

JUN 23 1975

June 28 1975

SUBJECT: Food Additive Regulation for Chlorpyrifos

FROM : TB

TO : PM

Petition No.: 5H5080

Petitioner : Dow Chemical Company

Chemical Name: Chlorpyrifos [0,0-diethyl0-(3,5,6-trichloro-2-pyridyl) phosphorothioate]

Trade Name : Dursban

Recommendation: Establish regulation.

Related Petitions: 9F0817, 3F1306, 3F1370, 4F1445, 5G1595

Established Tolerances: 40CFR 180.342

1.5 parts per million in the meat, fat, and meat byproducts of cattle.

1 part per million in or on lima bean forage and snap bean forage.

0.25 part per million in or on bananas of which not more than 0.05 part per million (negligible residue) shall be present in the pulp after the peel is removed and discarded.

0.25 part per million in milk fat (reflecting negligible residues of 0.01 part per million in whole milk).

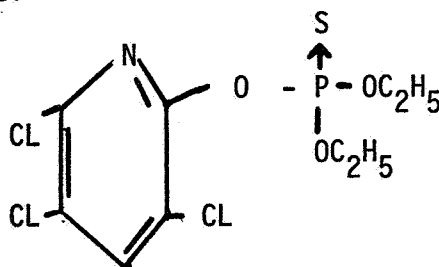
0.2 part per million in the meat, fat, and meat byproducts of turkeys.

0.1 part per million (negligible residue) in or on field corn grain, fresh corn including sweet corn (kernels plus cob with husk removed), and corn fodder and forage.

0.1 part per million (negligible residue) in meat, fat, and meat byproducts of goats, hogs, horses, and sheep.

0.05 part per million (negligible residue) in or on lima beans, peaches, and snap beans.

Chemical Structure:



Molecular Weight: 350.62

Melting Point: crystals 41-42°C

Background Toxicity Data

The following toxicity data have been reviewed during past evaluations of this chemical.

<u>Acute Oral Toxicity</u>		<u>Material in which</u>	<u>LD50 mg/kg body weight</u>
<u>Species</u>	<u>Sex</u>	<u>Chlorpyrifos Administered</u>	<u>(95% confidence limits)</u>
Rat	M	Corn oil	163 (97-276)
		Corn oil	245 (219-273)
		Corn oil	118 (77-181)
		Dursban 24E	713
		Peanut oil	115 (132-181)
		Dursban 25W	410
	F	Water-gum acacia	151
		Corn oil	137 (97-188)
		Dursban 25W	200
		Dursban 24E	356 (243-523)
Guinea Pig	M	Peanut oil	82 (69-97)
Rabbit (white)	M	Corn oil	504 (299-850)
Mouse (white)	M&F	Corn oil	1000-2000
Mouse (white-footed)	M	Water-gum tragacanth	102 ± 8.3*
Chick (leghorn)	M	Corn oil	62
Chicken (white rock)	M	Capsule	32 (14-72)
		Capsule	25.4 (20.8-30.9)
Chick (leghorn)	M	Capsule	25.4 (20.8-30.9)
Chicken (white rock)	M	Capsule	62
Turkey (poult)	M	Capsule	32 (14-72)
(2 wk old)	M	Capsule	25.4 (20.8-30.9)
(12 wk old)	M	Capsule	62

* 24 hour LD50

<u>Species</u>	<u>Sex</u>	<u>Material in which Chlorpyrifos Administered</u>	<u>LD50 mg/kg body weight (95% confidence limits)</u>
Duckling (mallard)	M&F	Water-gum acacia	167 (78.3-357)
Duck (mallard)	M&F	Capsule	75.6 (35.4-161)
Pheasant	M	Capsule	8.41 (2.77-25.5)
	F	Capsule	17.7
Chukar	M	Capsule	61.1 (47.5-78.6)
	F	Capsule	60.7 (43.8-84.1)
Goat	F	Capsule	500-1000

