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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Chlorpyrifos Registration Standard Follow-up. Dow's response of July 1986 with hen metabolism study. Accession No. 264029, RCB No. 1429

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Dow Chemical Company has submitted a hen metabolism study in response to the chlorpyrifos Registration Standard Guidance package issued September 28, 1984.

Chlorpyrifos is the common name for the insecticide 0,0-diethyl-0-(3,5,6-trichloro-2-pyridyl) phosphorothioate. Tolerances have been established in terms of the parent compound and its metabolite 3,5,6-trichloro-2-pyridinol (TCP) in 40 CFR 180.342 and 21CFR 193.85 and 561.98.

The hen metabolism study is the only data gap the registrant addresses in this submission (part of Section 158.125, guidelines reference 171-4).

The hen metabolism Study No. 6148-102 was conducted by Hazleton Laboratories and dated July 3, 1986. Sixteen hens were divided into 4 groups of 4 birds each. One group served as a control and the other three groups were fed an average dietary level of 20 ppm ring-labeled ^{14}C-chlorpyrifos for 10 days. The poultry diet could contain 4-5 ppm chlorpyrifos (based on established tolerances). Eggs were collected twice daily and egg, excreta, blood, gastrointestinal tract contents and ova were pooled and analyzed by subset. Other tissue samples from the three treated groups were combined before analysis. Tissue samples were collected 12 hours after the last treatment.

Ten percent of the total activity was excreted per day. Total activity calculated as chlorpyrifos was 0.15 ppm in egg yolks and 0.02 ppm in egg whites (after plateauing), 0.198 pm in fat, 0.154 pm in kidney, 0.126 ppm in skin, 0.068 ppm in heart, 0.054 ppm in liver, 0.024 ppm in gizzard, 0.015 ppm in thigh muscle and 0.01 ppm in breast muscle. Total activity averaged 0.037 ppm in blood, 0.28 ppm in gastrointestinal tract contents and 0.169 ppm in ova, calculated as chlorpyrifos.

Total activity in egg white and muscle were considered too low to warrant characterization of the residue. The residue in kidney, egg yolk, liver, skin, fat and excreta was further characterized by TLC and HPLC. In skin and fat, the majority of the residue is chlorpyrifos while the major residue is the pyridinol in the other tissues examined.

In skin, 92% of the activity was extracted with 7% remaining in the tissue; of the total activity, chlorpyrifos was 62% (HPLC) or 77% (TLC) and the pyridinol was 17% (HPLC) or 11% (TLC) with 9% unresolved by HPLC.

In fat tissue essentially all the activity was extracted with 87-88% identified as chlorpyrifos and less than 1% as the pyridinol with 6-7% unresolved.

In kidney, 85% activity was extracted and 8% remained in the tissue. The pyridinol was identified as 71-72% of the total activity, less than 1-2% was chlorpyrifos and 7-8% was unresolved.

Ninty-nine per cent of the activity in egg yolk was extracted with 30-33% identified as chlorpyrifos, 45% (HPLC) or 54% (TLC) as the pyridinol and 12% (HPLC) unresolved.

In excreta, 67% of the activity was extracted with chlorpyrifos as 5% of the total activity, 43% as the pyridinol and 15% unresolved material before hydrolysis. After hydrolysis, less than 1% of the total activity was chlorpyrifos, 51% was the pyridinol and 4% was unresolved.

Liver tissue was also examined before and after hydrolysis. Before hydrolysis, 69% of the activity was extracted with 12% remaining in the tissue; less than 1% each was identified as chlorpyrifos, the pyridinol and origin material with 10% as metabolite D, 7% as metabolite E and 13% unresolved. The material called metabolites D and E did not correspond with available standards and are not identified. The available standards, besides the parent and the pyridinol were 2-methoxy-3,5,6-trichloropyridine, 0,0-diethyl 0-(3,5,6-trichloro-2-pyridyl)phosphate and 0-ethyl 0-(3,5,6-trichloro-2-pyridyl) sodium phosphorothioate. After hydrolysis, 81% of the activity was extracted, 6% of which was aqueous souble and 12% remained in the tissue. This residue consisted of 62% pyridinol with less than 1% of the parent and 4% unresolved material. Apparently, the origin material, metabolites D and E and some of the unresolved residue was converted to the pyridinol by the hydrolsis step.

In summary 74-88% of the residues in skin, fat, kidney and egg yolk were identified as chlorpyrifos or its pyridinol metabolite and sixty-two percent of the residue in liver was hydrolyzable to the pyridinol metabolite.

Conclusion

1. The metabolism of chlorpyrifos in poultry has been adequately determined. Chlorpyrifos and its metabolite 3,5,6-trichloro-2-pyridinol (TCP) are the components of concern.

2. As has been previously concluded (R. Loranger memo 3/25/85 and N. Dodd memo 7/15/85) the animal metabolism data gap still needsan adequate dermal (pour-on) cattle study to resolve this deficiency. The registrant should be reminded that the Registration Standard suggested that the additional metabolism study include specific and sensitive analysis for the thiomethyl metabolite, 0,0-diethyl 0-(dichlorothiomethyl, 2-pyridyl) phosphorothioate.

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cc: R.S. File, Chlorpyrifos SF, RF, circu, M.Bradley
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