Image 5

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Date: 17/July/00

SUBJECT: **Disodium Methanearsonate (DSMA) Reregistration.** 860.1520: Processed Food and Feed Study on Citrus Fruit.

Reregistration Case No.: 2395.
PC Code: 013802.
DP Barcode No.: D232748.
MRID No.: 44195901.

FROM: Sherrie L. Kinard, Chemist Sherrie L. Kinard
Reregistration Branch II
Health Effects Division [7509C]

THROUGH: Alan Nielsen, Branch Senior Scientist A. Nielsen 7/17/2000
Reregistration Branch II
Health Effects Division [7509C]

TO: Tom Myer, Chemical Review Manager
Accelerated Reregistration Branch
Special Review and Reregistration Division [7508W]

Attached is a review prepared by Dynamac Corporation of studies submitted for the processed food and feed residues of DSMA in/on citrus. This information has undergone secondary review in Reregistration Branch 2 and is consistent with current Agency policies.

(1)

EXECUTIVE SUMMARY

1. 860.1520 - *DSMA Citrus Processed Food/Feed (MRID No.:* 44195901*):*

Analytical Method:
The analytical method, used for determining residues of DSMA (calculated as MSMA) and cacodylic acid in/on orange processed commodities which are evaluated in this document, was a gas chromatography method with electron capture detection (GC/ECD). The reported limits of quantitation (LOQ) were 0.04 ppm for orange juice and 0.05 ppm for oranges, wet and dried pulp, molasses, and oil. Based on acceptable method recoveries, the GC/ECD method is adequate for data collection purposes.

Residue Data:
The orange processing data are acceptable and may be used to satisfy reregistration requirements. Residues of DSMA (determined as MSMA) and cacodylic acid were each less than the analytical method's LOQ in/on orange fruits harvested 0-days following the last of three broadcast spray applications, with 79 and 110 day retreatment intervals, of the 81% SC formulation of DSMA at 24.3 lb ai/A/application (5x the maximum registered single and seasonal rates).

Residues of DSMA (determined as MSMA) and cacodylic acid were also below the LOQ in juice and oil processed from orange fruits treated at 5x the maximum registered single and seasonal rates; however, the combined residues of DSMA and cacodylic acid concentrated 2.0x in dried pulp processed from orange fruits treated at 5x the maximum registered single and seasonal rates.

The results of the orange processing study tentatively suggest that a tolerance for the combined residues of MSMA and cacodylic acid (expressed as As_2O_3) in citrus dried pulp may be needed. A definitive regulatory conclusion concerning the need for a tolerance on citrus dried pulp will be made when the HAFT residue in/on the RAC has been determined from the requested confirmatory field study. A tolerance for molasses need not be proposed since this item has been deleted from Table 1 (OPPTS 860.1000) as a processed fraction of citrus fruit.

DEFICIENCIES

Deficiencies in 860.1520 - *DSMA Citrus Processed Food/Feed (MRID No.:* 44195901*):*
There are no deficiencies that would seriously compromise the interpretation of these data; **however, the combined residues of DSMA and cacodylic acid concentrated 2.0x in dried pulp processed from orange fruits treated at 5x the maximum registered single and seasonal rates. There are some concerns that since the third application was done on the day of harvest, there was not adequate time for translocation of DSMA to the**

2

citrus fruit; however, the US FDA Total Diet Study-Market Baskets 91-3 through 97-1 demonstrates that it is unlikely to find residues of arsenic in/on citrus fruit. Therefore, we can assume that the third application of DSMA is unlikely to increase the residue levels over tolerance in processed citrus fruit.

Assuming that the established tolerance for the RAC (citrus fruits) remains at 0.35 ppm, a section 409 tolerance (or section 407 MRL) need not be established for citrus dried pulp. This determination is based on the fact that the established tolerance of 0.35 ppm is less than the number obtained by multiplying the observed concentration factor (2.0x) and the HAFT (highest average field trial) combined residues (<0.16 ppm) reported from the citrus field trials (MRID 43605901 and 43683101; DP Barcodes D214330 and D216740).

cc: Sherrie L. Kinard (RRB2), DSMA List B File, DSMA Subject File, RF, LAN. RDI: RRB2 Res. Chem. Team (7/13/00).

