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

APR - 7 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Methanearsonate (MSMA/DSMA) Livestock Metabolism Studies; Chemical No. 13803; Case No. 2395; Branch No. 8647; MRID Nos. 420097-01 and -02: DP Barcode No. D168990

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The Methanearsonate (MAA) Task Force Three has submitted ruminant and laying hen metabolism studies. These studies were required for the reregistration of the methanearsonates, including monosodium methanearsonate (MSMA) and disodium methanearsonate (DSMA). Translation of MSMA metabolism studies to DSMA is acceptable, according to the Phase 4 response (C. Olinger 3/26/91).

The methanearsonates are selective herbicides used on turf and agricultural crops. Tolerances are established in 40 CFR 180.289 for residues of methanearsonic acid (calculated as arsenic trioxide) on cottonseed and citrus at 0.7 ppm and 0.35 ppm, respectively. A feed additive tolerance for cottonseed hulls (at 0.9 ppm) has been established in 40 CFR 186.4050.

CONCLUSIONS

1. Most of the [^{14}C]-MSMA fed to the livestock was excreted.

2. Residues in milk plateaued at days 3 or 5.

3. Residues in egg yolk increased throughout the seven-day dosing period. No plateau was observed but the increase exhibited linearity.

4. Residues of [^{14}C]-MSMA were found in goat leg muscle, goat milk, poultry skin/fat, and egg yolk.

5. Residues of cacodylic acid were found in liver (goat and poultry), kidney (goat and poultry), goat muscle (leg and loin), milk, poultry muscle (breast and thigh), poultry skin/fat, egg white, and egg yolk.

6. Most of the radioactivity in goat and poultry muscle (>60%TRR) was associated with the post-extraction solids and was not hydrolyzed or characterized.

7. Unknown metabolites comprising >20% of the TRR were found in poultry breast muscle and egg white.

8. Approximately 17% of the TRR in egg yolks was tentatively identified as lipid conjugates.

RECOMMENDATIONS

Using mass spectrometry or another appropriate technique the registrant should attempt to identify the unknown metabolites. The registrant should attempt to release the radioactivity from the post-extraction solids of ruminant and poultry muscle tissue using acidic, basic, and/or enzymatic hydrolysis. The hydrolysates should be characterized. Confirmation of lipid conjugation in egg yolks should be provided. The registrant should also present a discussion on any potential differences in metabolism between DSMA and MSMA. Copies of the references cited describing the methylation of arsenical compounds should be sent with the additional data requested. Tissues, milk, and eggs should be analyzed by data collection and enforcement methods and the results should be compared to identifications made in the metabolism study and to the TRR.

Note to SRRD: The entire review should be sent to the registrants.

DETAILED CONSIDERATIONS

MRID No. 42009701 Metabolism of [^{14}C]-MSMA in Lactating Goats

In-Life Phase

The dosing and sample collections was done by Bio-Life Associates, Ltd. Two lactating goats were dosed once a day with [^{14}C]-MSMA orally for seven days. Each dose capsule contained approximately 75 mg of [^{14}C]-MSMA, equivalent to approximately 42 ppm MSMA in the diet, which is equivalent to 45-48x the maximum dietary burden. No significant differences were noted in the animal weights, milk production, and excreta production before and after dosing. Twenty-two hours after the final dose, the dosed animals and a control animal were sacrificed.

The specific activity of the [^{14}C]-MSMA was 2.4 mCi/mMole. Only hot material was dosed; there was no apparent dilution with cold material.

Extraction and Hydrolysis

The total radioactive residues (TRR) were determined by combustion/liquid scintillation spectrometry (LSS), except for milk and fat samples. Milk was analyzed directly by LSS and the fat was extracted with hexane, and the TRR was determined in the hexane supernatant and the solids. Results are presented in Table 1.

