PP#1F03969
11-17-93

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

NOV 17 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Triadimefon.** Storage Stability Study. Reregistration Case No. 2700. Chemical No. 109901. MRID #428574-01. DP Barcode D194783. CBRS #12,528.

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Miles Inc. (formerly Mobay Corporation) has submitted a storage stability study (1993; MRID 42857401) in support of the reregistration of triadimefon.

Tolerances for residues of triadimefon [1-(4-chlorophenoxy)-3,3-dimethyl-1-(1*H*-1,2,4-triazol-1-yl)-2-butanone] in/on raw agricultural commodities are expressed in terms the combined residues of triadimefon and its metabolites containing chlorophenoxy and triazole moieties, expressed as triadimefon [40 CFR §180.410 (a) and (b)]. Food/feed additive tolerances are currently expressed in terms of the combined residues of triadimefon and its metabolite triadimenol [β-(4-chlorophenoxy)-α-(1,1-dimethylethyl)-1*H*-1,2,4-triazole-1-ethanol] [40 CFR §185.800 and 40 CFR §186.800]. The Pesticide Analytical Manual (PAM, Vol. II, Section 180.410) includes GC/MS Methods I and II for the enforcement of tolerances of triadimefon residues in/on animal tissues, milk, and eggs. The method determines triadimefon, triadimenol, KWG 1323, and KWG 1342, and is reportedly applicable to plants, but validation data are still required.

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Recommendations

This study is not adequate for reasons stated in Conclusions 1 and 3. Additional data, as specified in the Conclusions are required before requirements for Guideline 171-4(e) are fulfilled. Results for triadimefon metabolism studies will soon be presented to the HED Metabolism Committee. Any additional metabolites requiring regulation will be determined by the Committee. If new metabolites which require regulation are identified by the Committee, then storage stability data may need to be developed for them.

Conclusions

1. CBRS concludes that the test system was not adequate since storage stability data for only plant commodities were provided. As noted in the Phase 4 Review (1/31/91), storage stability studies need to be conducted on animal commodities. Representative commodities to be examined should include muscle (cattle or poultry), liver (cattle or poultry), milk, and eggs. Storage stability of triadimefon and its regulated metabolites in these commodities can be determined either in conjunction with the magnitude of the residue studies in meat, milk, poultry, and eggs, or in a separate storage stability study. Storage conditions and storage time should represent the longest frozen storage time of any commodity in the meat, milk, poultry, and eggs magnitude of the residue study. Also, as noted in a previous CBRS review (S. Hummel, 12/22/92, CBRS Nos. 8566 and 9929), storage stability data will be needed on almond commodities if all almond uses are not concelled and storage stability data will be needed for an oilseed crop and its processed commodities if any oilseed is to be registered. Storage stability data required on pineapple processed commodities are still outstanding (F.Toghrol, 9/18/92, CBRS No. 9547).

2. The analytical method used was adequate for purposes of this study.

3. The registrant stated that each analysis set contained a concurrent fortification at 0.3 ppm, however, results for only a few concurrent recoveries were presented. This is a deficiency. All of the results for concurrent recovery samples must be submitted.

4. Results for the analysis of storage stability samples are presented in Table 2. Triadimefon, triadimenol and KWG 1323 were stable in all matrices examined over all time periods examined. KWG 1342 was not stable in asparagus, wheat bran, and coffee beans, with residues declining by 34%, 54%, and 79% of initial values respectively after 40 days of frozen storage. KWG 1342 was stable in wheat grain dust for 110 days; after 181 days of frozen storage residues had declined 33% from the initial value. KWG 1342 was stable in grape juice for 186 days; after 354 days of frozen storage, residues had declined by 47% from initial the value.