7509C: RRB2: S. Kinard: CM#2:Rm 722B: 703-305-0563: 7/17/00.

DISODIUM METHANEARSONATE (DSMA)

(PC Code 013802; Case 2395)

(DP Barcode D232748)

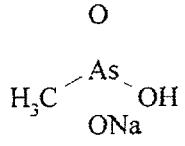
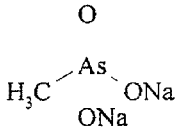
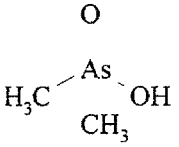
REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

In support of reregistration, the Methanearsonic Acid (MAA) Research Task Force Three submitted the results of an orange processing study (1996; MRID 44195901). The Phase 4 Reviews for DSMA (C. Olinger, 3/26/91) required that a processing study must be conducted for a representative citrus fruit. The submitted orange processing data are evaluated in this document for adequacy in fulfilling residue chemistry data requirements for the reregistration of DSMA.

The qualitative nature of the residue in plants is adequately understood. In a 12/19/94 meeting of the HED Metabolism Committee, it was determined that the residues of concern (i.e., those that should be included in the tolerance expression and are of toxicological concern) associated with the use of monosodium methanearsonate (MSMA) and disodium methanearsonate (DSMA) are MSMA and cacodylic acid (CA). [This conclusion is based on the low rate or lack of demethylation of CA to methanearsonic acid (MAA), and on the inability to distinguish between background arsenic and arsenic resulting from pesticidal use]. The molecular structures of MSMA, DSMA, and cacodylic acid are depicted below.

Figure 1. Chemical structures of MSMA, DSMA, and cacodylic acid.

		
MSMA	DSMA	Cacodylic acid (CA)

Tolerances are currently established for the selective postemergence herbicide methanearsonic acid (calculated as As_2O_3) resulting from application of the disodium and monosodium salts of methanearsonic acid [40 CFR §180.289]. Currently, a colorimetric method is published in PAM, Vol. II as Method I. The Phase 4 Reviews for MAA and cacodylic acid requested that the registrant submit new enforcement methods for determination of residues of concern in/on plant commodities.

Currently, for data collection purposes, residues of MSMA and cacodylic acid on cotton and citrus are quantified using a GC/ECD. Depending on the matrix, the reported LOQs of the analytical method were 0.04-0.05 ppm. The method was adequately validated by the registrants. Radiovalidation data have also been submitted and reviewed; the data indicate that the GC/ECD can adequately and separately quantitate residues of MSMA and cacodylic acid in/on aged samples of lemons generated from a citrus metabolism study.

Because the enforcement methods listed in PAM Volume II are colorimetric methods, the Agency recommends that this GC/ECD method be proposed as an enforcement method. The registrant is referred to OPPTS 860.1340 for specific requirements concerning regulatory methods. OPPTS 860.1340 requires that any proposed enforcement method be subjected to an independent laboratory validation (ILV) as per PR Notice 96-1. If the Agency determines that the registrant has submitted the results of a successful ILV trial by an independent laboratory, then the method will be validated by Agency chemists.

CONCLUSIONS AND RECOMMENDATIONS

1. The analytical method, used for determining residues of DSMA (calculated as MSMA) and cacodylic acid in/on orange processed commodities which are evaluated in this document, was a GC/ECD. The reported limits of quantitation (LOQ) were 0.04 ppm for orange juice and 0.05 ppm for oranges, wet and dried pulp, molasses, and oil. Based on acceptable method recoveries, the GC/ECD method is adequate for data collection purposes.

2a. The orange processing data are acceptable and may be used to satisfy reregistration requirements. Residues of DSMA (determined as MSMA) and cacodylic acid were each less than the analytical method's LOQ in/on orange fruits harvested 0-day following the last of three broadcast spray applications, with 79 and 110 day retreatment intervals, of the 81% SC formulation of DSMA at 24.3 lb ai/A/application (5x the maximum registered single and seasonal rates).