Table 1. Total Radioactive Residues in Tissues after Dosing with ^{14}C-MSMA

Matrix	Goat #178, ppm	Goat #67, ppm
Loin Muscle after 2/4/91	0.088 0.085	0.092 0.089
Leg Muscle after 2/4/91	0.105 0.106	0.104 0.103
Liver	0.249	0.215
Kidney	0.335	0.292
Fat	0.012	0.012
Milk Day 1	0.021	0.015
Milk Day 2	0.028	0.021
Milk Day 3	0.030	0.025
Milk Day 4	0.032	0.022
Milk Day 5	0.030	0.038
Milk Day 6	0.034	0.021
Milk Day 7	0.030	0.022

Liver, kidney, and muscle samples were first subjected to a modified Bligh-Dyer extraction. Tissues were blended with 11:5:5 Methanol (MeOH):H_2O:$CHCl_3$ and the mixture was

centrifuged. The solids were extracted again with $CHCl_3$ and the solids were separated from the extract by centrifuging. The supernatants were combined and the $MeOH/H_2O$ layer was partitioned from the $CHCl_3$. Results are presented in Table 2.

Table 2. Results of Bligh-Dyer Extractions (Goat #178)

Matrix	PES		$MeOH/H_2O$		$CHCl_3$		% Method Recovery
	%TRR	ppm[1]	%TRR	ppm	%TRR	ppm	
Liver	57.40	0.142	37.54	0.093	5.84	0.014	100.78
Liver Fort	7.11	0.020	99.05	0.283	ND	--	106.16
Kidney	43.46	0.146	53.21	0.178	8.09	0.027	104.76
Leg Muscle	82.96	0.087	24.79	0.026	3.82	0.004	111.57
Loin Muscle	103.6	0.092	23.68	0.021	6.16	0.005	133.44

[1]TRR and ppm values calculated by reviewer from dpm values found in flow charts.

Liver was subjected to a base hydrolysis in an attempt to release additional radioactivity. 2 N NaOH was added to homogenized liver and the mixture was heated to 91°C for three hours. Attempts to separate the solids using centrifugation and filtration were unsuccessful. The mixture was neutralized with HCl and passed through a C_{18} Sep-Pak cartridge. Water was used to elute the cartridge but most of the solids absorbed onto the frit. The aqueous eluent was further cleaned-up by ion exchange chromatography.

The final attempt to release radioactivity employed water sonication. Tissue samples were sonicated for 30 minutes with water. After centrifuging the solids were extracted two more times with water and the radioactivity remaining in the solids was quantified by combustion/LSS. The radioactivity in the aqueous phase was determined directly. A solvent blank and control liver sample were fortified with [^{14}C]-MSMA and subjected to a similar clean-up. Generally good agreement between the two test animals was obtained. Results are presented in Table 3.

Table 3. Comparison of Extractable Radioactivity between Goats dosed with [^{14}C]-MSMA[1]

			Aqueous Fraction		Post-Extraction Solids	
Tissue	Goat ID#	TRR	%TRR	ppm	%TRR	ppm
Liver	178	0.249	67.07	0.167	0.204	0.051
	67	0.215	86.83	0.187	30.13	0.065
Kidney	178	0.335	102	0.341	7.62	0.026
	67	0.292	97.09	0.283	5.19	0.015
Leg Muscle	178	0.106	50.34	0.053	65.56	0.069
	67	0.104	46.98	0.049	71.68	0.075
Loin Muscle	178	0.085	67.71	0.058	48.02	0.041
	67	0.089	44.94	0.040	61.80	0.055
Control Liver	Fortif.	0.319	94.67	0.302	ND	ND

[1]TRR and ppm values calculated by reviewer from dpm values found in flow charts.

Fat samples were extracted with hexane and filtered. The solids were then extracted with MeOH/H_2O and filtered, and the final extraction of the solids used H_2O. The solvent fractions were counted directly for one test animal, but the fractions from the other animal were analyzed by combustion /LSS due to excessive chemiluminescence. Results are presented in Table 4.

