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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: June 11, 2001

MEMORANDUM

SUBJECT: Metalaxyl/Mefenoxam Storage Stability in Livestock Commodities.

DP Barcode:	D248748	PRAT Case:	819456
Submission No.:	S547725	Caswell No.:	None
PC Code:	113501 and 113502	Class:	Fungicide
Trade Name:	Not Applicable	EPA Reg. No.:	Not Applicable
40 CFR:	180.408 and 180.546		
MRID Nos.:	44316102 and 44617001		

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06/19/2001

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INTRODUCTION

Syngenta (formerly Novartis Crop Protection, Inc. and formerly Ciba Crop Protection) submitted storage stability data for the fungicide mefenoxam [(R)-2-[(2,6-dimethylphenyl)-methoxyacetylamino]-propionic acid methyl ester; CGA-329351] in livestock commodities. The storage stability data were requested under the metalaxyl reregistration process [D197066, S. Hummel, 2/17/94; and the Product and Residue Chemistry Chapters for the Metalaxyl Reregistration Eligibility Decision (RED) Document (DP Barcodes D197037 and D197066, CBRS #12906 and 12907, issued on 6/16/94)]. Mefenoxam is the R isomer; metalaxyl (CGA-48988) is a mixture of the R and S isomers.

A time-limited tolerance (to expire on December 31, 2001) for mefenoxam and its metabolites containing the 2,6-dimethylaniline moiety, and *N*-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)-alanine methyl ester, each expressed as mefenoxam equivalents, in/on canola at 0.05 ppm has been established [*FR Vol. 65, 57550-57557*; 40 CFR § 180.546 (b)] in connection with a Section 18 emergency exemption for use of mefenoxam as a seed treatment on canola in ND. A permanent tolerance is pending for the combined residues of (R)- and (S)-2-[(2,6-dimethylphenyl)-methoxyacetylamino]-propionic acid methyl ester, its metabolites containing the 2,6-dimethylaniline moiety, and *N*-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)alanine methyl ester, each expressed as mefenoxam equivalents, on canola at 0.05 ppm (D254225, N. Dodd, 11/13/00). No other tolerances have been established for mefenoxam.

Permanent tolerances have been established for the combined residues of metalaxyl [*N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl) alanine methyl ester] and its metabolites containing the 2,6-dimethylaniline moiety, and *N*-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)-alanine methyl ester, each expressed as metalaxyl equivalents, in/on a number of plant and livestock commodities [40 CFR §180.408 (a, c, and d)]. Tolerances have been established on plant commodities at levels ranging from 0.1 ppm in/on beets (sugar and garden), *Brassica* leafy vegetables, cereal grains, cottonseed, pineapples, sunflowers, and papaya to 25 ppm in/on grass hay. Tolerances have been established for livestock commodities at 0.4 ppm in the fat, kidney, and liver of cattle, goats, hogs, horses, poultry, and sheep; 0.05 ppm in meat and meat byproducts (except kidney and liver) of cattle, goats, hogs, horses, poultry, and sheep; 0.02 ppm in milk, and 0.05 ppm in eggs.

Tolerances for residues of metalaxyl in/on raw and processed plant commodities and livestock commodities are currently expressed in the CFR in terms of the combined residues of metalaxyl [*N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl) alanine methyl ester] and its metabolites containing the 2,6-dimethylaniline moiety, and *N*-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)-alanine methyl ester, each expressed as metalaxyl equivalents. However, the HED Metabolism Committee (now called Metabolism Assessment Review Committee) determined in a meeting on 9/8/93 that the residues to be regulated in livestock commodities are metalaxyl, metabolites that can be converted to 2,6-dimethylaniline (2,6-DMA), and those metabolites containing the 2-

hydroxymethyl-6-methylaniline (HMMA) moiety (S. Hummel, 9/10/93).

The Metabolism Assessment Review Committee (D269910, N. Dodd, 10/27/00) discussed mefenoxam on 10/24/00 and concluded that the residues to be regulated for the tolerance expression and for dietary risk assessments would be the following:

Plants

(R)- and (S)-2-[(2,6-dimethylphenyl)-methoxyacetylamino]-propionic acid methyl ester, its metabolites containing the 2,6-dimethylaniline moiety, and *N*-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)alanine methyl ester*, each expressed as mefenoxam equivalents

[* *N*-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)alanine methyl ester is CGA-94689.]