2b. Residues of DSMA (determined as MSMA) and cacodylic acid were also below the LOQ in juice and oil processed from orange fruits treated at 5x; however, the combined residues of DSMA and cacodylic acid concentrated 2.0x in dried pulp processed from orange fruits treated at 5x. Assuming that the established tolerance for the RAC (citrus fruits) remains at 0.35 ppm, a section 409 tolerance (or section 407 MRL) need not be established for citrus dried pulp. This determination is based on the fact that the established tolerance of 0.35 ppm is less than the number obtained by multiplying the observed concentration factor (2.0x) and the HAFT (highest average field trial) combined residues (<0.16 ppm) reported from the citrus field trials (MRID Nos. 43605901 and 43683101; DP Barcodes D214330 and D216740).

DETAILED CONSIDERATIONS

Residue Analytical Methods

Samples of processed orange commodities from the submitted study were analyzed for residues of DSMA and cacodylic acid by PTRL East, Inc. (Richmond, KY) using a GC/ECD. Using this method, DSMA residues are converted to MSMA during an extraction process; consequently, samples are analyzed for residues of MSMA and cacodylic acid.

Briefly, samples of orange peel and dried pulp were extracted twice with water, centrifuged, and filtered. Dried pulp samples were initially treated with hexane to enhance extractability. The combined filtered extract was made basic (pH 11-12) with 10% NaOH and concentrated by rotary evaporation. The concentrated extract was then acidified with HCl, and the resulting precipitate was removed by filtration. The extract was further purified by C-18 solid phase extraction (SPE). Residues were eluted with water, and the eluate was made basic with 10% NaOH and then concentrated. The concentrated extract was acidified with HCl, and residues were derivatized with methylthioglycolate (MTG). The derivatized residues of MSMA and cacodylic acid were partitioned into hexane. The aqueous:hexane mixture was centrifuged to eliminate any emulsion for phase separation. The hexane phase was analyzed for residues of MSMA and cacodylic acid by GC/ECD. The reported LOQs were 0.04 ppm for orange juice and 0.05 ppm for all other orange matrices.

Samples of orange oil and molasses were partitioned with water, and the aqueous layer was acidified with concentrated HCl. The acidified aqueous phase was purified by C-8 SPE, and residues were eluted with pH 2 water. The eluate was partitioned with hexane, and the aqueous phase was derivatized with MTG as described above for analysis by GC/ECD. Samples of orange juice were acidified with concentrated HCl and derivatized with MTG. The derivatized residues were partitioned with hexane, and the hexane phase was analyzed by GC/ECD.

Concurrent method recovery data were submitted for oranges and each processed commodity. Untreated samples of oranges and orange juice, molasses, wet and dried pulp, and oil were fortified with DSMA and cacodylic acid at various levels, and analyzed using the GC/ECD method described above. The results of concurrent method analyses of fortified untreated samples are presented in Table 1. Based on acceptable method recoveries, the GC/ECD method is adequate for determining residues of MSMA and cacodylic acid in/on oranges, and in orange juice, molasses, wet and dried pulp, and oil.

Table 1. Concurrent method recoveries of DSMA and CA from fortified untreated samples of processed orange commodities.

Crop	Fortification Levels (ppm)	% Recoveries	
		DSMA (Determined as MSMA Equivalents)	Cacodylic Acid
Orange	0.05, 0.10	119; 122	93, 96
Juice	0.04	100	95
Wet pulp	0.05	119	120
Dried pulp	0.05	110	78
Molasses	0.05	103	78
Oil	0.05	94	72

Storage Stability Data

The harvested samples of orange fruits from the processing study were boxed after harvest and shipped overnight at ambient conditions to the Citrus Research and Education Center (Lake Alfred, FL) for processing. At the processing facility, the treated and untreated whole orange samples were stored in cold storage until processing into juice, molasses, wet and dried pulp, and oil. Processing was completed within five days of harvest. The processed samples were frozen (-10 C) and shipped to PTRL East, Inc. for analysis and were stored frozen until residue analysis. The maximum storage intervals between harvest and analysis were 10-14 months for orange fruit, 15 months for wet and dried pulp, and 14 months for juice, molasses, and oil.