Table 4. Extraction of Fat

	PES		Hexane		MeOH/H_2O		% Method Recovery
Matrix	%TRR	ppm	%TRR	ppm	%TRR	ppm	
Goat #178	18.45[1]	0.002	ND	ND	83.27	0.010	101.72
Goat #67	8.63	0.001	16.67	0.002	53.40	0.006	78.70
Control Fortif.	12.86	0.002	ND	ND	94.80	0.012	107.66

[1]TRR and ppm values calculated by reviewer from dpm values found in flow charts.

Extracts were not further characterized. No additional characterization is required since the concentration of radioactivity in the extracts and post-extraction solids are sufficiently low such that further identification would be difficult.

Milk samples were extracted with acetonitrile (ACN) and centrifuged. The solids were extracted first with 5:1 ACN:H_2O, followed by hexane, and finally H_2O. ACN was removed from the ACN/H_2O phase and the resulting aqueous fraction was partitioned with hexane. The aqueous fraction was concentrated to dryness, which the registrant reported as lactose. The lactose was rinsed with methanol and dissolved in water. Due to poor recovery of the radioactivity the flask was washed with 0.1 N NaOH. Day-5 milk samples were used since these samples exhibited the highest level of radioactivity.

Prior to the HPLC and TLC analyses, extracts were cleaned-up first using a cellulose column, followed by an XAD-2 column, and finally preparative cellulose TLC. The cellulose column was eluted with 3:1:1 MeOH:butanol:H_2O. Fractions containing radioactivity were combined. The radioactive eluent was applied to an XAD-2 column and eluted with H_2O. the fractions containing radioactivity were combined, concentrated, and applied to a cellulose TLC plate. After elution with solvent system A (3:1:1 MeOH:BuOH:H_2O) and/or B (3:2:1 ethyl acetate:acetic acid:H_2O) the radioactive bands were scraped off the plate and eluted with solvent A.

The registrant found that [^{14}C]-MSMA would adhere to the glassware. Flasks used to concentrate samples were first saturated with cold MSMA. In addition, 3-4 drops of 0.005 M dodecyltriethyl ammonium phosphate added to a solvent phase prior to concentration helped to reduce the loss.

Characterization of Residues

Thin-layer chromatography with cellulose plates and solvent systems A and B were used for identification of metabolites. The R_f values varied considerably due to matrix effects, so co-chromatography was used with unlabeled standards for identification. HPLC was used for confirmation of metabolite identification on a few fractions. A reverse phase C_{18} HPLC column was eluted isocratically with 0.005 M dodecyltriethyl ammonium phosphate. Results are presented in Table 5. Values presented in this table are directly from the report. The registrant apparently normalized the TLC and LSS results to 100%TRR accountability. TLC results (dpm values) were not reported so concentrations and %TRR could not be confirmed.

Table 5. Metabolite Identification in Goat Tissues and Milk after Dosing with [^{14}C]-MSMA[1]

Metabolite	Liver		Kidney		Loin Muscle		Leg Muscle		Milk[2]	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Extractable[3]										
MSMA	ND[4]	--	ND	--	ND	--	34.17	0.032	33.60	0.013[5]
Cacodylic Acid	74.24	0.160	85.16	0.249[5]	31.47	0.033	7.86	0.007	15.12	0.006
Unknown	--	--	9.76	0.028	8.12	0.008	--	--	--	--
Not Analyzed	N/A[6]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	48.97[7]	0.019
Post-Extraction Solids	25.76	0.055	5.08	0.015	60.41	0.063	57.97	0.053	2.34	0.001

1. All samples from Goat 67.

2. Aqueous fractions from methanol/water extractions analyzed.

3. All extractable metabolites were identified in the aqueous phase after water sonication unless otherwise indicated. All released radioactivity was generally found in a single band after preparative TLC. If two bands were found value represents combination of metabolites found in each extract after TLC.

