sevin showed slight erythrocyte cholinesterase inhibition (67% of the predosed mean three hours after dosing of 33% inhibition).

With guinea pigs an oral dose of 300 mg/kg Sevin produced a marked effect on erythrocyte, plasma and brain cholinesterase.

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One dog per level received 5, 10, 15 mg of Sevin iv. After 24 hours there was 82% inhibition of plasma cholinesterase of the dog receiving 15 mg and 66% inhibition of the plasma cholinesterase of the dog receiving 10 mg. There was no significant effect on the erythrocyte cholinesterase.

Subacute Toxicity

Subcutaneous injections of 0.2 ml of 0.05% Sevin in agar for twenty weeks produced no apparent increase in tumor incidence in groups of 10 G3H or A/Jax mice.

Five female and 5 male rats were placed on the following levels of Sevin for 90 days. The levels were 0.10, 0.033, 0.011, 0.0035, 0%. There was no effect on mortality, body weight gain, weight of liver or kidneys, micropathology of lung, liver, kidneys or appetite.

In addition 5 female and 5 male rats per group were fed 0.15 and 0.225% Sevin for 96 days. The body weight gain of the females at 0.225% was depressed and the mean liver weight of the males was significantly increased. The mean kidney weight of the females at both levels increased significantly. There was a diffuse cloudy swelling of the kidney tubules. There was no inhibition of the cholinesterase of the brain, liver, erythrocyte or plasma at the end of the 96 day feeding study.

Chronic Toxicity

20 female and 20 male rats per level were fed 0.04, 0.02, 0.01, and 0.005% for two years. In addition to these, additional rats were started and killed at 6, 9, 12, and 24 months of feeding at these levels. There was no effect on the hemocrits of each level at 89, 180, 269, 358, 543, and 726 days of age. After 1 year there was cloudy swelling of the convoluted and loop tubules, primarily in the proximal tubules, in the rats on 0.04% Sevin. At the end of 2 years, there was cloudy swelling of the central hepatic cords of the rats on 0.04% Sevin. In addition the male rats on this same level had decreased body weight gain. Examination of the eyes of the rats receiving Sevin for one year and 36 days showed no cataracts. The "no effect" level in rats was 200 ppm. There was no indication of any carcinogenic effect of Sevin.

Groups of 3 or 4 dogs were fed capsules containing 7.2, 14.4, 0.45 and 0 milligrams of Sevin per kilogram body weight 5 days per week for one year. These dosages approximated 400, 100, 25 and 0 ppm in the dry diet. The organochlorine concluded that there were no gross changes nor permanent degenerative changes in the tissues of any of the dogs which could be charged to treatment. There is mention, however, that sections of the kidneys of dogs which had received the equivalent of 400 ppm in the diet showed cloudy swelling of the convoluted and loop tubules. They state that similar lesions although less severe were present in control dogs. From the examination of the blood on changes in individual dogs Dr. Nelson concluded that there is slight kidney damage, the exact degree of which cannot be determined with the few dogs in this experiment. No blood changes were observed at any dosage level.

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The "no effect" dosage level for the one year dog study lies between 100 and 400 ppm. Due to the very slight effect at 400 ppm we can reasonably assume that 200 ppm Sevin fed for one year would be a "no effect" level in dogs.

Discussion

As stated in our memo on P.P. #193 a residue tolerance of 10 ppm on all fruits and vegetables would allow for a margin of safety of at least 100 fold. Tolerances were established on numerous fruits and vegetables. The extension of the residue tolerances requested in P.P. #318 to additional vegetables will result in the margin of safety remaining greater than 100. The requested tolerance for poultry meat will lower the margin of safety somewhat, but it will remain sufficiently large, within the order of 100 fold.

Conclusion

The proposed tolerances of 5 ppm Sevin on poultry meat and 10 ppm Sevin on various vegetables are safe.

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