Livestock

(R)- and (S)-2-[(2,6-dimethylphenyl)-methoxyacetylamino]-propionic acid methyl ester, its metabolites containing the 2,6-dimethylaniline moiety, and its metabolites containing the 2-hydroxymethyl-6-methylaniline moiety, each expressed as parent equivalents

Rotational Crops

(R)- and (S)-2-[(2,6-dimethylphenyl)-methoxyacetylamino]-propionic acid methyl ester, its metabolites containing the 2,6-dimethylaniline moiety, and *N*-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)alanine methyl ester, each expressed as parent equivalents, except that 2-[(methoxyacetyl)(2-methoxy-1-methyl-2-oxoethyl)amino]-3-methylbenzoic acid (CGA-108905) and *N*-(3-hydroxy-2,6-dimethylphenyl)-*N*-(methoxyacetyl)alanine methyl ester (CGA-100255) will be considered in risk assessments involving the foliar use of mefenoxam.

Metalaxyl is a List A chemical. A Metalaxyl Reregistration Standard and Guidance Document was issued on 12/81. Product and Residue Chemistry Chapters of the Metalaxyl Registration Standard were issued on 6/22/87. The Metalaxyl Final Reregistration Standard and Tolerance Reassessment (FRSTR) Guidance Document was dated 9/88. The Metalaxyl Product Chemistry and Residue Chemistry Reregistration Standard Updates were issued on 3/13/91. There is a Metalaxyl Product Chemistry and Residue Chemistry Registration Standard Update dated 4/92. The Product and Residue Chemistry Chapters for the Metalaxyl Reregistration Eligibility Decision Document (DP Barcodes D197037 and D197066, CBRS #12906 and 12907) were issued on 6/16/94.

The structure of metalaxyl/mefenoxam is shown in Figure 1 below.

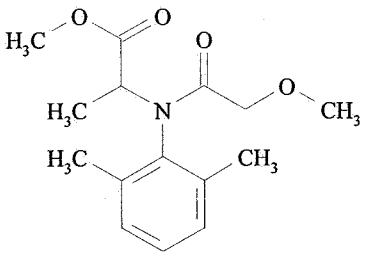


Figure 1. Metalaxyl/Mefenoxam

CONCLUSIONS

OPPTS GLN 860.1380: STORAGE STABILITY DATA - LIVESTOCK

1. Residues of CGA-329351, CGA-62826, and CGA-94689 in beef muscle, beef liver, and milk and residues of CGA-329351 and CGA-62826 in eggs, determined as 2,6-dimethylaniline, are stable in frozen storage (at approximately -20°C) for at least 18 months.

2. Residues of CGA-94689 in eggs, determined as 2,6-dimethylaniline, were stable in frozen storage (at approximately -20°C) for 3 months but declined at 6 months (-28%), 12 months (-16%), 18 months (-31%), and 23 months (-17%).

3. The recoveries for CGA-62826 in eggs and for CGA-94689 in all matrices tested in this submission are low for both fresh fortifications and stored samples. The above conclusions regarding the storage stability are based on the measure of stability as defined in OPPTS 860.1380 for the storage stability tables: "The values in the second column from the right represent the apparent recovery in the stored samples. These can be divided by the recoveries obtained in the freshly fortified samples to determine the corrected recovery, the measure of the stability of the residue in storage....".

4. Storage stability data are needed for P1 and P2 in livestock commodities stored frozen for one year, as requested in the metalaxyl reregistration process.

RECOMMENDATIONS

The registrant/petitioner should be informed of the status of the livestock storage stability data as stated in Conclusions 1, 2, 3, and 4 above.

DETAILED CONSIDERATIONS

See Attachment 1 for the chemical names and structures of mefenoxam and its metabolites which are discussed in this review.

OPPTS GLN 860.1380: STORAGE STABILITY DATA

LIVESTOCK (MRID 44316102 and MRID 44617001)

For reregistration of metalaxyl, storage stability data on livestock commodities representing one year of frozen storage were required (The Product and Residue Chemistry Chapters for the Metalaxyl Reregistration Eligibility Decision Document, DP Barcodes D197037 and D197066, CBRS #12906 and 12907, issued on 6/16/94).