4. ND = not detected

5. Confirmed by HPLC.

6. N/A = not applicable.

7. Represents a combination of hexane, suspension, and two of the solids fractions.

Structures of cacodylic acid and MSMA are shown if Figure 1. Additional work is needed before the metabolism of MSMA can be considered adequately delineated. Most of the radioactivity in the loin and leg muscle samples was not released from the post-extraction solids. An attempt should be made to hydrolyze the remaining radioactivity using acidic, basic, or enzymatic hydrolysis. Hydrolysates should be characterized. The unknown extractable radioactivity should be identified using mass spectrometry.

The proposed metabolic pathway is shown in Figure 2. The registrant states that arsenical compounds can be readily methylated and cited two papers in support of their statement. Conjugation of MSMA was not discussed, despite the considerable amount of activity which was not extracted from the muscle tissues. The registrant should also discuss any potential differences in metabolites between DSMA and MSMA. For example, since one of the ionic oxygens was exchanged for a methyl group, could this potentially occur with both of them?

The investigators did not validate any data collection and/or enforcement methods using the tissues from the metabolism studies. Tissues and milk should be analyzed by these methods and the results should be compared to identifications made in the metabolism study and to the TRR.

Fortifications

Liver, fat, and milk samples were fortified with [^{14}C]-MSMA and put through the same extraction procedures as the treated samples. All of the radioactivity was extractable when liver was sonicated with water, and was identified (by TLC) as MSMA. When subjected to the Bligh-Dyer extraction the radioactivity was distributed between the MeOH/H_2O and post-extraction solids.

Difficulty was experienced with the milk fortifications. The [^{14}C]-MSMA adhered to the glassware and the extraction procedures were modified (as described above) to enhance the recovery. Approximately 67% of the radioactivity was recovered and identified as MSMA.

Most of the radioactivity in the fortified fat was recovered in the MeOH/H_2O phase. No further characterization was done.

MRID No. 42009702 Metabolism of [^{14}C]-MSMA in Laying Hens

In-Life Phase

The dosing and sample collections was done by Bio-Life Associates, Ltd. Ten laying hens were dosed once a day with [^{14}C]-MSMA orally for seven days. Each dose capsule contained approximately 6 mg of [^{14}C]-MSMA, equivalent to approximately 42 ppm MSMA in the diet. The registrant estimated this to be 34x the maximum dietary burden, based on a diet of 100% cottonseed with residues at the tolerance level. No significant differences were noted in the animal weights, egg production, and excreta production before and after dosing. Twenty-four hours after the final dose, the dosed animals and five control animals were sacrificed. The tissues and eggs were pooled by treatment group.

The specific activity of the [^{14}C]-MSMA was 2.4 mCi/mMole. Only hot material was dosed; there was no apparent dilution with cold material.

Extraction and Hydrolysis

The total radioactive residue (TRR) in tissues (except fat), eggs, and post-extraction solids was determined by combustion/LSS. Fat was extracted with hexane and the TRR in the hexane supernatant and post-extraction solids was determined separately. Results are presented in Table 6.

Table 6. Total Radioactive Residues in Tissues and Eggs of Hens dosed with [^{14}C]-MSMA

Tissue	TRR, ppm
Breast Muscle	0.119
Thigh Muscle	0.083
Liver	0.101
Kidney	0.158
Preformed Egg	0.345
Fat	0.023

	Egg Yolk	Egg White
Day of Dosing	TRR, ppm	TRR, ppm
Day 1	0.003	0.002
Day 2	0.023	0.039
Day 3	0.090	0.090
Day 4	0.156	0.103
Day 5	0.234	0.106
Day 6	0.308	0.096
Day 7	0.340	0.108

Most of the dose (87%) was recovered in the excreta. Less than 0.25% of the dose was recovered in the tissues and eggs.