Data investigating the frozen storage stability of residues of MSMA, DSMA, and cacodylic acid in the processed fractions of citrus fruits and cottonseed are unavailable. Storage stability data (MRID 43605901; DP Barcodes D214330 and D216740) for the RAC indicate that residues of MSMA are stable under frozen conditions for up to 15 months in/on oranges, grapefruit, and lemons. Additionally, the registrant stated that the frozen storage stability of cacodylic acid for up to one year was demonstrated by data submitted in conjunction with a citrus metabolism study (MRID 42391201). The registrant asserted that the stability data for MSMA are indicative of the storage stability of DSMA, as both dissociate to methanearsonic acid when dissolved in water.

OPPTS GLN 860.1520: Processed Food/Feed

Citrus Fruits Group

Established tolerance: A crop group tolerance has been established for residues of methanearsonic acid (calculated as As_2O_3) in/on citrus fruit at 0.35 ppm resulting from application of the DSMA and MSMA in/on citrus fruits [40 CFR §180.289]. No tolerances are established for the processed commodities of citrus fruits.

Registered use patterns: Active DSMA end-use products registered to MAA Task Force Three members were identified as MSMA 4 and 6 lb/gal SC/L formulations and a 6 lb/gal EC (California only) registered for application to citrus orchards, including orange, grapefruit, tangerine, lemon, and lime, at 2-4 lb ai/A/application in 50-100 gal of water per acre (GPA). The 81% SC/S formulation of DSMA is registered for virtually identical use on citrus at 4.9 lb ai/A/application. These MSMA and DSMA application rates are equivalent in terms of total arsenic in water-soluble form at ~2 lb ai/A (expressed as elemental). A maximum of three applications per year are permitted. No PHI has been established.

Discussion of data: The MAA Research Task Force Three has submitted data (1996; MRID 44195901) from an orange processing study. In one trial conducted in FL during the 1993-1994 growing season, samples of mature orange fruits were harvested at 0-days following the last of three broadcast spray applications, with 79 and 110 day retreatment intervals, of the 81% SC formulation of DSMA at 4.9 lb ai/A/application (1x the maximum registered single and seasonal rates) or 24.3 lb ai/A/application (5x the maximum registered single and seasonal rates). Each spray application was made to the base of the trees using ground equipment in 50 GPA of water. On the day of harvest, orange fruits were shipped to the Citrus Research and Education Center, University of Florida (Lake Alfred, FL) for processing. Field samples of treated and untreated oranges were also frozen and shipped directly to the analytical laboratory (PTRL East).

At the processing facility, the treated and untreated whole orange samples were processed into juice, molasses, wet and dried pulp, and oil using a small scale processing procedure which according to the registrant simulated standard industrial processing conditions. Briefly, the harvested oranges were washed and rinsed. The juice was extracted from the washed oranges using a Commercial FMC 391B In-Line-Juice-Extractor. Excess pulp was removed, and fresh juice was collected. The oil/water/peel-frit emulsion from the FMC extractor was passed through a finisher equipped with a 0.02-inch screen, and peel frits and the oil/water emulsion were separately collected. The oil was centrifuged and frozen to remove water and to produce cold-pressed oil. The peel residue (peel-membrane-seed) from the FMC extractor was transferred to a hopper and chopped to a uniform size. After addition of a liquid lime slurry, the wet pulp was passed through a continuous press which separated the wet pulp into press cake and press liquor. The press cake was dried to produce dried citrus pulp. The press liquor was heated to boiling under vacuum and concentrated to produce molasses. The processed samples were shipped to PTRL East for residue analysis. Residues in/on treated and untreated oranges and its processed commodities were determined using the GC/ECD method previously discussed.

