12-15-88

Erratum

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

DEC 15 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Subject: CHLORPYRIFOS Registration Standard - Revision to Exclu TCP Metabolite from Existing Tolerances; Identifying N 3F2884; Record No. 233507; HED Project No. 9-0196; Caswell No. 219AA.

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To: Dennis Edwards - PM 12
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and

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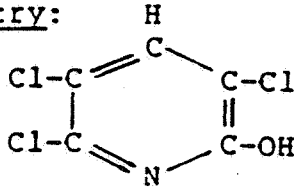
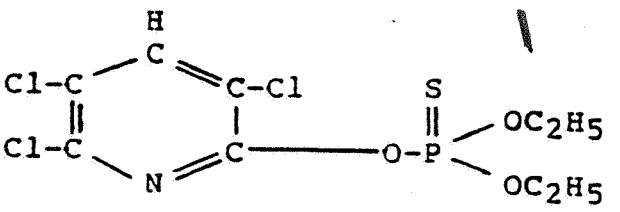
Background: CHLORPYRIFOS tolerances included the parent compound (CHLORPYRIFOS) as well as the metabolite 3,5,5-trichlor 2-pyridinol (TCP). The Registrant has submitted animal data for TCP in anticipation of reregistering CHLORPYRIFOS to exclude the metabolite in the calculatic of the tolerances.

Chemistry:



3,5,6-trichloro-2-pyridinol
[TCP]



O,O-diethyl O-(3,5,6-trichloro-2-pyridyl phosphorothioate
[CHLORPYRIFOS]

Toxicology: A comparison of the data for CHLORPYRIFOS and TCP is tabulated below:

Parameter	CHLORPYRIFOS	TCP
Oral LD50 Mice	M=62 mg/kg	M=380 (333-433)mg/kg F=415 (367-469)mg/kg flacid paralysis,dyspnea
Oral LD50 Rats	M=163 (97-276)mg/kg F=137 (97-188)mg/kg	M=794 (709-889)mg/kg F=870 (758-1009)mg/kg flacid paralysis,dyspnea slight salivation
90-Day Rat Feeding	None Required	Doses: 10,30,100 mg/kg NOEL = 30; LEL = 100 apparent increase liver and kidney weights
Chronic Dog	2-Year; doses:0.01,0.03, 0.1,1.0,3.0 mg/kg; increase liver weight 3.0; ChE NOELs: plasma= 0.01, RBC=0.1, Brain=1.0	1-Year; doses:3,12,48 mg/kg; NOEL=3; LEL=12; decrease in BW gain at 12 & 48; alk. phos. & ALT elevated M at 48 & F at 12 & 48
Oncogenic Mice	Doses:0.5,5.0,15.0 ppm (0.075,0.75,2.25 mg/kg No systemic or oncogenic effects	Not Performed
Tox./Oncogenic Rat	Awaiting Report	Not Performed
Teratology Rat	Doses:0.1,3.0,15.0 mg/kg Maternal NOEL=0.1,LEL= 3.0 (ChE inhibition); Developmental NOEL=>15	Doses:50,100,150 mg/kg Maternal NOEL=50, LEL= 100 (decrease BW gain); Developmental NOEL >150
Teratology Mouse/Rabbit	Mouse Doses:1,10,25 mg/kg At 25, increase in maternal deaths & incidence of minor skeletal variations as well as decrease in fetal length; additional dose levels of 0.1,1.0, 10 mg/kg for ChE NOEL plasma & RBC= 0.1.	Rabbit Doses:25,100,250 mg/kg Maternal NOEL=100, LEL= 250 (BW loss during dosing); Developmental NOEL=25, LEL=100 (incr. # fetuses & litters with hydrocephaly or hydrocephaly/dilated ventricles increased in 100 & 250 groups.

Oral LD50, chronic dog and rat teratology data appear to indicate that TCP is less "toxic" (at least 1/4 - 1/6) than the parent compound, CHLORPYRIFOS. Cholinesterase inhibition signs were evident in the CHLORPYRIFOS studies, but not in the studies performed with TCP. The metabolite, TCP, is not an organophosphate chemical.

Conclusion and Recommendation:

From a toxicological standpoint, the Toxicology:Herbicide/Fungicide/Microbial Support Branch feels that the data available indicate that the TCP metabolite is less toxic than CHLORPYRIFOS, th parent compound. Further, TCP is not considered as a cholinesterase inhibitor metabolite. Dietary Exposure Branch permitting, Toxicolog has no objections to removing the term "and TCP metabolite" from the CHLORPYRIFOS tolerance calculations.