In response, storage stability studies (MRID 44316102, interim report; and MRID 44617001, final report) on mefenoxam (CGA-329351), CGA-62826 (which contains the dimethylaniline moiety), and CGA-94689 (which contains the 2-hydroxymethyl-6-methyl aniline moiety) in beef muscle, beef liver, milk, and eggs were submitted. The performing laboratory was Novartis Crop Protection, Inc., Greensboro, NC. The studies are cited below:

MRID 44316102 Eudy, L.W. (1997) Stability of CGA-329351, CGA-62826, CGA-94689 in Meat, Milk, and Eggs under Freezer Storage Conditions, Interim Report, Laboratory Project Identification No. (Report No.) ABR-97048, Study Number 230-96, unpublished study sponsored by Novartis Crop Protection, Inc., 80 pp.

MRID 44617001 Gruenwald, M.C. (1998) Stability of CGA-329351, CGA-62826, CGA-94689 in Meat, Milk, and Eggs under Freezer Storage Conditions, Laboratory Project Identification No. (Report No.) ABR-98053, Novartis Number 230-96, unpublished study sponsored by Novartis Crop Protection, Inc., 92 pp.

Samples of beef muscle, beef liver, milk, and eggs were fortified with mefenoxam (CGA-329351), CGA-62826, or CGA-94689 and stored frozen (at approximately -20°C) in polyethylene bottles. Samples of beef muscle and beef liver were ground before fortification. Samples of milk and eggs were homogenized by shaking before fortification. Samples were extracted at 0-day and at 3, 6, 12, 18 and 23 months. For muscle, liver, and egg samples, analytical Method AG-576 was used to determine residues. For milk samples, the acetonitrile extraction and acetonitrile:hexane partition steps described in AG-349 were combined with the methanesulfonic acid reflux, cleanup, and chromatographic steps described in AG-576. Residues were determined as 2,6-dimethylaniline (DMA) and then converted to CGA-329351, CGA-62826, or CGA-94689 equivalents using the factors 2.305, 2.189, or 2.437, respectively.

Table1. Storage Stability Fortification Recovery Data for CGA-329351 in Beef Muscle								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
beef muscle	CGA-329351	2.0	0	9	1.931, 1.732, 1.466 (av 1.710)	89, 92, 76 (av 86)	86	100
			3.2	13	1.607, 1.495 (av 1.551)	85, 84 (av 84)	78	93
			5.9	8	1.588, 1.765 (av 1.676)	80, 85 (av 82)	84	102
			12.6	4	1.726, 1.608 (av 1.667)	90, 87 (av 88)	83	94
			17.9	3	1.818, 1.670 (av 1.744)	87, 78 (av 82)	87	106
			21.6	7	1.499, 1.378 (av 1.438)	82, 78 (av 80)	72	90

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 2.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 2. Storage Stability Fortification Recovery Data for CGA-329351 in Beef Liver								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
beef liver	CGA-329351	2.0	0.0	6	2.051, 1.812, 1.666 (av 1.843)	81, 93, 87 (av 87)	92	106
			3.2	22	1.835, 1.765 (av 1.800)	86, 87 (av 86)	90	105
			6.0	12	1.632, 1.693 (av 1.662)	86, 87 (av 86)	83	97
			12.6	3	1.822, 1.920 (av 1.871)	97, 98 (av 98)	94	96
			17.9	5	1.737, 1.810 (av 1.774)	100, 86 (av 93)	89	96
			21.6	8	1.466, 1.415 (av 1.440)	83	72	87

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 2.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 3. Storage Stability Fortification Recovery Data for CGA-329351 in Milk								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
milk	CGA-329351	2.0	0.0	11	1.505, 1.504, 1.294 (av 1.434)	61, 66, 72 (av 66)	72	109
			3.2	7	1.603	80, 80 (av 80)	80	100
			6.0	13	1.492, 1.403 (av 1.448)	71, 69 (av 70)	72	103
			12.4	3	1.816, 1.865 (av 1.840)	90, 98 (av 94)	92	98
			17.8	4	1.846, 1.795 (av 1.820)	82, 87 (av 84)	91	108
			21.5	6	1.827, 1.771 (av 1.799)	82, 85 (av 84)	90	107