Following treatment at 1x, residues of DSMA (determined as MSMA) and cacodylic acid were each less than the respective LOQs in/on two samples of oranges (one from the field and one from the processor) and in/on one sample each of washed fruit, juice, wet and dried pulp, and oil processed from treated oranges. Detectable residues (0.05 ppm) of cacodylic acid were reported in/on one molasses sample from the 1x treatment; residues of DSMA

8

(determined as MSMA) were less than the LOQ (<0.05 ppm) in that sample. The results of the orange processing study conducted at the 5x rate are presented in Table 2.

Table 2. Residues of DSMA and cacodylic acid in the processed commodities of oranges harvested 0-day following the last of three broadcast spray applications of the 81% SC formulation at 24.3 lb ai/A (5x the maximum registered single and seasonal rates).

Substrate	Residues (ppm)			Concentration/Reduction Factor [a]		
	DSMA [b]	Cacodylic Acid	Combined	DSMA	Cacodylic Acid	Combined
Oranges (from field)	<0.05	<0.05	<0.10			
Oranges (from processor)	<0.05	<0.05	<0.10	--	--	--
Washed fruit	<0.05	<0.05	<0.10	--	--	--
Juice [c]	<0.04	<0.04	<0.08	--	--	--
Molasses	<0.05	0.17	<0.22	--	3.4	2.2
Wet pulp	<0.05	0.05	<0.10	--	1.0	1.0
Dried pulp [c]	<0.05	0.15	<0.20	--	3.0	2.0
Oil [c]	<0.05	<0.05	<0.10	--	--	--

[a] Concentration/reduction factors were calculated using residues of oranges from the processor; concentration factors were not calculated for commodities for which residues were less than the LOQ.

[b] DSMA residues were determined as MSMA.

[c] According to Table 1 of OPPTS GLN 860.1000, the processed fractions of citrus fruits include dried pulp, oil, and juice. Molasses and wet pulp have been deleted from Table 1 as processed commodities of citrus fruits.

Apparent residues of DSMA (determined as MSMA) and cacodylic acid were each less than the respective LOQs (<0.04 ppm for juice and <0.05 ppm for fruit, wet and dried pulp, molasses, and oil) in/on two samples of **untreated** oranges (one from the field and one from the processor), and one sample each of juice, wet and dried pulp, molasses, and oil processed from **untreated** oranges.

Study summary: The orange processing data are acceptable and may be used to satisfy reregistration requirements. Residues of DSMA (determined as MSMA) and cacodylic acid were each less than the analytical method's LOQ in/on orange fruits (<0.05 ppm) harvested 0-day following the last of three broadcast spray applications, with 79 and 110 day retreatment intervals, of the 81% SC formulation of DSMA at 24.3 lb ai/A/application (5x the maximum registered single and seasonal rates).

Residues of DSMA (determined as MSMA) and cacodylic acid were also below the LOQ in juice (<0.04 ppm) and oil (<0.05 ppm) processed from orange fruits treated at 5x. However, the combined residues of DSMA and cacodylic acid concentrated 2.0x in dried pulp processed from orange fruits treated at 5x. Assuming that the established tolerance for the RAC (citrus fruits) remains at 0.35 ppm, a section 409 tolerance (or section 407 MRL) need

not be established for citrus dried pulp. This determination is based on the fact that the established tolerance of 0.35 ppm is less than the number obtained by multiplying the observed concentration factor (2.0x) and the HAFT (highest average field trial) combined residues (<0.16 ppm) reported from the citrus field trials (MRID 43605901 and 43683101; DP Barcodes D214330 and D216740; currently under secondary review).

EPA MEMORANDA CITED IN THIS REVIEW

CBRS No.: 15435 and 15796
DP Barcode: D214330 and D216740
Subject: Magnitude of the residue studies in citrus fruits
From: S. Kinard
To: T. Myer
Dated: 7/12/00
MRID(s): 43605901 and 43683101

MASTER RECORD IDENTIFICATION NUMBERS

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

44195901 Johnson, T. (1996) Disodium Methanearsonate: Field Crop Residue Trials for DSMA on Citrus (Processed Commodities): Final Report: Lab Project Number: 769: 1856: 769-21. Unpublished study prepared by PTRL East, Inc. 221 p.