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

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MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Malathion. Storage Stability Studies in Various Raw and Processed Commodities. GDLN 171-4(e). DP Barcodes: D213229 and D219313; CBRS Nos. 15273 and 16257; MRID Nos.: 435490-01 and 436848-01; Case No. 0248.

FROM: David J. Miller, HSO, US Public Health Service
Chemistry Pilot Review Team
Chemistry Branch II--Reregistration Support
Health Effects Division (7509C)

THRU: Edward Zager, Chief
Chemistry Branch II--Reregistration Support
Health Effects Division (7509C)

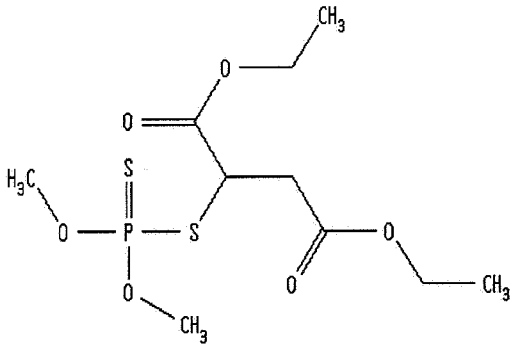
TO: Susan Jennings, PM Team 72
Reregistration Branch
Special Review and Reregistration Division (7508W)

In support of reregistration, Cheminova Agro (Cheminova) and its representative Jellinek, Schwartz, and Connolly, Inc., have submitted data on the storage stability of malathion and malaoxon in various food and feed commodities. Additional information regarding the storage interval used for the Magnitude of the Residue (MOR) studies in raw and processed commodities has also been provided. CBRS has been asked to review this material and evaluate the storage stability of parent malathion and its malaoxon metabolite in the raw agricultural commodities tested. CBRS has also been asked to determine if previously reviewed storage stability data in raw and processed commodities support the storage intervals used in the MOR trials.

Tolerances are currently established only for residues of malathion (or *O,O*-dimethyl dithiophosphate of diethyl mercaptosuccinate) *per se* in or on a multitude of agricultural commodities (40 CFR 180.111, 185.3850, 185.7000, and 186.3850). Tolerances range from 0.1 ppm in flax seed and eggs to as high as 135 ppm in many grass and non-grass forages. The HED Metabolism Committee has previously determined that the parent compound malathion and its malaoxon metabolite are the compounds to be regulated.

The structure of malathion is presented below:

(1)



CONCLUSIONS

1. *For storage stability purposes*, method performance was adequate for both parent malathion and the malaoxon metabolite. Recovery of parent malathion and metabolite malaoxon from fortified samples was acceptable, with average recoveries in all cases at least 80%.

2. CBRS concludes that malathion and its malaoxon metabolite are stable when stored frozen for periods of at least 6 months in raw agricultural commodities. CBRS will await the results from the ongoing 12 month storage stability study (expected January 31, 1996) before determining whether the 171-4(e) storage stability data adequately address potential concerns with respect to the storage periods associated with the rac field trials. If this data confirms that no significant declines with storage occur over a 12 month period, CBRS will not require further storage stability tests with malathion or its malaoxon metabolite. Following submission of acceptable 12 month stability data and for purposes of determining the adequacy of the crop field trials and processing studies, CBRS will conclude that the parent malathion compound and its malaoxon metabolite display sufficient storage stability on all racs such that new MOR trials or new storage stability studies are not required.

3. With respect to storage stability in *processed* commodities, CBRS has previously concluded that residues are stable in processed commodities of cottonseed, wheat and tomato stored frozen for 6 months. CBRS will await the pending 12 month storage stability data prior to determining whether the present storage stability data are adequate.

RECOMMENDATIONS

The registrant should be informed of the above conclusions, and is required to submit to the Agency results from the ongoing 12 month storage stability test. CBRS will extrapolate any 12 month data to 2-3 years and on this basis will conclude, upon the registrant's submission of adequate 12 month data, that residues of malathion and malaoxon are stable when stored frozen for a period of at least 2-3 years. Since in no case were residue and processing study field samples stored for longer than 2 years, CBRS will conclude (upon submission of adequate data) that there are no storage stability concerns associated with the submitted MOR field trial and processing study data and that GDLN 171-4(e) is considered satisfied.

