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Scratch File petition

EEE BRANCH REVIEW

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FISH & WILDLIFE ENVIRONMENTAL CHEMISTRY EFFICACY

FILE OR REG. NO. 464-448

PETITION OR EXP. PERMIT NO. 6F1838

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TYPE PRODUCT(S): (I) D, H, F, N, R, S

PRODUCT MGR. NO. 12-F. T. Sanders

PRODUCT NAME(S) Lorsban

COMPANY NAME Dow Chemical Company

SUBMISSION PURPOSE Midge Control on sorghum

CHEMICAL & FORMULATION Chlorpyrifos-
[O,O-Diethyl-O-(3,5,6-Trichloro-2-Pyridyl)
Phosphorothioate] and aromatic petroleum
derivative solvent

PP#6F1830: Chlorpyrifos in Sorghum. Evaluation of analytical method and residue data.

JUN 23 1976

Alfred Smith, Chemist, Chemistry Branch,
Registration Division (WH-567)

Product Manager No. 12 (Frank T. Sanders)
and Toxicology Branch

Chief, Chemistry Branch

The Dow Chemical Company proposes tolerances for combined residues of the insecticide chlorpyrifos, [0,0-diethyl 0-(3,5,6-trichloro-2-pyridyl) phosphorothioate], and its metabolite 3,5,6-trichloro-2-pyridinol at 0.75 ppm in or on sorghum grain and at 1.5 ppm in or on sorghum forage and fodder.

Tolerances are established for residues of chlorpyrifos (§180.342) on a variety of commodities at levels of 0.05-1.5 ppm. These include tolerances on meat, fat, and meat byproducts of cattle at 1.5 ppm; in milk fat at 0.25 ppm (reflecting negligible residues of 0.01 ppm in whole milk); meat, fat, and meat byproducts of turkeys at 0.2 ppm; meat, fat, and meat byproducts of goats, hogs, horses, and sheep at 0.1 ppm; eggs, meat, fat, and meat byproducts of poultry at 0.01 ppm.

Conclusions

1. The nature of the residue is adequately delineated. Chlorpyrifos and its metabolite 3,5,6-trichloro-2-pyridinol are the significant components of the residue.

2. Adequate analytical methods are available for enforcement of the proposed tolerances.

3(a). Residues in or on sorghum grain or sorghum forage and fodder are not likely to exceed the proposed tolerances. There are no residue data for sweet sorghum varieties or the byproduct syrup. However, label restrictions which prohibit the use of chlorpyrifos on sweet sorghum would alleviate our concern on this question.

3(b). We estimate that residues in hay or fodder will be about 6 ppm following drying of green plants. Therefore, a tolerance to cover such residues should be proposed.

3(c). No data are submitted for sorghum grain milling fractions (bran, germ, starch, flour). Since these items may be used as food or feed, data on the level of residues likely to occur are necessary. If residues in the fractions exceed those in the grain, then food additive tolerance(s) will be necessary to cover such residues (except flour).

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4. Residues could occur in eggs, milk, meat, fat, and meat byproducts of livestock [§180.6(a)(2)]; however, such residues would be adequately covered by existing tolerances.

Recommendations

We recommend against the proposed tolerances. A favorable recommendation is contingent upon resolution of the questions raised in Conclusions 3(a), ~~and~~ 3(b), ~~and~~ 5(c).

Additionally, we believe that the label should be revised to read as follows: "the treated crop is not to be used for forage/fodder, hay, or silage within 14 days after the last treatment.

EEE has raised questions concerning rotational crops. A favorable recommendation is also contingent upon the resolution of these questions.

Detailed Considerations

Proposed Use

Chlorpyrifos is formulated as LORSBAN 4E, an emulsifiable concentrate containing 41% active ingredient, for use on sorghum. (The directions suggest that chlorpyrifos is to be used on sorghum grown for grain instead of the sweet sorghum varieties. If this is the intent, then the label should specify that chlorpyrifos is not to be used on sweet sorghum varieties. Ground or aerial foliar applications are to occur at a broadcast rate of 0.25 lb act/A. First treatment is to occur when 30-50 percent of the seed heads are in bloom and midge adults are present. A second and third application may occur at 3-day intervals as needed, but no more than three applications are permitted.