<u>Species</u>	<u>No.</u>	<u>Dosage (mg/kg)</u>	<u>Formulation</u>	<u>Duration (days)</u>	<u>Deaths</u>
Calf	2	125	KM*	4	1
	2	100	KM	5	2
	1	75	Technical	5	0
	2	100	Technical	6	0
	1	500	Technical	3	1
	1	25	2 lb/gal E.C.	3	1
	1	2.5	2 lb/gal E.C.	3	0
	1	5.0	2 lb/gal E.C.	3	0
	3	2.5	2 lb/gal E.C.	3	0
	3	300	CO*	6	1
Cattle	1	250	CMEK*	-	0
	5	300	CMEK	6	2
	2	400	CMEK	9	2
	2	400	KM	-	0
	15	300	CMEK	7	5
	15	300	SM*	7	1
	15	300	KM	7	3
	15	300	CO	7	12
	25	250	KM	6	1
	25	250	KM	14	2
Sheep	25	200	KM	-	0
	25	200	KM	6	1
	4	200	25% WP	8	1
	5	150	25% WP	-	0
	5	100	25% WP	-	0
	5	50	25% WP	-	0
	25	200	KM	6	1
	25	200	KM	6	1

*KM = kaolin + methyl cellulose in water

CO = castor oil + ethanol (80:20)

CMEK = castor oil + methocel + ethanol + kaolin

SM = silica gel + methyl cellulose in water

Signs of toxicity included diarrhea, excessive salivation, labored and rapid respiration, fasciculations, stiffness in hindquarters, difficulty in standing, and anorexia due to loss of tongue control.

Acute Dermal Toxicity

<u>Species</u>	<u>No.</u>	<u>Formulation</u>	<u>Results</u>
Rabbit	3	Undiluted (intact skin)	0 died
	3	Undiluted (abraded skin)	2 died
	3	50% soln in [REDACTED] (intact skin)	2 died
	3	50% soln in [REDACTED] (abraded skin)	2 died
	4	Dursban 24E	LD ₅₀ 3360 (2000-5650) mg/kg
Rats	12	Dursban 25W	LD ₅₀ 2.83 g/kg
	40	Dursban	LD ₅₀ 202 (176-232) mg/kg
Turkey (8 wk old)	5/grp.	4, 8, 16 & 32 lb/A	No ill effects
	2	0.5% spray-saturated	2 died in 6 hours
	2	0.5% spray-mist on heads and backs	No ill effects
	2	0.25% spray-saturated	2 died in 8 hours
	2	0.25% spray-mist on heads and backs	No ill effects
	2	2 gm 25% WP	2 died in 8 hours
	2		
Turkey (10 wk old)	2	3750 mg 25% WP	2 died in 14 hours
	2	1000 mg 25% WP	2 died in 5 hours
	2	500 mg 25% WP	2 died in 4 hours
	2	100 mg 25% WP	1 died in 7 hours
	2	0.5% spray-wetheads & backs	2 died in 24 hours
	2		
Turkey (8 wk old)	5/grp.	4, 8, 16, & 32 lb/A	1 32 lb/A bird became ill
Turkey (20 wk old)	1	25 mg/kg of 25% WP	1 died in 24 hours
	4	20 mg/kg of 25% WP	3 died in 24 hours
	4	14 mg/kg of 25% WP	No ill effects
Calf	1	0.25%	ChE depression
	1	0.5%	Poisoned and survived; ChE depression
Cattle	44	0.1%	ChE depression
	8	0.05%	ChE depression
	16	0.01%	ChE depression
	8	0.005%	ChE depression
	8	0.025%, spray	No ill effects
	8	0.025%, dip	ChE depression
	8		

