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February 17, 1994

MEMORANDUM

SUBJECT: Metalaxyl (113501) Storage Stability Data Interim Report
[MRID No. 42919401; CB No. 12888; DP Barcode D197066]

FROM: Susan V. Hummel, Chemist
Special Review Section II
Chemistry Branch II-Reregistration Support
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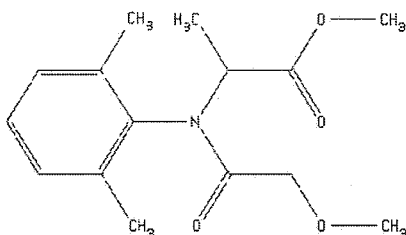
THRU: Francis B. Suhre, Section Head
Special Review Section II
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TO: Peg Perreault/Linda Propst, PM#73
Reregistration Branch
Special Review and Reregistration Division (H7508W)

Ciba Geigy Corporation has submitted an interim report on storage stability of total metalaxyl in weathered samples of cranberries, peppers, potatoes, and spinach, stored frozen for 24 months (18 months for cranberries). The study is planned to continue until 38 months of storage.

Metalaxyl is a fungicide used on numerous plant commodities. The structure is shown in Figure 1. Tolerances for residues in or on plant and animal commodities are currently expressed in terms of the combined residues of metalaxyl [N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-aniline methyl ester] and its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxy methyl-6-methyl-phenyl)-N-(methoxyacetyl)-alanine methyl ester (CGA-94689) (40 CFR §180.408[a]). Metalaxyl tolerances on plant commodities range from 0.1 ppm on grain and other crops to 20 ppm on alfalfa hay and other livestock feeds. Metalaxyl tolerances on livestock commodities range from 0.02 ppm on milk to 0.05 ppm on eggs and livestock tissues. 40 CFR §180.408[b] and [c] include tolerances for inadvertent residues on barley, oat, and wheat commodities and tolerances with regional registration, respectively. Food and feed additive tolerances have been established on apple, apricot, citrus, grape, hops, legume,

peanut, potato, prune, soybean, sugar beet, and tomato processed commodities (40 CFR §185.4000 and 40 CFR §186.4000).



Metalaxyl is on list A. The Metalaxyl Final Registration Standard and Tolerance Reassessment (FRSTR) Guidance Document was issued 9/88. A Residue Chemistry Reregistration Standard Update was issued 3/13/91.

CONCLUSIONS

1. Storage intervals and conditions are available to support all current metalaxyl tolerances.
2. Storage stability data are available to support residue data on raw agricultural commodities, except oilseeds and grains. Storage stability data for a representative oilseed (e.g., soybean or nut) and grain (e.g., wheat) are required, and can be submitted along with the required storage stability data for processed commodities (see conclusion 3a). Storage stability data would normally be required for all of the raw commodities associated with oilseeds and grains, but in the case of metalaxyl, we will translate from leafy greens to the forages and hays.
3. No storage stability data are available to support any processing studies. Storage stability data on processed commodities are required.
- 3a. Storage stability data are required for all processed commodities of at least three diverse crops. Storage stability data are needed for metalaxyl and representative

metabolites containing the dimethylamine moiety and CGA-94689 in processed commodities. The registrant should be referred to our recent additional guidance on storage stability data requirements. Storage Stability Studies must be conducted in all processed commodities of an oilseed (soybeans or peanuts recommended), a grain (wheat or corn recommended) and a fruit or fruiting vegetable (citrus or tomatoes recommended).