The treated crop is not to be used for forage or silage within 14 days after the last treatment or for fodder within 70 days after the last treatment.

The formulation's inert ingredients are cleared for use under §180.1001.

The manufacturing process for technical chlorpyrifos and its impurities have been discussed in previous petitions (PP #s 4F1445, 6F1673). The impurity [redacted] The formulation will contain [redacted] at a maximum level of about [redacted] Because of the quantity involved and the dilution factor, the impurity [redacted] and the remaining impurities are not expected to produce a residue problem.

INFORMATION ON PRODUCT IMPURITIES IS NOT INCLUDED

Nature of the Residue

We have discussed the nature of plant (beans, corn) and animal residues in PP #4F1445 and PP #3F1306 [J. Agr. Fd., Chem., 15, 127 (1967)]. Metabolism studies with radio-labelled chlorpyrifos and its metabolite 3,5,6-trichloropyridinol (TCP) show that chlorpyrifos is absorbed from soil and foliar applications and translocated in plants. Chlorpyrifos is metabolized and/or degraded in soil and plants to yield TCP which could be conjugated. (The residue method could determine bound residues.) TCP is metabolized via dechlorination and formation of diols and triols with subsequent cleavage of the pyridine ring. The oxygen analog of chlorpyrifos has not been noted.

In animals (rats, cows, pigs, chicken), metabolism occurs via oxidation and hydrolysis to water-soluble phosphoric acid derivatives, and such components are excreted primarily in the urine. The hydrolysis product, TCP, is excreted either intact or is further metabolized to small carbon fragments. The oxygen analog of chlorpyrifos has not been noted. The significant components of animal residues are the parent and its metabolite TCP.

A question has been raised in previous reviews concerning an unidentified 3,5,6-trichloro-2-pyridinol (TCP) derivative (PP #3F1306, memo 5/6/76, R. D. Schmitt; PP #6F1745, memo 6/1/76, A. Smith). This TCP derivative comprised a major portion of the residue in a corn metabolism study. The petitioner was asked to identify this component.

The corn metabolism study was repeated by the petitioner using ring-labelled ^{14}C-chlorpyrifos. The major component of the plant residue was shown to be the parent compound chlorpyrifos. Minor components of the residue included the metabolite TCP and possibly its glucose conjugate (see amendment to PP #6F1745, dated 9/9/76). This alleviates our concern on this point.

Characterization was performed by thin-layer and paper chromatography using radioautographic techniques and combined gas chromatography-mass spectrometry analytical techniques.

The nature of the residue is adequately delineated. Chlorpyrifos and its metabolite 3,5,6-trichloro-2-pyridinol are the significant components of the residue.

Analytical Methods

Chlorpyrifos - a sample of grain, forage, or fodder is extracted by blending with acetone, filtering, and concentration of the filtrate. The residue is partitioned into hexane and cleaned up using a hexane/acetonitrile partitioning followed by a silica gel column treatment. The

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hexane eluate is evaporated to dryness, and the residue is taken up with acetone. Chlorpyrifos is determined in an aliquot by gas-liquid chromatography (GLC) using a flame photometric detection system.

The presence of chlorpyrifos in a sample is confirmed by alkaline hydrolysis of the final solution. The hydrolysis yields TCP. The trimethyl silyl derivative of TCP is formed by treatment with N,O-bis(trimethylsilyl) acetamide. The derivative is then determined by GLC using an electron capture detection system.

Untreated (control) samples of sorghum grain, green and dry plants, and silage had average chlorpyrifos-equivalent residues of <0.001-0.05 ppm. (Samples from Stoneville, Mississippi had occasionally high and variable control values for both chlorpyrifos and TCP. The values were inconsistent when compared with controls from other areas. The pattern strongly suggest contamination and/or mishandling of samples. The high control values were not included in the calculation of averages. Moreover, the presence of these values do not adversely affect the overall validation procedure or residue data.)

Samples of grain, green and dry plants, and silage were fortified with chlorpyrifos at levels of 0.01-5.0 ppm. Recoveries averaged 72-102%.