Inert Ingredient Information is not Included

Eye Irritation (Tech) - slight pain and irritation
Eye Irritation (25W) - moderate irritation and transient corneal haziness for 48 hours
Acute Mice I.P. LD50 - 30.8 mg/kg
Acute Rat S.C. LD50 - >200 mg/kg
Acute Rat Inhalation LC50 - >5 mg/L
Acute Rabbit Dermal (24 E) - moderate to severe irritation
Neurotoxicity In Hens - no paralysis noted

Subacute Toxicity

21 Day Rat Inhalation - a 7 hr/day exposure to 0.007 µg/L produced no deaths or ChE effects
Subacute Rabbit Dermal (Tech) - three to ten applications produced slight hyperemia and slight burns.
Area healed in 21 days.
21 Day Rabbit Dermal (25W) - Produced no irritation
90-Day Rat Feeding - NEL less than 10 ppm (ChE)
NEL 100 ppm (systemic)
20 Week Rat Feeding - NEL 0.03 mg/kg/day
6 month Rat Feeding - NEL 0.15 mg/kg/day
6 Month Monkey Feeding - NEL 0.08 mg/kg/day
2 Year Rat Feeding - systemic NEL >45 ppm (3.9 mg/kg/day)
ChE NEL 2 ppm (0.1 mg/kg/day)
2 Year Dog Feeding - systemic NEL 40 ppm (1.0 mg/kg/day)
ChE NEL 4 ppm (0.1 mg/kg/day)
3 Generation Rat Reproduction ChE-NEL 0.1 mg/kg
NEL for reproductive effects - >1 mg/kg
12 Hour Human Dermal - ChE-NEL less than 5 mg/kg (lowest level tested)

Present Action

Dow Chemical Company has requested that a food additive regulation be established for chlorpyrifos, pursuant to Section 409 of the FDC Act, by addition to 21 CFR 121, Subpart D (food additives permitted in food for human consumption).

The grounds in support of this request are as follows:

--Notice was given in the August 10, 1973 issue of the Federal Register authorizing the use of 16 residual insecticides including chlorpyrifos for crack and crevice treatment in food areas of food handling establishments until October 1974 during which time applicants were advised to submit residue data adequate to support food additive regulations. On June 4, 1974 notice was issued in the Federal Register advising applicants of the availability of a protocol designed to obtain data on the possible transference and levels of residues in food resulting from proper use of residual insecticides in food handling establishments.

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Accordingly, the registrant conducted the required residue studies using a 0.25 or 0.50% water or oil-base spray of chlorpyrifos. According to the registrant, no quantifiable residues of the compound was found in 288 of 289 samples of food prepared, processed, held or served in food handling establishments treated with the insecticide. The one sample contained 0.1 ppm chlorpyrifos, the validated sensitivity of the method.

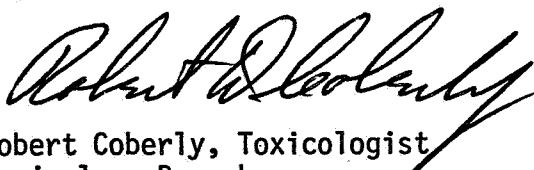
Discussion:

In general, the establishment of chlorpyrifos under a Food Additive Regulation is dependent upon several factors:

- 1) The use of the formulation will not produce undue human health hazards.
- 2) Residues of the active ingredient when applied as directed will not exceed the levels found during the recommended residue study.
- 3) The use concentration will not exceed that used to determine the residues when used according to directions.
- 4) Clearance of the inert ingredients of each formulation under 40 CFR 180.1001(c).
- 5) Adequate label restrictions to prevent the pesticide's contact with food or food contacting surfaces.
- 6) Label restriction permitting only spot or crack and crevice application.
- 7) Label restriction not to treat area more often than every 7 to 14 days.

Conclusion:

The toxicity data and general information supplied by the petitioner will support the request for the establishment of the food additive regulation.


Robert Coberly, Toxicologist
Toxicology Branch
Registration Division

cc: Branch Reading File
RCoberly:BOA:6/18/75
Initials: O.E. Paynter