The increase of the TRR in the egg yolks was linear throughout the seven-day dosing period. When conducting the poultry feeding studies (which the registrant committed to do in Phase 3) the registrant should ensure the residues in the eggs have plateaued after the 28-day dosing. If a plateau has not been reached by 28 days, the study dosing should be continued until a plateau is reached.

Liver, kidney, and muscle samples were homogenized with water and sonicated for 30 minutes. The aqueous extract was separated from the solids by centrifugation and the extraction procedure was repeated twice. Radioactivity in the post-extraction solids was quantified by combustion/LSS. Results are presented in Table 7.

Table 7. Distribution of Radioactivity in Liver, Kidney, and Muscle

Tissue	Aqueous Extractable		Post-Extraction Solids		Totals	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Liver	102[1]	0.103	22.28	0.023	124	0.101
Kidney	95.69	0.151	21.40	0.034	117	0.158
Breast Muscle	42.22	0.050	70.55	0.084	113	0.119
Thigh Muscle	38.16	0.032	64.28	0.053	102	0.083

[1]TRR and ppm values calculated by reviewer from dpm values found in flow charts.

Fat samples were extracted with hexane and filtered. The solids were blended with 11:5 MeOH:H_2O and filtered. A final extraction of the solids with H_2O was conducted. Results are presented in Table 8.

Table 8. Distribution of Radioactivity in Fat

Fraction	% TRR	ppm
Hexane	17.67[1]	0.004
MeOH/H_2O	40.16	0.007
Post-Extraction Solids	82.34	0.014

[1]TRR and ppm values calculated by reviewer from dpm values found in flow charts.

Egg yolk and egg white samples were extracted three times with 6:5:1 hexane:ACN:H_2O. Extracts were separated from the solids by centrifugation and the hexane layer was separated from the ACN/H_2O layer. The hexane layer was saponified if significant radioactivity was found in this fraction. The hexane extract was concentrated to a low volume, KOH was added, and refluxed for three hours. The KOH extract was partitioned with hexane, acidified with HCl, and partitioned again with hexane. Results are presented in Table 9.

Table 9. Distribution of Radioactivity in Eggs[1]

	Egg White		Egg Yolk	
Fraction	%TRR	ppm	%TRR	ppm
ACN/H_2O	61.51	0.067	34.33	0.117
Hexane	ND[2]	ND	0.056	16.33
Hexane	N/A[3]	N/A	ND	ND
KOH	N/A	N/A	0.057	16.64
HCl	N/A	N/A	0.030	8.76
Hexane	N/A	N/A	0.027	7.88
Post-Extraction Solids	29.69	0.032	47.06	0.160

[1]Values calculated by reviewer from dpm values in flow chart.

[2]ND = not detected [3]N/A = not available

Prior to the HPLC and TLC analyses extracts were cleaned-up using first a cellulose column, followed by an XAD-2 column, and finally preparative cellulose TLC. The cellulose column was eluted with 3:1:1 MeOH:butanol:H_2O. Fractions containing radioactivity were combined. The radioactive eluent was applied to an XAD-2 column and eluted with H_2O. the fractions containing radioactivity were combined, concentrated, and applied to a cellulose TLC plate. After elution with solvent system A (3:1:1 MeOH:BuOH:H_2O) and/or B (3:2:1 ethyl acetate:acetic acid:H_2O) the radioactive bands were scraped off the plate and eluted with solvent A.

The registrant found that [^{14}C]-MSMA would adhere to the glassware. Flasks used to concentrate samples were first saturated with cold MSMA. In addition, 3-4 drops of 0.005 M dodecyltriethyl ammonium phosphate added to a solvent phase prior to concentration helped to reduce the loss.