4. No storage stability data are available to support the livestock feeding studies. Storage stability data on livestock commodities are required, representing one year of frozen storage.
- 4a. Storage stability data are needed for metalaxyl and representative metabolites containing the dimethylaniline moiety and CGA-94689 in livestock tissues. The registrant should be referred to our recent additional guidance on storage stability data requirements. Storage stability data are required for muscle (cattle or poultry), liver (cattle or poultry), milk, and eggs. If residues are stable in these matrices, analyses of other tissues (fat, kidney) will not be needed. Data on cattle tissues is preferred, since cattle tissues were stored longer than poultry tissues

RECOMMENDATIONS

We recommend that the registrant be informed that adequate storage stability data are available to support residue studies on raw agricultural commodities, with the exception of oilseed and grain crops. We recommend that the registrant be advised to submit storage stability data for processed commodities (including an unprocessed oilseed and grain) and livestock commodities as specified in conclusions 2, 3a, and 4a.

Detailed Considerations

Storage stability data were required for metalaxyl in the Metalaxyl Update dated 3/13/91, footnote 6 (and earlier in the Metalaxyl FRSTR Residue Chemistry Chapter (6/22/87):

Storage stability data in support of all required and previously submitted residue data reflecting the actual storage conditions and intervals for samples used to generate the residue data. If residue depletion occurs, data will be required which depict the decline in levels of metalaxyl residues of concern in commodities stored under the range of conditions and for the range of intervals

specified. Crop samples bearing measurable weathered residues or fortified with metalaxyl residues of concern must be analyzed immediately after harvest or fortification and again after storage intervals that allow for reasonable unforeseen delays in sample analysis. In laboratory tests using fortified samples, the pure active ingredient and pure metabolites must be used. However, if field weathered samples are used, the test substance must be a typical end-use product. For additional guidance on conducting storage stability studies, the registrant is referred to an August 1987 Position Document on the Effects of Storage Validity of Pesticide Residue Data available from NTIS under order No. PB 88112362/AS.

Storage Intervals and Conditions

The Metalaxyl FRSTR required information on storage intervals and conditions for all studies used to support tolerances. In response to the FRSTR, Ciba Geigy submitted storage intervals and conditions for most of the studies cited in the FRSTR (R. Perfetti, DEB 7193, 1/15/91, MRID 41449001). Shortly thereafter, Ciba Geigy submitted storage intervals and conditions for the rest of the residue studies cited in the FRSTR (J. Abbotts, CB 8166, 4/16/92, MRID 41912902). Storage conditions for residue samples were reported to be -15 C. The storage lengths were tabulated in the aforesaid reviews. Fortified storage stability studies for metalaxyl and metabolites were conducted for 18 months at -15 C. These storage stability studies have been included in numerous MRIDs and cited in numerous reviews. Residues of metalaxyl and its metabolites were stable for the 18 month period of frozen storage, except for CGA-94689 in leafy vegetables.

Since the FRSTR, a number of tolerances for residues of metalaxyl have been established or increased, and additional residue studies have been submitted in response to the FRSTR. The storage temperature for these studies is assumed to be -15 C, the same as reported by the registrant earlier. The storage times for the studies not cited in the FRSTR are tabulated below in crop group order.

Storage Lengths for Samples from Studies not cited in the FRSTR

<u>Crop Matrix</u>	<u>MRID</u>	<u>Storage Length (months)</u>
Sugar beets and tops	40569301	14
Legumes and foliage	40569303	14
Apricots	Acc265764	5
Cherries	Acc265764	6

Plums and Peaches	Acc265764	3
Blueberries	Acc265763	12
Cranberries	41996401	7
Grapes	41150101	17
Raspberries	41150101	17
Strawberries	Acc265765	4
Almonds	Acc265765	6
Walnuts	Acc265765	4
Grass Forage, Fodder, and Hay	40569302	36
(pending tolerance)	42134501	19
Non-grass animal feeds		
(tolerance proposal deleted)	40569302	36
Alfalfa	40832901	14
Asparagus	Acc260563	10
Ginseng	41688901	6
Papaya	40490501	4
Peanuts	41870306	13
Corn processed products	41870301	3 (after processing)