Detailed Considerations

Test System

Homogenized wheat straw, wheat bran, wheat flour, wheat grain dust, sugarbeet tops, sugarbeet roots, sugarbeet molasses, coffee beans, asparagus, apple, cucumber, pineapple, grape juice, grape wet pomace (79% moisture), grape dry pomace (22% moisture), and raisins were fortified at 1.0 ppm with triadimefon, triadimenol, KWG 1342, and KWG 1323 and then stored in a freezer at - 20 C. Samples were removed from the freezer at approximately 1, 3, 6, and 12 months (except for grape dry and wet pomace which were not analyzed at 12 months) and analyzed for each of the test compounds.

The Phase 4 Review (1/31/91) noted the following data gap concerning storage stability, "Storage stability studies must be conducted on all crops and processed commodities for which a field trial and/or processing study has been (or will be) conducted, as well as representative livestock commodities. Storage stability studies are needed for wheat (straw, grain, grain dust, bran, flour, middlings, shorts), barley (grain, grain dust, straw, forage, hulls, bran, flour, and pearl barley), sugar beets (root, tops, pulp, molasses, refined sugar), almonds (nutmeats, hulls), pineapple, pear, cattle (milk), cucurbits, processed grape products (raisin, wet and dry pomace, raisin waste, juice), raspberries, seed grass, poultry (meat, fat, eggs), and chick peas."

Since the Phase 4 Review, additional guidance for conducting storage stability has been issued (Pesticide Reregistration Rejection Rate Analysis Residue Chemistry, EPA 737-R-93-001, 2/93). This guidance suggested that storage stability studies be conducted using at least five diverse crops, including (1) and oilseed (or soybean or nut), (2) a non oily grain, (3) a leafy vegetable, (4) a root crop, and (5) a fruit or fruiting vegetable. Storage stability studies for processed commodities should use oilseeds, grains, and fruits/fruiting vegetables. With respect to animal commodities, representative commodities to be examined should include muscle (cattle or poultry), liver (cattle or poultry), milk, and eggs.

CBRS concludes that the test system was not adequate. Storage stability studies need to be conducted on animal commodities. Representative commodities to be examined should include muscle (cattle or poultry), liver (cattle or poultry), milk, and eggs. Storage stability of triadimefon and its regulated metabolites in these commodities can be determined either in conjunction with the magnitude of the residue studies in meat, milk, poultry, and eggs, or in a separate storage stability study. Storage conditions and storage time should represent the longest storage time of any commodity in the meat, milk, poultry, and egg magnitude of the residue study. Also, as noted in a previous CBRS review (S. Hummel, 12/22/92, CBRS Nos. 8566 and 9929), storage stability data will be needed on almond commodities if all almond uses are not concelled and storage stability data will be needed for an oilseed crop and its processed commodities if any oilseed is to be registered.Storage stability data required on pineapple processed commodities are still outstanding (F.Toghrol, 9/18/92, CBRS No. 9547).

Test Substances

Triadimefon from Lot No. 82R82-127 (99.5% purity) or Lot No. 88R264, Vial K-57 (95.4% purity) was used. Triadimenol used was from Lot No. 82R82-109 (95.6% purity). KWG 1323 was from Lot No. 86R-264, Vial K-71 (95.0% purity). KWG 1342 was from Lot No. 86R-264, Vial 456B(K-74) (96.6% purity).

Analytical Method

Miles analytical method No. 80488 was used for all analyses. A summary of this method was submitted as part of the Phase 3 Response and assigned MRID #92188-042. Briefly, triadimefon and metabolite residues were extracted using 7:3 (v:v) methanol:water. The extract was then heated at reflux for 1.5 hours, cooled, and filtered. The MeOH in the extract was removed using a rotovap. The extracts were then buffered and incubated overnight with cellulase enzyme. Residues were then extracted into methylene chloride and cleaned-up using gel permeation chromatography (GPC). A semi-preparative HPLC column was used to separate the residues into parent (triadimefon and triadimenol) and metabolite (KWG 1342 and KWG 1323) fractions. The parent fraction was diluted with toluene and quantitated using GC with NPD (Varian 3700 GC, 10% SP-2100 + 1.5% SP-2401 Packed Column, 6 ft. x 2 mm. The metabolite fraction was diluted with acetone and an aliquot was transferred to a reacti-vial. Keeper (1-decanol) and trifluoroacetic acid were added, followed by addition of trifluoroacetic anhydride. The solution was heated at 45 C for one hour to produce trifluoroacyl derivatives. The metabolite derivatives were quantitated using the same GC as for the parent fraction.