Characterization of Residues

Thin-layer chromatography with cellulose plates and solvent systems A and B were used for identification of metabolites. The R_f values varied considerably due to matrix effects, so co-chromatography was used with unlabeled standards for identification. HPLC was used for confirmation of metabolite identification on a few fractions. A reverse phase C_{18} HPLC column was eluted isocratically with 0.005 M dodecyltriethyl ammonium phosphate. Results are presented in Table 5. Values presented in this table are directly from the report. The registrant apparently normalized the TLC and LSS results to 100%TRR accountability. TLC results (dpm values) were not reported so concentrations could not be confirmed. Results are presented in Table 10.

Table 10. Characterization of Radioactivity in Tissues and Eggs from Hens Dosed with [^{14}C]-MSMA

Metabolite	Liver		Kidney		Breast Muscle		Thigh Muscle		Skin/Fat		Egg White		Egg Yolk	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Extractable														
MSMA	--	--	--	--	--	--	--	--	17.42	0.004	--	--	21.26	0.072
Cacodylic Acid	68.31	0.069	81.72	0.129	12.10	0.014	27.71	0.023	11.23	0.003	39.08	0.042	13.87	0.047
Unknown	13.80	0.014	--	--	25.34	0.030	9.54	0.008	--	--	28.36	0.031	--	--
Lipid Conjugated[1]	--	--	--	--	--	--	--	--	--	--	--	--	16.71	0.057
Not Analyzed	--	--	--	--	--	--	--	--	12.61	0.003	--	--	--	--
Non-Extractable	17.89	0.018	18.28	0.029	62.56	0.074	62.75	0.052	58.74	0.014	32.56	0.035	48.16	0.164

[1]Represents the final hexane fraction from saponification that was not analyzed and the HCl fraction that was inconclusive.

Only the identifications in the egg yolk were confirmed by HPLC. Additional work is needed before the metabolism of MSMA in poultry can be considered adequately delineated. Most of the radioactivity in the breast and thigh muscle samples was not released from the post-extraction solids. An attempt should be made to hydrolyze the remaining radioactivity using acidic, basic, or enzymatic hydrolysis. Hydrolysates should be identified. The unknown extractable radioactivity should be identified using mass spectrometry. The registrant has not provided an adequate justification for the identification of some of the radioactivity as "lipid conjugated". Confirmation of lipid conjugation is required.

Tissue and egg samples from the poultry metabolism study were not analyzed by data collection or enforcement methods to ensure adequate recovery of the residues of concern.

Storage Stability

Control liver, egg white, and egg yolk samples were fortified with [^{14}C]-MSMA, placed into frozen storage, and analyzed ten weeks later. Analyses were also conducted soon after fortification.

The distribution of radioactivity is shown in Table 11. Results of TLC analyses for residues of MSMA may be found in Table 12.

Table 11. Distribution of Radioactivity in [^{14}C]-MSMA Fortified Liver, Egg White, and Egg Yolk Samples

	Aqueous		ACN/H_2O		Hexane		Non-extractable		Totals	
Tissue	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Liver t_0	90.37	0.114	N/A[2]	N/A	N/A	N/A	1.95	0.002	92.32	0.126
Liver t_{10}	126	0.118	N/A	N/A	N/A	N/A	1.56	0.001	127	0.094
Egg Yolk t_0	N/A	N/A	49.57	0.170	11.72	0.040	45.72	1.57	107	0.343
Egg Yolk t_{10}	N/A	N/A	77.11	0.244	13.24	0.042	23.58	0.057	114	0.316
Egg White t_0	N/A	N/A	90.51	0.103	ND[3]	ND	14.04	0.016	105	0.114
Egg White t_{10}	N/A	N/A	92.34	0.095	ND	ND	30.13	0.031	123	0.103

[1]TRR and ppm values calculated by reviewer from dpm values found in flow charts.

