2,4-D/TOX

Dr. Parkin (12)

Inert ingredient information deleted from page 4.

ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

releasable

Date: December 18, 1972

Reply to Attn of:

Subject: Request to extend the residue tolerance of 5 ppm for 2,4-D acid and its isopropyl ester in or on citrus to include the 2,4-D butoxyethanol ester from preharvest application.

To: Mr. Lee E. TerBush, Acting Chief
Coordination Branch
Registration Division

Pesticide Petition No. 3E1326

Interregional Research Project No. 4
Rutgers University
New Brunswick, New Jersey 08903

Related Petitions:
167, 272, 414, 6F0459, 6F0477, 7F0589, 8F0670, 1E1046, 1E1122, 1E1136, and 2E1293.

Existing Tolerances:40 CFR 180.142 and 40 CFR 180.165

Use - Weedone LV-4 was applied to the grove floor of citrus groves at a maximum dosage level of 2 lb/acre to kill vine and broadleaf weeds. Two applications will be permitted/year at 30 day intervals with no applications to be made within 5 months of harvest.

TOXICOLOGICAL EVALUATION

No new toxicological data was presented in this petition. Evaluation of the safety of 2,4-D must be conducted from material submitted and reviewed in previous petitions.

I. Pesticide Petition No. 162 reviewed by Dr. O. G. Fitzhugh (5/2/58). Citing no-effect levels of 300 ppm in rats fed 2,4-D for 113 days and 400 ppm in dogs fed for 90 days as well as a Department of Pharmacology study where only minimal changes occurred in the bone marrow of rats fed 1,000 ppm of 2,4-D for 32 weeks, Dr. O. G. Fitzhugh concluded that a tolerance of 5 ppm of 2,4-D (or its sodium salt) on or in asparagus was safe.

II. Pesticide Petition No. 272 and 414 by Dr. G. E. Whitmore (12/5/63)

Chronic toxicity study - dogs (2,4-D) no-effect level 500 ppm

Oyster shell growth - 2,4-D no effect at 2 ppm
2,4-D dimethylamine salt no-effect at 2 ppm
2,4-D butoxyethanol 50% growth decrease 3.75 ppm

Juvenile white mullet fish (2,4-D) no kill at 50 ppm

Longnose kill fish - 2,4-D glycol butyl ether LC_{50} = 4.5 ppm
2,4-D butoxyethanol LC_{50} = 5.5 ppm

Natural phytoplankton communities (4 hr.) - 2,4-D no-effect at 1 ppm
2,4-D dimethylamine salt no-effect at 1 ppm

Mallard ducks (100 days) - 2,4-D acetamide no-effect level 500 ppm
2,4-D butoxyethanol no-effect level 500 ppm
2,4-D dimethylamine no-effect level <500 ppm

Relative toxicity (with DDT = 1) rats 0.2
bobwhites 0.5
pheasants 0.5
mallards 0.5
bluegills 0.1

22-week cattle feeding study (5 doses/week) no-effect at 50 mg/kg

LD_{50} oral rat 2,4-D 300-470 mg/kg
2,4-D sodium salt 610-1060 mg/kg
2,4-D isopropyl ester 570-869 mg/kg
2,4-D mixed butyl esters 320-950 mg/kg
2,4-D mono, bi, tripropylene glycol butyl ether ester 510-640 mg/kg

Dr. Whitmore concluded that a mammalian reproduction study would be necessary to approve tolerance of 5 ppm in or on Irish potatoes and post-harvest use on lemons.

III. Pesticide Petition No. 459 by Dr. O. G. Fitzhugh (3/11/66)

The rat reproduction experiment exhibited no effect levels at 100 and 500 ppm but the 1500 ppm level was very toxic. Dr. Fitzhugh concluded that the proposed tolerance of 0.5 ppm on wheat, barley, rye, and oats is safe (acid form or various salts or esters listed under 40 CFR 180. 142(b)).

IV. Pesticide Petition No. 477 by Dr. G. E. Whitmore (12/20/65)

No new toxicological data submitted so the proposed amendment to include pre-harvest use of 2,4-D on citrus fruit was considered to represent no hazard to the public.

V. Pesticide Petition No. 7F0589 by Dr. M. L. Quaife (5/1/67)

No new toxicological data submitted so the tolerance of 2 ppm in or on apricots was judged safe.