DETAILED CONSIDERATIONS

A freezer storage stability study was conducted by EN-CAS Analytical Laboratories in Winston-Salem, NC. The study was entitled "Stability of Malathion and Malaoxon in Various Raw Agricultural Commodities During Six Months of Frozen Storage" (MRID 43549001; 1995). The objective of the submitted study was to determine the storage stability of malathion and its malaoxon metabolite in/on fortified raw agricultural commodities. Residue stabilities in the various sample matrices were monitored over a 6 month period of time. The registrant has indicated that it intends to provide EPA with a 12 month storage stability report and anticipates being able to submit these data to the Agency by January 31, 1996. This 12 month test interval in some cases is not adequate to cover the time periods elapsed between sampling and analysis in the crop Magnitude of the Residue (MOR) field trials. However, CBRS believes that demonstrated storage stability over a 12 month period in many cases can be legitimately extrapolated to cover crop field trial sample storage intervals of at least 2 to 3 years.

The study was designed using the combined crop grouping system detailed in Chemistry Branches' January 14, 1993 memorandum entitled "Guidance on Generating Storage Stability Data in Support of Pesticide Residue Chemistry Studies." Cottonseed was selected to represent the oil seed crop, wheat (grain, forage, and straw) represented the non-oily grain group, leaf lettuce represented the leafy vegetable group, potato tubers were selected to represent the root crop group, and tomatoes represented the fruiting vegetable crop group.

Sample Preparation and Analysis

Untreated control samples of each matrix were obtained from various field trials conducted by the sponsor from 1992 to 1994. Upon receipt by EN-CAS laboratories, the untreated samples were transferred to a laboratory freezer for storage where they remained frozen until homogenization and subsampling.

For the determination of storage stability, the stored samples were homogenized with dry ice, subsampled, and separately fortified with either 0.5 ppm malathion or 0.5 ppm malaoxon and stored frozen at less than -5 °C until analysis. Additional samples were stored for use as controls and for determination of concurrent procedural recoveries.

At specific time intervals after storage (e.g., 0 days, and 1-, 2-, 3-, and 6- months), 3 non-fortified control samples, 2 malathion (only)-fortified samples, and 2 malaoxon (only)-fortified samples were removed from freezer storage: one of the three non-fortified stored control samples was left unfortified for use as a blank to monitor any background that developed in the sample matrix during storage, while the remaining two unfortified control samples were used for fresh fortifications (procedural recovery samples) to monitor the analytical procedure for recovery of the compounds of interest. The 4 fortified stored samples (2 malathion-fortified and 2 malaoxon-fortified) served to monitor any losses of malathion or malaoxon during storage.

Following removal from the freezer at the specified time intervals, samples were blended with acetonitrile/water or 100% acetonitrile for 2 minutes, evaporated to aqueous, mixed with deionized water and NaCl, partitioned with dichloromethane, and concentrated by evaporation. The resulting extract was mixed with acetone and activated charcoal, filtered, evaporated to dryness, redissolved in acetone/dichloromethane, and passed through a silica gel column. After redissolving the extract in polyethylene glycol/acetone, analysis was performed by GC.

The potato tuber, tomato fruit, leaf lettuce, and wheat (grain, forage, and straw) extracts as well as the 1 and 2 month cottonseed samples were analyzed on a Tracor 540 gas chromatograph equipped with a 15 m x 0.53 mm DB-5 megabore column. Detection was with a flame photometric detector (FPD) operated in the phosphorus mode. The 0, 3, and 6 month cottonseed extracts were analyzed on a HP-5890 gas chromatograph equipped with a 30 m x 0.32 mm DB-5 capillary column. Detection in this case was also with an FPD operating in the phosphorus mode. Quantitation limits for the analytical method were estimated to be 0.05 ppm by the performing laboratory.

For storage stability purposes, method performance was adequate for both parent malathion and the malaoxon metabolite. Mean

percent recoveries and standard deviations of the fresh fortification recovery samples are shown in Table 1 on the following page.

Table 1. Mean Recoveries of Malathion and Malaoxon from Fresh Fortification Recovery Samples Fortified (separately) at 0.5 ppm.

Commodity	Percent Recovery of Malathion		Percent Recovery of Malaoxon	
	Mean±SD[a]	Range	Mean±SD[a]	Range
Cottonseed	84±7.2	68-92	100±18	73-135
Wheat Grain	91±5.0	82-100	95±4.7	89-100
Wheat Forage	87±5.5	81-97	88±5.3	81-97
Wheat Straw	75±6.4	67-83	91±4.6	83-96
Leaf Lettuce	91±9.3	77-107	94±7.9	81-106
Potato Tubers	85±7.8	70-91	91±6.9	78-98
Tomato Fruit	82±8	65-93	79±8.5	62-91

[a] Represents mean ± one standard deviation. N=10 for all commodities.

As can be seen, recovery of parent malathion and metabolite malaoxon were acceptable, with average recoveries in all cases of at least 80%.