[2]N/A = not applicable [3]ND = not detected

Table 12. Characterization of Radioactivity in Fortified Liver, Egg Yolk, and Egg White Samples

	MSMA		Cacodylic Acid		Not Analyzed		Lipid Conjugated[1]	
Tissue	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Liver t_0	97.88	0.123	ND[2]	ND	N/A[3]	N/A	N/A	N/A
Liver t_{10}	98.77	0.093	ND	ND	N/A	N/A	N/A	N/A
Egg Yolk t_0	46.32	0.159	ND	ND	N/A	N/A	10.95	0.038
Egg Yolk t_{10}	67.68	0.214	ND	ND	11.62	0.038	N/A	N/A
Egg White t_0	86.58	0.099	ND	ND	N/A	N/A	N/A	N/A
Egg White t_{10}	75.40	0.078	ND	ND	N/A	N/A	N/A	N/A

[1]Represents the final hexane fraction from saponification that was not analyzed and the HCl fraction that was inconclusive.

[2]ND = not detected [3]N/A = not applicable

The registrant states that samples were stored for no more that 10 weeks prior to extraction. According to the dates in the report samples were stored up to four months prior to extraction. Incomplete recovery of MSMA was obtained for egg yolk at the initial fortification and ten weeks. This method does not appear adequate to assess the storage stability of MSMA in egg yolks since most of the radioactivity at t_0 was found with the post-extraction solids.

CODEX CONSIDERATIONS

Codex MRLs have not been established for residues of MSMA or DSMA.

TOLERANCE CONSIDERATIONS

Once the additional characterization has been completed and the analytical method(s) have been validated (using tissues from the metabolism studies) the Agency and the registrants must consider the impact of the metabolism studies on the tolerance expression. Cacodylic acid is a pesticide for which a tolerance has also been established on cottonseed (2.8 ppm, 40 CFR 180.311). Tolerances for cacodylic acid are also established in animal commodities. The enforcement methods for both MSMA/DSMA and cacodylic acid involve conversion to As_2O_3 and quantitation of total arsenic. If TOX is concerned about differentiating between MSMA/DSMA and cacodylic acid, confirmation methods differentiating the two compounds would be required. The tolerance expression would also need to differentiate MSMA/DSMA residues from cacodylic acid residues.

cc: CLOlinger (CBRS), Circulate, List B File, RF, SF, C. Furlow (PIB/FOD)
H7509C:CBRS:CLOlinger:clo:CM#2:Rm 803C:305-5406: 3/30/92
RDI: ARRathman: 4/02/92 MMetzger: 4/06/92 EZager: 4/06/92

Figure 1. Structures of MSMA and Cacodylic Acid

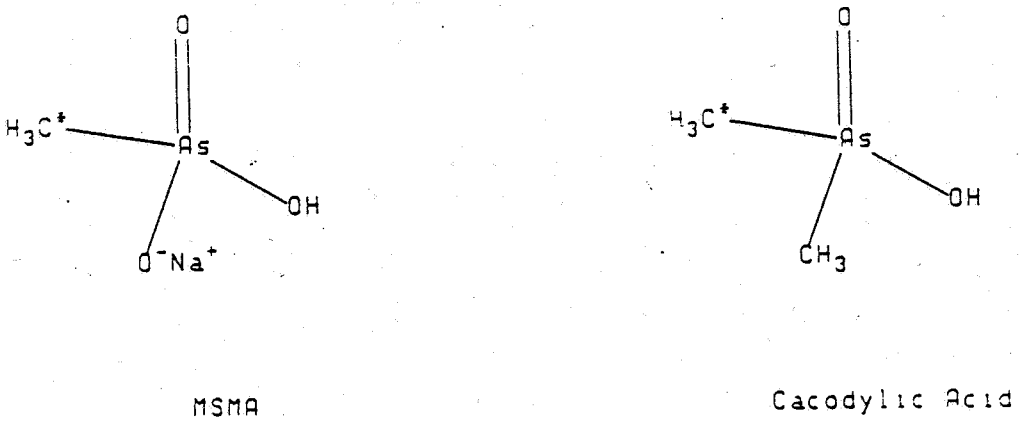

Figure 2. Proposed Metabolic Pathway