VI. Pesticide Petition No. 8F0670

A. Reviewed by Dr. G. E. Whitmore (3/22/68)

Groups of purebred beagles were fed 0, 10, 50, 100, and 500 ppm 2,4-D for 2 years with no effects noted. Twenty-five rats/sex were fed 0, 5, 25, 125, 625, and 1250 ppm 2,4-D for 2 years also with no effect. Dr. Whitmore adjudged the proposed tolerances of 0.5 ppm on flax seed and rice and 0.2 ppm on grapes, blueberries, cranberries, raspberries, strawberries, corn (field, pop, and sweet), sorghum (milo, milo maize), soybeans, sugar cane, potatoes, alfalfa, clover, trefoil, and soybean hay to be safe.

B. Amendment to include a tolerance of 300 ppm in or on rangeland grasses or pasture grasses reviewed by Dr. C. H. Williams (7/15/71). Summary of previously submitted data presented along with reprints of several published articles describing 2,4-D toxicity in cattle, sheep, and chickens. Dr. Williams concluded that the requested tolerances on the berries and grains were safe but that insufficient data relating to the residues present in meat and milk was available to consider the range grass and forage crops safe.

VII. Pesticide Petition No. 1E1046 by Dr. R. Engler (11/22/71).

No new toxicological data was submitted and that previously submitted supported the request tolerances of 1 ppm in or on fish and 1 ppm in or on crop plants (corn, soybeans, sugar beets).

VIII. Pesticide Petition No. 1E1122 by Dr. W. E. Parkin (2/16/72).

No new toxicity data was submitted but the data previously submitted supported a negligible residue tolerance of 0.1 ppm on or in potato tubers.

IX. Pesticide Petition No. 1E1136 by Dr. C. H. Williams (6/2/71).

No new toxicity data was submitted but Dr. Williams found that the data currently in our files supported the negligible residue tolerance of 0.1 ppm on numerous raw agricultural commodities resulting from the application of 2,4-D to irrigation ditch banks.

X. Pesticide Petition No. 2E1293 by Dr. W. E. Parkin (8/14/72).

No new toxicity data was submitted in this petition. The data previously submitted supported the requested tolerance of 2 ppm in or on apricots (fresh and dry).

DISCUSSION

The ADI for a 60 kg man is 7.5 mg 2,4-D/day based upon a 500 ppm systemic no-effect level in a 2 year dog feeding study. The request to extend the residue tolerance of 5 ppm for 2,4-D acid and its isopropyl ester in or on citrus to include the butoxyethanol ester will not increase the theoretical maximum daily intake of 2,4-D. The theoretical maximum daily intake of 2,4-D is 0.5451 mg - a level well below the ADI (see PP# 2F1293, memo dated 8/14/72).

In their Chemistry Branch memo dated 5/3/66 (PP# 6F0459) Mr. A. E. Houk and Mr. J. Alpert concluded that the miscellaneous esters (including the butoxyethanol ester) were hydrolyzed to the acid during plant metabolism. Animal metabolism studies indicated that no intact ester was eliminated in the urine and the reviewers presumed that the remainder of the ester fed was excreted in the feces. Unless Chemistry Branch now believes that the metabolism of the butoxyethanol ester differs from what was earlier described, TB does not feel that this ester is any more toxic than the acid form or its isopropyl ester.

At TB's request, the petitioner submitted the formulation sheet for Weedone LV-4:

	%/wt.
Active Ingredient	
2,4-Dichlorophenoxyacetic acid, butoxyethyl ester	63.82
Inert Ingredients	[redacted]

All inert ingredients have been granted exemptions from tolerances under 40 CFR 180.1001(c) or (b.3.).

Inert ingredient information deleted.

RECOMMENDATION

TB finds the proposed extension of the tolerance on citrus fruits at 5 ppm to include the butoxyethyl ester to be safe.

William E. Parkin, D.V.M., D.P.H.
Toxicology Branch
Registration Division

cc: Chemistry Branch
Ecological Effects Branch
Division Reading File
Branch Reading File
PP# [redacted] 3E1326

R/D Init:CHWilliams 12/15/72
WEParkin:dtb 12/19/72
Init:C HWilliams
CHW 12/20/72