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 2.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 4. Storage Stability Fortification Recovery Data for CGA-329351 in Eggs								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
eggs	CGA-329351	2.0	0.0	15	1.579, 1.553, 1.552 (av 1.561)	76, 80, 86 (av 81)	78	96
			3.1	13	1.495, 1.745 (av 1.620)	85, 94 (av 90)	81	90
			6.1	7	1.702, 1.755 (av 1.728)	81, 87 (av 84)	86	102
			12.7	8	1.988, 1.880 (av 1.934)	98, 87 (av 92)	97	105
			18.0	4	1.734	82, 91 (av 86)	87	101
			22.1	3	1.481, 1.644 (av 1.562)	78, 76 (av 77)	78	101

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 2.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 5. Storage Stability Fortification Recovery Data for CGA-62826 in Beef Muscle								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
beef muscle	CGA-62826	2.0	0.0	8	1.467, 1.455 (av 1.461)	80, 78, 77 (av 78)	73	94
			2.8	12	1.486, 1.385 (av 1.436)	79, 76 (av 78)	72	92
			6.0	20	1.322, 1.316 (av 1.319)	78, 81 (av 80)	66	82
			11.8	7	1.706, 1.617 (av 1.662)	84, 86 (av 85)	83	98
			18.0	3	1.552, 1.587 (av 1.570)	86, 80 (av 83)	78	94
			23.0	8	1.524, 1.631 (av 1.578)	88, 84 (av 86)	79	92

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 2.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 6. Storage Stability Fortification Recovery Data for CGA-62826 in Beef Liver								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
beef liver	CGA-62826	2.0	0.0	15	1.375, 1.368, 1.537 (av 1.427)	57, 58, 78 (av 64)	71	111
			2.9	14	1.378, 1.505 (av 1.442)	76, 72 (av 74)	72	97
			6.1	29	1.410, 1.534 (av 1.472)	75, 77 (av 76)	74	97
			12.0	11	1.638, 1.635 (av 1.636)	80, 81 (av 80)	82	102
			18.1	16	1.680, 1.758 (av 1.719)	86	86	100
			23.2	7	1.629, 1.658 (av 1.644)	89, 87 (av 88)	82	93

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 2.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 7. Storage Stability Fortification Recovery Data for CGA-62826 in Milk								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
milk	CGA-62826	2.0	0.0	24	1.653, 1.399, 1.423 (av 1.492)	81, 77, 70 (av 76)	75	99
			3.2	12	1.418, 2.260 (av 1.839)	118, 70 (av 94)	92	98
			6.4	13	1.191, 1.170 (av 1.180)	56, 58 (av 57)	59	104
			12.1	20	1.282, 1.273 (av 1.278)	66, 64 (av 65)	64	98
			19.0	6	1.568, 1.619 (av 1.594)	87, 80 (av 84)	80	95
			23.4	4	1.489, 1.474 (av 1.482)	81, 65 (av 73)	74	101

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 2.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 8. Storage Stability Fortification Recovery Data for CGA-62826 in Eggs								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
eggs	CGA-62826	2.0	0.0	7	1.055, 1.040, 0.964 (av 1.020)	48, 51, 50 (av 50)	51	102
			2.8	12	1.009, 1.090 (av 1.050)	50, 51 (av 50)	52	104
			6.0	8	1.074, 1.038 (av 1.056)	51, 51 (av 51)	53	104
			11.8	11	0.954, 1.069 (av 1.012)	52, 47 (av 50)	51	102
			18.0	2	1.000, 0.955 (av 0.978)	48	49	102
			23.1	7	1.088, 1.071 (av 1.080)	56, 56 (av 56)	54	96

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 2.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 9. Storage Stability Fortification Recovery Data for CGA-94689 in Beef Muscle								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
beef muscle	CGA-94689	5.0	0.0	8	2.457, 2.577, 2.640 (av 2.558)	57, 58, 54 (av 56)	51	91
			2.8	26	2.588, 2.679 (av 2.634)	60, 38 (av 49)	53	108
			6.0	29	2.876, 2.672 (av 2.774)	56, 58 (av 57)	55	96
			11.8	7	2.521, 2.488 (av 2.504)	53, 51 (av 52)	50	96
			18.6	15	2.943, 2.651 (av 2.797)	33, 41 (av 37)	56	151
			23.0	9	1.924, 1.144 (av 1.534)	30, 35 (av 32)	31	97