The Day 0 recovery data for the 0.3 and 1.0 ppm fortifications served as method validation. For samples fortified at 1.0 ppm, recoveries for triadimefon ranged from 61% (in coffee beans) to 101% (in grape juice); recoveries for triadimenol ranged from 76% (in wheat grain dust) to 106% (in grape juice); recoveries for KWG 1342 ranged from 61% (in wheat straw) to 120% (in coffee beans); recoveries for KWG 1323 ranged from 69% (in sugarbeet tops) to 117% (in grape wet pomace). Representative chromatograms were presented for wheat flour, sugar beet tops and raisins.

A control and concurrent recovery (fortified with each of the test compounds at 0.3 ppm) were analyzed with each analysis set as a check on method performance.

CBRS concludes that for the method used for analysis of samples in this study is adequate. However, CBRS notes that the triadimefon Phase 4 Review (1/31/91) concluded that the methods summarized in MRID 92188042 are acceptable <u>for review</u> as data collection methods, but must be validated for apples, almonds, cucurbits, sugar beets, pineapples, and grapes. Furthermore, the submitted regulatory method requires an independent laboratory validation as described in PR Notice 88-5. If new metabolites which require regulation are found in the plant metabolism studies, then analytical method(s) must be developed for them as well. Results for triadimefon metabolism studies will soon be presented to the HED

Metabolism Committee. Any additional metabolites requiring regulation will be determined by the Committee.

Results

Results for the analyses of concurrent fortifications (at 0.3 ppm), expressed as percent recoveries are presented in Table 1. CBRS notes that results for all concurrent recoveries were not presented. This is a deficiency. The registrant stated that each analysis set contained a concurrent fortification at 0.3 ppm. All of the results for concurrent recovery samples must be submitted.

Results for the analysis of storage stability samples are presented in Table 2. Triadimefon, triadimenol and KWG 1323 were stable in all matrices examined over all time periods examined.

KWG 1342 was not stable in asparagus, wheat bran, and coffee beans, with residues declining by 34%, 54%, and 79% of initial values respectively after 40 days of frozen storage. KWG 1342 was stable in wheat grain dust for 110 days; after 181 days of frozen storage residues had declined 33% from the initial value. KWG 1342 was stable in grape juice for 186 days; after 354 days of frozen storage, residues had declined by 47% from initial the value.

Table 1. Results, expressed as percent recovery, for analysis of concurrent fortifications. Control samples for each commodity were fortified with 0.3 ppm each of triadimefon, triadimenol, KWG 1342, and KWG 1323 on the day of analysis.

Commodity	Concurrent Recovery Sample Analyzed with Sample Stored for Indicated Number of Days	Triadimefon (% recovery)	Triadimenol (% recovery)	KWG 1342 (% recovery)	KWG 1323 (% recovery)
Sugar Beet Top	105	68	87	80	72
	187	83	98	87	75

Commodity	Concurrent Recovery Sample Analyzed with Sample Stored for Indicated Number of Days	Triadimefon (% recovery)	Triadimenol (% recovery)	KWG 1342 (% recovery)	KWG 1323 (% recovery)
Wheat Straw	110	78	82	98	94
Coffee Beans	105	73	80	82	79
Apple	220	96	104	79	80
	342	85	83	99	77
Grape Juice	92	100	100	75	101
	186	115	115	115	124
	354	82	71	93	85

Table 2. Results for storage stability study. All samples were fortified with 1.0 ppm each of triadimefon, triadimenol, KWG 1342, and KWG 1323 on Day 0 and stored frozen (-20 C) until analysis at specified intervals.

