

2-17-94
(1-2-94)

MEMORANDUM

SUBJECT: Response to the Malathion Reregistration Standard: Radiovalidation of method in plants. (MRID No. 42894601, CBRS No. 12,855, Barcode: D196878).

FROM: R. B. Perfetti, Ph.D., Chemist
Reregistration Section 1
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

THRU: Paula A. Deschamp, Section Head
Reregistration Section 1
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

TO: Lois Rossi, Chief
Reregistration Branch
Special Review & Reregistration Division (H7508C)

Attached is a review of a radiovalidation study in plants submitted by A/S Cheminova in response to the malathion Reregistration Standard. This review was completed by Dynamac Corporation under supervision of CBRS, HED. It has undergone secondary review in the branch and has been revised to reflect Agency policies.

1. The radiovalidation data for the proposed GLC/FPD method (Method M-1886) are adequate to satisfy radiovalidation data requirements in plants. The method adequately recovered residues of malathion and malaoxon from samples of alfalfa hay treated with ¹⁴C-malathion (from the alfalfa metabolism study). No additional radiovalidation data are required.
2. When the tolerance expression is revised to include both malathion and malaoxon, an adequate enforcement method to determine both malathion and malaoxon in plant commodities will be needed. Before the proposed method can be considered suitable for enforcement purposes, independent laboratory validation, in accordance with PR Notice 88-5 dated 7/15/88, is required. The Registrant should be informed that this independent laboratory validation should be initiated **as soon as possible**. Once a successful confirmatory trial has been received, the method will be validated by the Agency and included in PAM, Vol. II as an enforcement method.

A revised Residue Chemistry summary sheet is included.

If you need additional input please advise.

①

malathion. 01/8

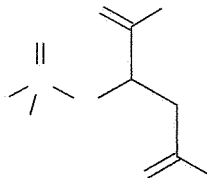
Attachment 1: Malathion Residue Chemistry Review.

cc (With Attachment 1): RBP, Malathion Reregistration
Malathion Subject File, Circulation and Dynamac.

Standard File,

cc (Without Attachment): RF.

MALATHION



Shaughnessy No. 057701; Case 0248

(CBRS No. 12855; DP Barcode D196878)

Task 4

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

An Agency memorandum (CBRS 9969, DP Barcode D178988, 7/30/92, R. Perfetti) required that representative samples from the alfalfa metabolism study be analyzed by the residue analytical methods developed for data collection and tolerance enforcement to assure that these methods are capable of adequately recovering malathion and malaoxon. In response, Cheminova Agro A/S has submitted (1993; MRID 42894601) a description of and radiolabeled validation data for a proposed enforcement method for the determination of malathion and malaoxon in/on alfalfa forage and hay. The Conclusions and Recommendations stated below apply only to radiovalidation of the proposed method. All other residue chemistry data requirements stated in the Malathion Reregistration Standard Guidance Document are not addressed herein.

The qualitative nature of malathion residues in alfalfa, lettuce, cotton, and wheat is adequately understood. The qualitative nature of the residue resulting from oral dosing of ruminants and poultry is adequately understood. However, if the direct livestock treatment uses of malathion are supported, appropriate dermal metabolism studies are required.

Tolerances for residues in/on food/feed commodities are expressed in terms of malathion (O,O-dimethyl dithiophosphate of diethyl mercaptosuccinate) [40 CFR

§180.111, §185.3850, §185.7000, and §186.3850]. The HED Metabolism Committee has determined that the parent compound malathion and the malaoxon metabolite are the compounds to be regulated. Codex MRLs exist for residues of malathion *per se* in/on various plant and processed commodities. The Codex MRLs and the U.S. tolerances will be incompatible when the U.S. tolerance expression for plant commodities is revised to include both residues of malathion and the metabolite malaoxon.

Adequate methods are available for the enforcement of current tolerances. The Pesticide Analytical Manual (PAM) Vol. II lists a TLC method, a GLC method with KCl thermionic detection, and a spectrophotometric method as Methods I, II, and III, respectively, for the enforcement of malathion tolerances. The Residue Chemistry Science Chapter of the Malathion Reregistration Standard, dated 7/87, recommends use of the GLC method for tolerance enforcement. When the tolerance expression is revised to include both malathion and malaoxon, new enforcement methodology may be required.

CONCLUSIONS AND RECOMMENDATIONS

1. The radiovalidation data for the proposed GLC/FPD method (Method M-1886) are adequate to satisfy radiovalidation data requirements in plants. The method adequately recovered residues of malathion and malaoxon from samples of alfalfa hay treated with ¹⁴C-malathion (from the alfalfa metabolism study). No additional radiovalidation data are required.
2. When the tolerance expression is revised to include both malathion and malaoxon, an adequate enforcement method to determine both malathion and malaoxon in plant commodities will be needed. Before the proposed method can be considered suitable for enforcement purposes, independent laboratory validation, in accordance with PR Notice 88-5 dated 7/15/88, is required. The Registrant should be informed that this independent laboratory validation should be initiated **as soon as possible**. Once a successful confirmatory trial has been received, the method will be validated by the Agency and included in PAM, Vol. II as an enforcement method.

DETAILED CONSIDERATIONS

Radiovalidation of analytical method

Cheminova has submitted radiolabeled validation data (1993; MRID 42894601) for a GLC/flame photometric detection (FPD) method, American Cyanamid Method M-1886. This GLC method is a new method and is not included in the PAM Vol. II as an enforcement method.