Storage Lengths for Samples from Studies not cited in the FRSTR,
continued

<u>Crop Matrix</u>	<u>MRID</u>	<u>Storage Length (months)</u>
Cotton processed products	41870305	11 (after processing)
Grape processed products	41150101	17
Legume cannery waste	40569303	14
Pineapple processed products	42233601	3
Pineapple processed products	42498701	3
Potato processed products	41870307	14
Rice processed products	41870303	6 (after processing)
Sorghum processed products	41870302	20
Prunes	Acc265764	3
Sunflower processed products	41870304	13

Storage Stability of Metalaxyl Residues in Raw Agricultural Commodities

The registrant submitted a protocol for storage stability data for plant raw agricultural commodities (W. O. Smith memo of 1/22/92, CB No. 8723, Barcode D169714). The registrant concluded that, assuming complete stability of total metalaxyl residues in all crops, the long term weathered residue stability study, in concert with previously reported fortified studies, will provide a storage stability data base sufficient to bridge to all other crops for which metalaxyl has existing or pending tolerances. We concluded that we cannot officially concur with the registrant's conclusion prior to completion of studies and review of all data. We did agree with the registrant that if metalaxyl residues of

concern are completely stable in all crops tested, it would be reasonable to allow translation of these data to other crops for which tolerances are established.

The Agency has recently provided additional guidance on storage stability data requirements. For raw agricultural commodities, at least five diverse crops need to be tested. If a pesticide is to be applied to all types of crops, suggested crops for a storage stability study are (1) an oilseed (or soybean or nut), (2) a non-oily grain (or corn), (3) a leafy vegetable, (4) a root crop, and (5) an acidic fruit or fruiting vegetable (e.g., citrus or tomatoes). The crop parts to be examined in these studies are those used for food and food (the same plant parts on which residue data are generated and tolerances established). If residues are found to be stable in all five diverse crops, then no additional storage stability data will be needed for racs. If, however, residues are found to be unstable, then storage stability data will be needed on at least one crop from each crop group for which the pesticide is registered.

Storage stability data have been provided previously for metalaxyl, per se, and 5 metabolites individually fortified in strawberries, apples, cabbage, lettuce, and potatoes stored frozen 12 months (MRID 40106691).

This submission (MRID 42919401) includes storage stability data for weathered samples field treated with metalaxyl. The study included cranberries, peppers, potatoes, and spinach stored frozen at approximately -20 C for 24 months (only 18 months for cranberries). The study reportedly will be continued to 38 months of frozen storage. Total metalaxyl residues were determined as 2,6-dimethylaniline. The results of the weathered storage stability study is shown in the table below. Residues reported are the average of duplicate analyses and are corrected for average procedural recoveries.

STORAGE STABILITY OF WEATHERED SAMPLES FIELD TREATED WITH METALAXYL

Commodity	Total Metalaxyl Residues (ppm) at Storage time (months)						
	0	1	6	9	12	18	24
Cranberries	0.44	0.63	0.54	--	0.50	0.63	--
Peppers	0.48	0.56	0.27	0.54	0.48	0.59	0.52
Potatoes	0.24	--	0.17	--	0.20	0.16	0.24
Spinach	2.2	1.9	2.9	--	3.0	2.3	2.2

These data will satisfy the storage stability data requirements for raw agricultural commodities stored less than 24 months at temperatures of -20 C or less, except for oilseeds and grains. Ordinarily, storage stability data for all raw agricultural commodities of an oilseed and a grain would be required, including the forage and hay; however, the storage stability data on spinach will suffice for the forages and hays. Storage stability data on an oilseed and a grain should be provided along with the required storage stability data on processed commodities.

Storage Stability of Metalaxyl Residues in Processed Commodities

The Chemistry Branches have no record of any response to the requirement for storage stability data for processed commodities. (Storage stability data are required in support of all required and previously submitted residue data reflecting the actual storage conditions and intervals for samples used to generate the residue data.)

