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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#3F4185 and ID# 062719-EEG. (CBTS #'s 11516 and 11799; Barcode #'s D188957 and D190750). DE-498 (Flumetsulam) on Field Corn (MRID #'s 426778-00, -01, -02, and -03).

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and

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DowElanco has submitted an amendment to their petition for permanent tolerances for DE-498 (flumetsulam) on field corn (PP#3F4185, formerly combined with soybeans in PP#2F4036). The amendment was submitted in response to a review of PP#2F4036 dated 4/14/93 (N. Dodd). The amendment consists of a letter dated 2/19/93, frozen storage stability data, a processing study, additional residue data, and a revised Section F.

CONCLUSIONS

(The numbering below corresponds to the numbering of the deficiencies in the 3/27/92 review by N. Dodd of PP#1G4006.)

12b. A revised Section F has been submitted as requested.

14b. Flumetsulam per se has been determined to be the residue of concern in field corn.

15. Since residues on field corn grain, forage, and fodder resulting from the proposed use will be <0.05 ppm, the nature of the residue in animals is adequately defined for the proposed use. The residue of concern in ruminants is flumetsulam per se. The residues of concern in poultry are flumetsulam per se and the 5-hydroxy metabolite.

16i. Since flumetsulam per se has been determined to be the residue of concern in field corn, enforcement methods for other residues in field corn will not be needed.

18. Since residues on field corn grain, forage, and fodder resulting from the proposed use will be <0.05 ppm and tolerances for animal commodities are not needed, analytical methods for animal commodities will not be required.

20/21g. Adequate storage stability data are available for flumetsulam on corn grain, forage, and fodder. Flumetsulam is fairly stable for at least 555 days. Based on the corrected average residues at 0 and 555 days, losses were 4% for grain, 5% for forage, and 13% for fodder during frozen storage for 555 days.

21a. Residue data have been submitted from the requested states. Adequate geographic representation has now been provided. Residues in field corn grain, forage, and fodder will not exceed 0.05 ppm as a result of the proposed use. The forage samples containing residues >0.05 ppm were treated at 3X the proposed application rate.

22b. The processing study was conducted on corn which contained essentially no residues (reported as 0.000 or 0.001 ppm before correction for recovery and as not detectable [<0.002 ppm] after correction for recovery). Unless the 3X application rate was chosen because of phytotoxicity, the application rate for the processing study normally should have been 5X or higher. However, based on the results of this processing study and the properties of flumetsulam (see page 10 of this review), CBTS can conclude that food or feed additive tolerances are not necessary.

26. Since residues in feed items as a result of the proposed use on field corn will be <0.05 ppm and animal metabolism data show little transfer of residues, animal feeding studies and tolerances on animal commodities will not be required.

RECOMMENDATIONS

TOX considerations permitting, CBTS recommends for the proposed permanent tolerances for DE-498 (flumetsulam) on field corn grain, forage, and fodder.

DETAILED CONSIDERATIONS

Deficiencies from the review on field corn dated 4/14/93 (PP#2F4036, N. Dodd) will be repeated below, followed by the petitioner's responses and CBTS's discussions/conclusions. (The numbering below corresponds to the numbering of the deficiencies in the 3/27/92 review by N. Dodd of PP#1G4006.)

Deficiency #12b

The petitioner should submit a revised Section F listing the field corn commodities as follows:

commodity	ppm
corn, field, grain	0.05
corn, field, fodder	0.05
corn, field, forage	0.05

Petitioner's Response to Deficiency #12b

A revised Section F has been submitted.

CBTS's Conclusion #12b

Deficiency #12b is resolved by submission of the revised Section F as requested.

Deficiency #14b

The nature of the residue in corn is adequately understood. The major residues in corn are parent, the free and conjugated 5-CH_2OH metabolite (N-(2,6-difluorophenyl)-5-hydroxymethyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide), and the free and conjugated 4-OH metabolite (N-(2,6-difluoro-4-hydroxyphenyl)-5-methyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide). The residues of concern in corn will be determined by the HED Metabolism Committee.

If residues other than parent are determined to be of concern in corn, analytical methods would be needed for those residues of concern. Independent laboratory validations and possibly EPA validations would be needed for those methods. Use of an extraction solvent which would extract more of the aged residues may be desired.

The metabolic pathway for flumetsulam metabolism in corn is different from that in soybeans. Therefore, if the petitioner seeks to register uses on additional species (i.e., plants in crop groups other than those containing corn and soybeans) in the

future, additional metabolism studies on those new species may be required.

Petitioner's Response to Deficiency #14b

None. However, the HED Metabolism Committee decided on 4/21/93 that flumetsulam per se is the residue of concern in field corn.