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 5.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 10. Storage Stability Fortification Recovery Data for CGA-94689 in Beef Liver								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
beef liver	CGA-94689	5.0	0.0	19	1.188, 1.482, 1.394 (av 1.355)	21, 20, 30 (av 24)	27	112
			2.9	15	1.184, 1.172 (av 1.178)	28, 24 (av 26)	24	92
			6.1	3	1.239, 1.298 (av 1.268)	21, 29 (av 25)	25	100
			12.0	12	1.215, 1.250 (av 1.232)	24, 26 (av 25)	25	100
			18.1	31	0.905, 1.152 (av 1.028)	23, 23 (av 23)	21	91
			23.2	8	0.904, 0.540 (av 0.722)	20, 23 (av 22)	14	64

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 5.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 11. Storage Stability Fortification Recovery Data for CGA-94689 in Milk								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
milk	CGA-94689	5.0	0.0	25	3.161, 3.195, 3.376 (av 3.244)	72, 64, 64 (av 67)	65	97
			3.2	26	3.042, 3.302 (av 3.172)	57, 61 (av 59)	63	107
			6.4	20	2.491, 2.176 (av 2.334)	53, 53 (av 53)	47	89
			12.1	22	2.122, 2.623 (av 2.372)	44, 44 (av 44)	47	107
			19.3	5	1.725, 1.440 (av 1.582)	35, 26 (av 30)	32	107
			23.4	4	0.772, 0.951 (av 0.862)	43, 36 (av 40)	17	42

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 5.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Table 12. Storage Stability Fortification Recovery Data for CGA-94689 in Eggs								
Commodity	Analyte	Residue Level Added (ppm)	Storage Period, Fortification to Extraction (months)	Storage Period, Extraction to Analysis (days)	Residue Level Found, Uncorrected[1] (ppm)	Fresh Fortification Recovery[2] (%)	Apparent Recovery in Stored Sample (%)	Corrected Recovery[3] in Stored Sample (%)
eggs	CGA-94689	5.0	0.0	9	2.561, 2.781, 2.850 (av 2.731)	50, 56, 53 (av 53)	55	104
			2.8	12	2.351, 2.267 (av 2.309)	49, 44 (av 46)	46	100
			6.0	35	0.782, 1.025 (av 0.904)	27, 23 (av 25)	18	72
			11.8	12	2.067, 2.082 (av 2.074)	48, 50 (av 49)	41	84
			18.0	6	1.015, 0.781 (av 0.898)	27, 24 (av 26)	18	69
			23.1	12	1.208, 0.653 (av 0.930)	27, 19 (av 23)	19	83

[1] Residue levels found were not corrected for controls or fresh fortification recoveries.

[2] The fortification level was 5.00 ppm. Results are not corrected for controls.

[3] apparent recoveries ÷ fresh fortification recoveries X 100

Discussion

The ChemSAC determined in a meeting on 2/28/01 that the plant storage stability data for CGA-94689 are acceptable despite the low fresh fortification recoveries since 1) parent and the other metabolites are stable; 2) there was a high degree of consistency in recoveries; and 3) CGA-94689 is not of particularly high toxicological concern.

Summary

Storage stability data were submitted for mefenoxam (CGA-329351), CGA-62826 (which contains the dimethylaniline moiety), and CGA-94689 (which contains the 2-hydroxymethyl-6-methyl aniline moiety) in beef muscle, beef liver, milk, and eggs. Ground muscle and liver and homogenized eggs and milk were fortified with CGA-329351, CGA-62826, or CGA-94689 and stored at -20°C for 21-23 months. Residues were determined using method AG-576 for muscle, liver, and eggs and a combination of methods AG-349 and AG-576 for milk. Residues were detected as 2,6-dimethylaniline (DMA) and then converted to CGA-329351, CGA-62826, or CGA-94689 equivalents. Residues of CGA-329351 are stable in beef muscle, beef liver, milk, and eggs stored frozen (-20°C) for at least 21 months. Residues of CGA-62826 are stable in beef muscle, beef liver, milk, and eggs stored frozen (-20°C) for at least 23 months. Residues of CGA-94689 are stable in beef muscle stored frozen (-20°C) for at least 23 months. Residues of CGA-94689 were stable in beef liver stored frozen (-20°C) for 18 months but declined (-36%) at 23 months storage. Residues of CGA-94689 were stable in milk stored frozen (-20°C) for 18 months but declined (-58%) at 23 months storage. Residues of CGA-94689 were stable in eggs stored frozen (-20°C) for 3 months but declined at 6 months (-28%), 12 months (-16%), 18 months (-31%), and 23 months (-17%).