3,5,6-Trichloro-2-pyridinol(TCP) - samples of sorghum grain, green and dry plants, and silage are extracted by heating with alcoholic sodium hydroxide which hydrolyzes any chlorpyrifos present to TCP. (The method involves assay for total TCP. Thus, chlorpyrifos is determined separately, and TCP originally in the sample is determined by difference.) The mixture is filtered, and an aliquot is concentrated, acidified with hydrochloric acid, and the TCP is extracted into benzene. The benzene extract is cleaned up on an alumina column using ethyl ether/buffer as the eluting solvent. The TCP residues are extracted into sodium bicarbonate which is acidified and extracted with benzene. An aliquot of the benzene phase is treated with N,O-bis(trimethylsilyl) acetamide to form the pyridinol trimethylsilyl derivative. The derivative is determined by GLC using an electron capture detector.

Control samples of sorghum grain, green and dry plants, and silage had average chlorpyrifos-equivalent residues of 0.004-0.059 ppm. (For a discussion of control values, see under chlorpyrifos determination.)

Control samples of grain, green and dry plants, and silage were fortified with TCP, chlorpyrifos, or TCP and chlorpyrifos at levels of 0.05-3.0 ppm. Recoveries averaged 73-94%.

Successful method trials have been performed with chlorpyrifos on peaches at levels of 0.025 ppm and 0.05 ppm and beef fat at levels of 0.1 ppm and 0.5 ppm (PP #3F1306, memo 6/12/73, J. E. Mayes). A successful

trial has been performed on bananas with TCP at levels of 0.05 ppm and 0.10 ppm (PP #3F1370, memo 9/25/73, F. D. R. Gee) and beef fat at levels of 0.1 ppm and 0.5 ppm (PP #3F1306, memo 11/1/73, F. D. R. Gee).

We believe the results of the method trials can be extended to include sorghum grain and forage and fodder.

Adequate analytical methods are available for enforcement of the proposed tolerances.

Residue Data

Treatments are to occur when 30-50% of the seed heads are in bloom and at 3-day intervals to a maximum of three applications. This procedure provides a built in PHI for the grain of about 30 days or more.

Samples were obtained from crops which had been treated in the proposed manner. The grain had combined residues of <0.05-0.58 ppm at intervals of 38-72 days after the last treatment. As a result, we conclude that residues in sorghum grain are not likely to exceed the proposed tolerance (0.75 ppm) from the proposed use. There are no data for sorghum grain milling fractions (bran, germ, starch, flour). Such data are necessary since such items may be used as food or feed. If residues in the fractions exceed those in the grain, then a food additive tolerance will be necessary to cover such residues.

Green plants had combined residues of 1.68-5.18 ppm at 0-day, 0.53-0.66 ppm at 2 days after the last treatment, and 0.16-1.34 ppm at 7-15 days after the last treatment. Silage stage green plants had combined residues of 0.29-0.74 ppm at 28 and 29 days after the last application. The dry plant had <0.07-1.98 ppm at 38-47 days, and 0.34-1.25 ppm at 72 days after the last application. The green plant is usually cut for fodder or hay at the dough stage and dried. No data are given for the level of residues expected in fodder or hay when dried. By using a dry down factor of 4, we estimate that residues in fodder or hay would be about 6 ppm. Therefore, a tolerance proposal is necessary for such residues.

We conclude that combined residues of chlorpyrifos and its metabolite TCP are not likely to exceed the proposed tolerance of 1.5 ppm for sorghum forage and fodder.

There are no data for sweet sorghum varieties or the byproduct syrup. Such data are necessary. As an alternative, label restrictions barring the use of chlorpyrifos on sweet sorghum varieties will be appropriate.

Livestock feeding studies (PP #3F1306)

Beef cattle - animals were fed chlorpyrifos in the daily diet at levels of 3, 10, 30, or 100 ppm for 30 days. The animals were slaughtered at the end of the feeding period, and tissue samples were taken for analyses.

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No residues of the oxygen analog was noted in any tissues. At the 3 ppm feeding level, maximum chlorpyrifos and TCP residues were 0.16-0.23 ppm (liver). Residues in the fat were < 0.01-0.05 ppm. At the 10 ppm feeding level, maximum residues noted were 0.54 ppm (kidney). At the 30 ppm feeding level maximum residues were noted in the liver and were 1.67 ppm. At the 100 ppm feeding level, maximum residues were noted in the fat and were 5.06 ppm. Residues decreased when chlorpyrifos feeding was terminated. At 35 days afterwards, maximum fat residues were 0.04 ppm from the 100 ppm feeding level.