CBTS's Conclusion #14b

Deficiency #14b is resolved since flumetsulam per se has been determined to be the residue of concern in field corn.

Deficiency #15

The nature of the residue in animals is adequately defined for this proposed use provided that no detectable or very low residues are found in feed items. The residue of concern in ruminants is flumetsulam per se. The residues of concern in poultry are flumetsulam per se and the 5-hydroxy metabolite.

For uses that may result in detectable residues in feed items, additional animal metabolism data on ruminants and poultry may be required.

Petitioner's Response to Deficiency #15

The petitioner has submitted the requested residue data on field corn.

CBTS's Conclusion #15

Deficiency #15 is resolved since residues on field corn grain, forage, and fodder resulting from the proposed use will be <0.05 ppm. The nature of the residue in animals is adequately defined for the proposed use. The residue of concern in ruminants is flumetsulam per se. The residues of concern in poultry are flumetsulam per se and the 5-hydroxy metabolite.

Deficiency #16i

The issues raised by ACS concerning the EPA method validation of ACR 91.6 on soybean grain and ACR 91.6.1S on corn grain and corn fodder have been satisfactorily addressed by the petitioner. Adequate enforcement methods (revised analytical methods ACR 91.6R on soybeans and ACR 91.6.S1R on field corn, both dated 4/7/93) are available for flumetsulam per se on soybeans and field corn. However, if additional residues besides parent are determined to be of concern, enforcement methods for those residues would be needed.

Petitioner's Response to Deficiency #16i

None. However, the HED Metabolism Committee decided on 4/21/93 that flumetsulam per se is the residue of concern.

CBTS's Conclusion #16i

Deficiency #16i is resolved since flumetsulam per se has been determined to be the residue of concern in field corn. Enforcement methods for other residues in field corn will not be needed.

Deficiency #18

No analytical methods have been submitted for animal commodities. Analytical methods for animal commodities will not be required provided that no detectable or very low residues are found in feed items and no detectable residues are expected to occur in animal commodities as a result of the proposed use.

Petitioner's Response to Deficiency #18

The petitioner has submitted the requested residue data on field corn.

CBTS's Conclusion #18

Deficiency #18 is resolved since residues on field corn grain, forage, and fodder resulting from the proposed use will be <0.05 ppm and tolerances for animal commodities are not needed. Analytical methods for animal commodities will not be required.

Deficiency #20/21g

The final frozen storage stability report on corn (summarized in Appendix C in MRID #424890-01) will be needed for review to support a permanent tolerance.

Petitioner's Response to Deficiency #20/21g

The petitioner has submitted MRID #426778-01 which contains a frozen storage stability study on corn grain, forage, and fodder.

CBTS's Discussion re. Deficiency #20/21g

Corn grain, forage, and fodder was fortified at 0.25 ppm, stored frozen below -15 °C in polyethylene bags, and analyzed after 92 days (grain), 105 days (forage, fodder), and 555 days (grain, forage, and fodder). The analytical method was ACR 91.6.S1. Results were corrected for average recoveries, which were determined by fortifying controls at the time of analysis. The range and average recoveries from fortifications are reported below:

corn grain - range 88-114%; average 92%, 112%, and 89% at 0, 92, and 555 days, respectively;

corn forage - 76-117%; average 77%, 94%, and 110% at 0, 105, and 555 days, respectively;

corn fodder - 83-95%; average 90%, 94%, and 83% at 0, 105, and 555 days, respectively.

Frozen storage stability data were reported as follows, with "ppm found" corrected for average recoveries (above) from spikes determined at the time of analysis:

		DE-498		
commodity	time interval (days)	ppm added	ppm found	% recovery
grain	0	0.251	0.225	90
		0.251	0.264	105
		0.251	0.222	88
				94
	92	0.251	0.234	93
		0.251	0.228	91
		0.251	0.251	100
				95
	555	0.251	0.227	90
		0.251	0.226	90
				90
forage	0	0.251	0.240	96
		0.251	0.253	101
		0.251	0.219	87
				95
	105	0.251	0.223	89
		0.251	0.219	87
		0.251	0.218	87
				88
	555	0.251	0.226	90
		0.251	0.228	91
				90

commodity	time interval (days)	DE-498 ppm added	DE-498 ppm found	DE-498 % recovery
fodder	0	0.251	0.224	89
		0.251	0.244	97
		0.251	0.244	97
				94
	105	0.251	0.215	86
		0.251	0.207	82
		0.251	0.210	84
				84
	555	0.251	0.199	79
		0.251	0.206	82
				81

Representative chromatograms (for DE-498 standard and for controls, spikes, and frozen samples of corn grain, forage, and fodder) were submitted. A calibration curve for DE-498 and sample calculations for determination of DE-498 in corn samples were also submitted.