Storage Stability

Recoveries of malathion and its malaoxon metabolite from cottonseed (representing oil seed crops), wheat grain, forage, and straw (representing non-oily grain crops), leaf lettuce (representing leafy vegetable crops), potato tubers (representing root crops), and tomatoes (representing fruiting vegetables) following various periods of storage are presented in summary form in Table 2. *With respect to malathion and its malaoxon metabolite*, CBRS judges these data to be acceptable and concludes that malathion and its malaoxon metabolite are stable when stored frozen for periods of least 6 months in raw agricultural commodities. CBRS notes that Cheminova intends to submit additional storage stability data covering a 12 month period, and has indicated that it anticipates submitting this data to the Agency by January 31, 1996. This data is required since in many cases RAC samples from crop field trials were stored for longer than 6 months (MRID 436848-01; 1995)

The registrant has indicated that the time between harvest of the rac field trial samples and extraction of these samples was in some cases as long as 772 days. According to the registrant, CBRS has previously indicated that storage stability data covering periods at least as long as the time interval over which racs from MOR trials have been stored must be submitted. The information provided by the registrant in its Table 1 indicates that in certain instances racs from field trials were stored considerably longer than the corresponding storage stability trial samples. The registrant, however, has indicated that the vast majority of MOR field trial samples were stored for less than 12 months. Since CBRS does not believe that the reviewed 6 month storage stability data reveal evidence of instability in any of the representative commodities and that storage stability data can in some instances be extrapolated from 12 months to 2-3 years, CBRS will only require that data from the ongoing 12 month storage stability study be submitted. Following submission of acceptable 12 month stability data and for purposes of determining the adequacy of the crop field trials and processing studies, CBRS will conclude that the parent malathion compound and its malaoxon metabolite display sufficient storage stability on all racs such that new MOR trials or new storage stability studies are not required.

With respect to storage stability in *processed* commodities, CBRS has previously concluded that residues are stable in cottonseed meal, hulls, and bleached and deodorized oils; wheat bran, flour, middlings, and shorts; and tomato dried pomace, catsup, and juice stored frozen for 6 months (K. Dockter, in review, CBRS No. 15843) [Cottonseed, wheat, and tomato represent an oil seed, a grain, and a fruiting vegetable, respectively, in Chemistry Branches' storage stability classification system for processed commodities]. However, these processed commodities were stored by the registrant prior to extraction for as long as 522 days (per registrant's Table 1). Since CBRS previously concluded that malathion and its malaoxon metabolite are stable in the tested representative commodities for a period of as least 6 months (see K. Dockter review), CBRS will await the pending 12 month storage stability data prior to determining whether the present storage stability data are adequate: if the 12 month data for the above-mentioned processed commodities show no significant residue declines, CBRS will conclude (by extrapolation) that the submitted storage stability data are adequate to cover all processed commodities of concern which were stored for periods of less than approximately 2-3 years.

RDI: Pilot Team:10/3/95; RPerfetti:10/4/95;EZager:10/5/95.
cc: RF, SF, List A Rereg. File, Circ., DJM

Table 2. Summary of Malathion (Mthion) and Malaoxon (Moxon) Storage Stability Data for Various Raw Agricultural Commodities[a].

Test Commodity	Chemical	Mean Percent Recovery From Test Commodity Fortified at 0.5 ppm[b]					
		Day 0	Month 1	Month 2	Month 3	Month 6	Month 12
Cottonseed	Mthion	89%	79%	108%	94%	91%	NR[c]
	Moxon	101%	57%	80%	99%	121%	NR
Wheat Grain	Mthion	94%	63%	68%	77%	76%	NR
	Moxon	98%	75%	77%	76%	78%	NR
Wheat Forage	Mthon	84%	76%	76%	70%	69%	NR
	Moxon	84%	90%	88%	82%	80%	NR
Wheat Straw	Mthon	72%	82%	102%	76%	83%	NR
	Moxon	86%	77%	89%	67%	103%	NR
Leaf Lettuce	Mthion	99%	NA	99%	97%	103%	NR
	Moxon	97%	NA	117%	99%	111%	NR
Potato Tubers	Mthion	88%	75%	83%	88%	100%	NR
	Moxon	92%	87%	93%	90%	91%	NR
Tomato Fruit	Mthon	83%	90%	96%	109%	100%	NR
	Moxon	77%	94%	107%	103%	75%	NR

[a] Data provided here are summary data. Raw data indicate that there is no interconversion of malathion and malaoxon.

[b] Mean percent recoveries of residues correct for control and concurrent procedural recoveries.

[c] Not Reported. Study is ongoing and registrant is required to submit these data to CBRS when it becomes available (anticipated January 31, 1996).