Dairy cattle - animals were fed chlorpyrifos at levels of 1, 3, 10, and 30 ppm in the daily diet for 14 days. Samples of whole milk and cream were collected and analyzed for residues of chlorpyrifos, its oxygen analog, and TCP. At the 1, 3, and 10 ppm feeding levels, no residues were noted in whole milk at any time. No residues of the oxygen analog or TCP were noted in the cream at any feeding level. No residues of chlorpyrifos were noted in cream at the 1 and 3 ppm feeding levels.

Maximum chlorpyrifos residues of 0.04 ppm were noted in cream at the 10 ppm feeding level while no residues were noted in whole milk. At the 30 ppm feeding level, trace residues (0.02 ppm) of chlorpyrifos was noted in whole milk, and maximum residues of 0.15 ppm were noted in cream on day 10. Residues disappeared rapidly after withdrawal of treated feed. After 1-5 days of the withdrawal period, no residues were noted in either whole milk or cream.

The study indicates that residues in whole milk are concentrated in the fat.

Swine feeding study

Pigs were fed chlorpyrifos in the daily diet at levels of 1, 3, and 10 ppm for 30 days. Samples of tissues were taken from slaughtered animals and analyzed for residues of chlorpyrifos and TCP.

No detectable residues were noted in any tissues at the 1 ppm feeding level. At the 3 ppm feeding level, maximum residues of 0.08 ppm were noted (liver). At the 10 ppm feeding level, maximum residues of 0.32 ppm were noted (liver). At 7 days after termination of feeding, detectable residues were noted in fat only (0.03 ppm). At 21 days after feeding was ended, no residues were detected in any tissues.

Poultry feeding study - laying hens were fed chlorpyrifos in the daily diet at levels of 0.3, 1, 3, and 10 ppm for 30 days. At the end of the feeding period, chickens were sacrificed, and tissue samples were taken for analyses. Eggs samples were also analyzed for residues of chlorpyrifos and TCP.

Chickens which had been fed at 10 ppm were continued on a chlorpyrifos free diet for 30 days. Tissue and egg samples were taken and analyzed for residues of chlorpyrifos and TCP.

No residues were noted in eggs of chickens fed at the 10 ppm level. No residues were noted in tissues of chicken fed at the 0.3 ppm level. Maximum residues of 0.11 ppm (kidney) were noted at the 1 ppm feeding level, 0.24 ppm at the 3 ppm feeding level, and 0.84 ppm at the 10 ppm feeding level. No residues were noted in any tissues at 7 days following withdrawal of treated feed.

Meat and Milk

Sorghum grain and fodder and forage are major livestock feed items. The grain can be fed at maximum dietary levels of 90% for swine, 80% for cattle, 60% for poultry and sheep, and 20% for horses. The hay is not fed to poultry, swine, or horses, but can be fed to cattle at maximum dietary level of 60%, and sheep at 40%. Silage is not fed to poultry or horses, but can be fed at maximum dietary levels of 50% to cattle, 40% to sheep, and 30% to swine.

By using the above maximum dietary levels, we can calculate maximum levels of residues of chlorpyrifos and its metabolite TCP likely to result in the daily diet of livestock. The following are the ingestion levels expected. Cattle (3.6 ppm), swine (0.675 ppm), sheep (2.40 ppm), poultry (0.45 ppm), and horses (0.15 ppm).

By using the residue deposition values obtained from the livestock feeding studies, we can estimate values likely to result in milk, eggs, and tissues thru extrapolation of the above ingestion levels. The following are the estimated levels. Cattle (0.3 ppm); swine (no detectable residue); sheep (0.1 ppm); poultry (0.02 ppm); and horses (NDR). Estimated levels for milk is NDR, cream (NDR), and eggs (NDR).

We can conclude that residues could occur in eggs, milk, meat, fat, and meat byproducts of livestock [§180.6(a)(2)]; however, such residues would be adequately covered by existing tolerances.

Alfred Smith

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