Commodity	Actual Storage Time (days)	Nominal Storage Time (months)	Triadimefon (ppm)	Triadimenol (ppm)	KWG 1342 (ppm)	KWG 1323 (ppm)
Sugar Beet Root	0	0	0.94	0.98	0.88	0.87
	35	1	0.93	0.97	0.87	0.86
	105	3	1.02	1.01	0.65	0.81
	187	6	0.93	1.06	0.98	0.89
Sugar Beet Top	0	0	0.92	1.02	0.88	0.70
	35	1	0.82	0.96	0.77	0.54
	105	3	0.87	0.97	0.76	0.75
	187	6	0.85	0.96	0.68	0.69
Sugar Beet Molasses	0	0	0.93	0.97	0.97	0.89
	35	1	0.94	0.96	0.91	0.88
	105	3	0.61	0.74	0.78	0.87
	187	6	0.95	1.06	0.83	0.85

Commodity	Actual Storage Time (days)	Nominal Storage Time (months)	Triadimefon (ppm)	Triadimenol (ppm)	KWG 1342 (ppm)	KWG 1323 (ppm)
Asparagus	0	0	0.93	1.00	1.00	0.97
	40	1	0.87	0.91	0.66	0.76
	110	3	0.78	0.86	0.75	0.81
	187	6	0.78	0.93	0.69	0.80
Wheat Straw	0	0	0.82	0.84	0.69	0.73
	40	1	0.84	0.90	0.68	0.73
	110	3	0.84	0.92	0.88	0.96
	181	6	0.79	0.89	0.86	0.81
Wheat Bran	0	0	0.62	0.77	1.04	0.89
	40	1	0.50	0.59	0.50	0.57
	110	3	0.75	0.85	0.62	0.73
	181	6	0.66	0.81	0.69	0.77
Wheat Flour	0	0	0.75	0.89	0.96	0.92
	40	1	0.69	0.76	0.78	0.79
	105	3	0.93	1.00	0.70	0.79
	181	6	0.70	0.82	0.71	0.91
Wheat Grain Dust	0	0	0.75	0.76	0.95	0.77
	40	1	0.72	0.66	0.73	0.59
	110	3	0.70	0.64	0.74	0.66
	181	6	0.77	0.80	0.62	0.75
Coffee Beans	0	0	0.66	0.77	1.16	0.88
	40	1	0.63	0.72	0.37	0.78
	105	3	0.32	0.58	0.46	0.69
	187	6	0.72	0.85	0.59	0.90
Apple	0	0	0.74	0.85	0.80	0.74
	92	3	0.89	0.93	0.74	0.82
	220	6	0.94	0.95	0.97	0.72
	342	12	0.90	0.97	1.06	0.86

Commodity	Actual Storage Time (days)	Nominal Storage Time (months)	Triadimefon (ppm)	Triadimenol (ppm)	KWG 1342 (ppm)	KWG 1323 (ppm)
Cucumber	0	0	0.96	0.97	0.99	0.77
	92	3	0.80	0.84	0.76	0.57
	186	6	0.95	1.00	1.14	0.76
	342	12	0.92	0.94	0.79	0.76
Pineapple	0	0	0.98	1.02	1.01	0.97
	92	3	0.87	0.93	0.76	0.95
	220	6	0.94	0.95	0.91	0.96
	342	12	0.82	0.95	0.80	0.93
Grape Juice	0	0	1.01	1.05	0.97	0.84
	92	3	0.97	0.98	0.93	0.96
	186	6	0.92	0.96	1.07	0.96
	354	12	0.96	0.98	0.50	0.84
Grape Wet Pomace	0	0	0.92	1.00	0.98	1.12
	92	3	0.90	0.91	0.99	0.91
	186	6	0.96	0.99	1.15	0.98
Grape Dry Pomace	0	0	0.86	0.88	0.75	0.77
	92	3	0.82	0.86	0.95	0.84
	186	6	0.80	0.85	0.93	0.92
Raisins	0	0	0.83	0.86	0.92	0.85
	92	3	0.86	0.93	0.96	0.80
	186	6	0.90	0.86	0.89	0.82
	354	12	0.76	0.86	0.67	0.84

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