There are three major types of crops for which processing studies are required: oilseeds (peanuts, soybeans), grains (wheat, corn), and fruits/fruited vegetables (citrus, apples, and tomatoes). Storage stability data will be required for all processed commodities for one crop of each of these three types. If residues are stable in processed commodities of these three types of crops, then no additional storage stability data will generally be required for processed commodities. If the pesticide is not registered for use on these three types of crops, but is registered for use on root crops, then storage stability data for processed commodities of root crops (potatoes or sugar beets) will be required. Metalaxyl is registered for use on a wide variety of crops, including oilseeds, grains, and fruits and fruited vegetables.

A number of processing studies were reviewed in J. Morales memo of 6/19/92 (CB No. 9011, DP Barcode D169779) and L. Cheng memo of 6/1/92 (CB No. 8043, DP Barcode D164655). We have re-examined the data to determine the length of storage after processing and prior to analysis. Samples of corn processed commodities were stored at -15 C for 10 months total, including 3 months after processing (MRID 41870301); potato processed commodities at 20 C for 14 months after processing (MRID

41870307); rice processed commodities at -20 C for 6 months after processing (MRID 41870303); cottonseed processed commodities at -20 C for 13 months, 11 months after processing (MRID 41870305); and sunflower processed commodities at -20 C for 13 months, 3 months after processing (MRID 41870304). In the FRSTR Residue Chemistry Chapter, and in subsequent reviews of storage intervals (R. Perfetti, 1/15/91 and J. Abbotts, 4/16/92), it was stated that citrus processed commodities were stored 8 months prior to analysis (MRID 0017969), apple processed commodities for 3 months (MRID 00126315), soybean processed commodities for 12 months (MRID 00071672), and tomato processed products for 3 months (MRID 00081615). In this review, storage times are provided for Grape processed products (17 months, MRID 41150101), Legume cannery waste, 14 months, MRID 40569303), Pineapple processed products (3 months, MRID 42233601,42498701), and Prunes (3 months, Accession No. 265764).

No storage stability data are available on processed commodities for these time frames. In a separate review of R. Perfetti (6/22/92, CB No. 9596, DP Barcode D175852), it was determined that storage stability data for pineapple processed commodities (MRID 42233501) may not be needed because of the relatively short storage interval of 3 months, provided residues on the rac were stable. This conclusion can be extended to metalaxyl residues on any processed commodities analyzed within 3 months of processing. However, at least some of the oilseed, grain, and fruit/fruited vegetable processed commodities were stored longer than 3 months.

Storage stability data are needed for metalaxyl and representative metabolites containing the dimethylamine moiety and CGA-94689 in processed commodities. The registrant should be referred to our recent additional guidance on storage stability data requirements. Storage Stability Studies must be conducted in all processed commodities of an oilseed (soybeans or peanuts recommended), a grain (wheat or corn recommended) and a fruit or fruited vegetable (citrus or tomatoes recommended).

Storage Stability of Metalaxyl Residues in Livestock Commodities

The Chemistry Branches have no record of any response to the requirement for storage stability data for livestock commodities. Requirements for storage stability data for metalaxyl residues (metalaxyl and representative metabolites) in livestock commodities were recently reiterated (S. Hummel memo of 9/15/93, CB No. 9102, Barcode D172350). Storage stability data are needed for metalaxyl and representative metabolites containing the dimethylamine moiety and CGA-94689. The registrant should be

referred to our recent additional guidance on storage stability data requirements.

To support livestock feeding studies, storage stability data are required for muscle (cattle or poultry), liver (cattle or poultry), milk, and eggs. If residues are stable in these matrices, analyses of other tissues (fat, kidney) will not be needed. Data on cattle tissues is preferred, since cattle tissues were stored longer than poultry tissues.

cc w/ attachment: addressee, S. Hummel, Metalaxyl RSF, R.F., circu, metalaxyl S.F.
RDI:FBS:02/14/94:MSM:02/16/94:EZ:02/17/94
H7509C:CBII:SVH:svh:RM:810:CM#2:02/17/94
DISK6:METALAXY.STA