Radiovalidation was conducted by EN-CAS Analytical Laboratories, Winston-Salem, NC using American Cyanamid Method M-1886 as modified by EN-CAS Laboratories. Samples of [¹⁴C]malathion-treated alfalfa hay homogenates, stored frozen, were obtained from the alfalfa metabolism study (MRID 42317404, CBRS No. 9969, DP Barcode D178988, 7/30/92, R. Perfetti). The samples were hydrated in water for 15 minutes and then homogenized in acetonitrile and filtered. The acetonitrile was removed by rotary evaporation, water and sodium chloride-saturated water were added, and the extract was partitioned three times with dichloromethane (DCM). The DCM fraction was evaporated to dryness by rotary evaporation, and the residue was redissolved in acetone and then cleaned with activated carbon for 35 minutes. Following vacuum filtration, the extract was reduced to dryness by rotary evaporation and a stream of nitrogen. The residue was redissolved in acetone and DCM, sodium sulfate was added, and the sample was applied to a silica gel Bond Elut column conditioned with acetone:DCM (10:90, v:v). Residues were eluted with the same solvent. The eluate was concentrated under a stream of nitrogen, reconstituted in acetone and 0.02% polyethylene glycol, and analyzed for malathion and malaoxon by GLC on a DB-5 fused silica capillary column using FPD in the phosphorus mode. The target limit of quantitation was 0.05 ppm for malathion and malaoxon. The hydration step prior to extraction with acetonitrile, the DCM partitioning step, and use of the DB-5 column are modifications of Method M-1886 as introduced by EN-CAS.

Sample calculations, standard curves, and representative chromatograms depicting GLC analyses of malathion and malaoxon in [¹⁴C]malathion-treated alfalfa hay samples were provided. The radiovalidation data comparing the results of the current GLC/FPD analysis to data obtained from the alfalfa metabolism study are presented in Table 1.

Table 1. Determination of malathion and malaoxon in samples of alfalfa hay from a metabolism study using HPLC radiochemical analysis and the proposed GLC/FPD enforcement methodology.

Sample/Method	Malathion (ppm)		Malaoxon (ppm)	
	Sample 1	Sample 2	Sample 1	Sample 2
HPLC Radiochemical Analysis (Metabolism study)	31.33	31.33	1.82	1.82
GLC/FPD Analytical Method (Proposed enforcement method)	27.91	33.66	0.67	0.86

The levels of malathion detected in [¹⁴C]malathion-treated alfalfa hay by the proposed GLC/FPD enforcement method were comparable to the levels of malathion determined by the HPLC method used in the metabolism study. However, the levels of malaoxon detected in [¹⁴C]malathion-treated alfalfa hay by the proposed GLC/FPD enforcement method were lower than the levels of malaoxon determined by the HPLC method used in the metabolism study. The registrant explains these results in several ways. First, the registrant asserts that malaoxon degraded during storage since the alfalfa hay samples from the metabolism study were stored frozen for 2.5 years prior to analysis in the current study using the GLC/FPD Method M-1886.

5

The registrant also provided method recovery data. Untreated control samples of alfalfa hay were fortified with malathion and malaoxon as a mixture and analyzed by Method M-1886 with EN-CAS modifications for malathion and its metabolite. The method recovery data are presented in Table 2. The recoveries of both malathion and malaoxon from fortified samples of alfalfa hay analyzed using the GLC/FPD method were excellent.

Table 2. Method recoveries of malathion and malaoxon from fortified alfalfa hay samples using American Cyanamid Method M-1886.

Metabolite	Fortification Level (ppm)	Percent Recovery ^a
Malathion	50	95
	10	92
Malaoxon	5	102
	1	110

^a Values were not corrected for background levels.

The radiovalidation data for the proposed GLC/FPD method (Method M-1886) are adequate to satisfy radiovalidation data requirements in plants. The method adequately recovered residues of malathion and malaoxon from samples of alfalfa hay treated with ¹⁴C-malathion (from the alfalfa metabolism study). No additional radiovalidation data are required.

When the tolerance expression is revised to include both malathion and malaoxon, an adequate enforcement method to determine both malathion and malaoxon in plant commodities will be needed. Before the proposed method can be considered suitable for enforcement purposes, independent laboratory validation, in accordance with PR Notice 88-5 dated 7/15/88, is required. The Registrant should be informed that this independent laboratory validation should be initiated **as soon as possible**. Once a successful confirmatory trial has been received, the method will be validated by the Agency and included in PAM, Vol. II as an enforcement method.

EPA MEMORANDA CITED IN THIS REVIEW

CBRS No.: 9969
DP Barcode: D178988
Subject: A/S Cheminova: Response to the Malathion Reregistration Standard:
Residue Chemistry
From: R. Perfetti
To: E. Saito and L. Rossi
Dated: 7/30/92
MRID(s): 42317401

6

MASTER RECORD IDENTIFICATION NUMBERS

A citation for the MRID document referred to in this review is presented below.

42894601 Barker, W. and Prohonic, K. (1993) Accountability Study of the Proposed Method for the Determination of Malathion (O,O-dimethyl phosphorodithioate of diethyl mercaptosuccinate) and Its Metabolite, Malaoxon, in/on Alfalfa Hay Treated with ¹⁴C-Radiolabeled Malathion. En-Cas Protocol Number 92-0106. Unpublished study conducted by En-Cas Analytical Laboratories, Winston-Salem, NC, and sponsored by Cheminova Agro A/S. 98 p.