Conclusions

Residues of CGA-329351, CGA-62826, and CGA-94689 in beef muscle, beef liver, and milk and residues of CGA-329351 and CGA-62826 in eggs, determined as 2,6-dimethylaniline, are stable in frozen storage (at approximately -20°C) for at least 18 months.

Residues of CGA-94689 in eggs, determined as 2,6-dimethylaniline, were stable in frozen storage (at approximately -20°C) for 3 months but declined at 6 months (-28%), 12 months (-16%), 18 months (-31%), and 23 months (-17%).

The recoveries for CGA-62826 in eggs and for CGA-94689 in all matrices tested in this submission are low for both fresh fortifications and stored samples. The above conclusions regarding the storage stability are based on the measure of stability as defined in OPPTS 860.1380 for the storage stability tables: "The values in the second column from the right represent the apparent recovery in the stored samples. These can be divided by the recoveries obtained in the freshly fortified samples to determine the corrected recovery, the measure of the stability of the residue in storage....".

Storage stability data are needed for P1 and P2 in livestock commodities stored frozen for one year, as requested in the metalaxyl reregistration process.

Attachment 1: Names and Structures of Mefenoxam, CGA-94689, CGA-62826, P1, and P2

cc: N. Dodd (810C), PM#21, PM#53, M. Rust (810J)
RDI: Chem Team:5/16/01: S. Dapson:6/11/01
7509C:RAB3:CM#2:Rm810C:305-5681:N. Dodd:nd:6/11/01

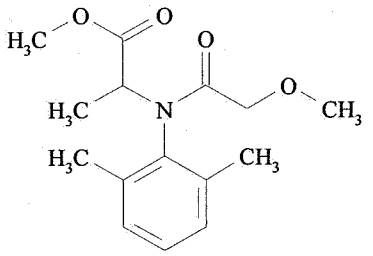
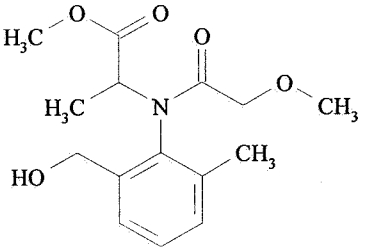
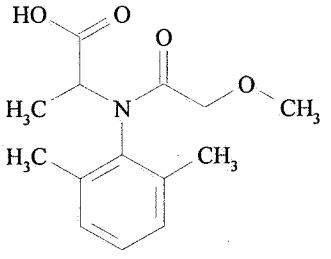
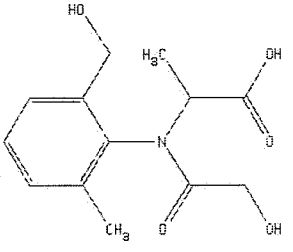
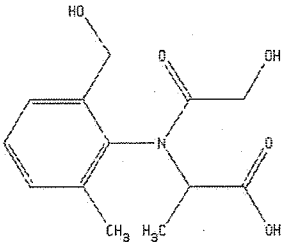
Table 13. Names and Structures of Mefenoxam, CGA-94689, CGA-62826, P1, and P2	
Chemical Name Common Name (Company Code)	Structure
(R)-2-[(2,6-dimethylphenyl)-methoxyacetylamino]-propionic acid methyl ester mefenoxam (CGA-329351)	
N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester (CGA-94689)	
N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine (CGA-62826)	
N-[2-(hydroxymethyl)-6-methylphenyl-N-(hydroxyacetyl)alanine[1] (P1)	

Table 13. Names and Structures of Mefenoxam, CGA-94689, CGA-62826, P1, and P2	
Chemical Name Common Name (Company Code)	Structure
N-[2-(hydroxymethyl)-6-methylphenyl]-N-(hydroxyacetyl)alanine[1] (P2)	

[1] P1 and P2 are isomers.