CBTS's Conclusion #20/21g

Deficiency #20/21g is resolved. Adequate storage stability data are available for flumetsulam on corn grain, forage, and fodder. Flumetsulam is fairly stable for at least 555 days. Based on the corrected average residues at 0 and 555 days, losses were 4% for grain, 5% for forage, and 13% for fodder during frozen storage for 555 days.

Deficiency #21a

Adequate geographic representation is not provided for field corn. Additional residue data should be obtained from TX, CA, MD, and WA.

Petitioner's Response to Deficiency #21a

The petitioner has submitted MRID #426778-03, which contains residue data obtained from TX, CA, MD, and WA.

CBTS's Discussion re. Deficiency #21a

Four residue studies on field corn were conducted in the states of CA, WA, TX, and MD (1 study in each state) (MRID #426778-03). XRM-5019 was mixed with water and applied preemergence as a broadcast spray or postemergence to 12-inch corn. Postemergence applications included the additive Ortho X-77. Only one application was made to each plot. The preemergence application

rates were 0.09, 0.14, and 0.27 lb XRM-5019/A (0.07, 0.11, and 0.20 lb ai/A). The postemergence application rates were 0.08, 0.12, and 0.24 lb XRM-5019/A (0.06, 0.09, and 0.18 lb ai/A). For both the preemergence and postemergence applications, the application rates were 1X, 1.5X, and 3X the maximum proposed use rates. The samples were frozen after analysis, shipped frozen, and stored at -20 °C until analysis. The samples were analyzed within 6 months of sampling. The samples were analyzed by method ACR 91.6.S1, with slight modifications to allow use of a laboratory robot. The method uses gas chromatography with mass selective detection (GC/MSD). The petitioner indicates that the limit of detection of the analytical method was 2 ppb and that the limit of quantitation was 7 ppb. The method was validated by EPA at 0.05 ppm, the proposed tolerance level. Residue data were reported as uncorrected and as corrected for recoveries. Recoveries were 71-104% for forage, 76-94% for grain, and 71-90% for fodder. All forage, grain, and fodder controls were <0.05 ppm. Representative chromatograms (for DE-498 standard and for controls, spikes, and samples of forage, grain, and fodder) were submitted. A calibration curve for DE-498 and sample calculations for determination of DE-498 in corn samples were also submitted. All residues on forage, grain, and fodder were <0.05 ppm except for the following residue data on forage in CA reflecting postharvest applications at a 3X rate:

lb ai/A	PHI (days)	Recovery(%)	Residues (ppm)	
			uncorrected	corrected
0.18	14	87, 94	0.1764-0.2184	0.2025-0.2318
0.18	28	87, 94	0.0538-0.0860	0.0571-0.0987

The petitioner indicates that the higher residues in CA may be due to furrow irrigation only. The corn received little or no overhead irrigation after application of the herbicide and minimal rainfall during the 1992 growing season.

The residue studies were conducted by DowElanco or coordinated by Stewart Agricultural Research Services, Inc. Samples were analyzed by North American Environmental Chemistry Laboratory, DowElanco. -

CBTS's Conclusion #21a

Deficiency #21a is resolved. Residue data have been submitted from the requested states. Adequate geographic representation has now been provided. Residues in field corn grain, forage, and fodder will not exceed 0.05 ppm as a result of the proposed use. The forage samples containing residues >0.05 ppm were treated at 3X the proposed application rate.

Deficiency #22b

For the permanent tolerance, a processing study is needed and food additive tolerances may be needed for processed fractions of corn grain. The theoretical concentration factor from corn grain to corn oil is 28X. However, the petitioner should apply the maximum practical exaggerated foliar application rate, which would be considered to be 5X or less if phytotoxicity occurs at 5X. Even if no detectable residues were found in corn grain after postemergence treatment at 5X, the corn grain should be processed since the theoretical concentration factor is 28X for corn oil. If no detectable residues are found in the processed products, then no food additive tolerance would be required. Processed commodities from field corn are starch, crude oil and refined oil from wet milling; and grits, flour, meal, crude oil and refined oil from dry milling. Grain dust residue data are not required for this use on corn since applications are preplant incorporated, preemergence, and early postemergence. "The grain dust data are needed only in those cases in which detectable, primarily surface residues are found on the grain." (Overview of Residue Chemistry Guidelines", R.D. Schmitt, 10/10/89).

Petitioner's Response to Deficiency #22b

The petitioner has submitted MRID #426778-02 which contains a dry milling and wet milling processing study.

CBTS's Discussion re. Deficiency #22b

Corn grain treated postemergence at 0.18 lb ai/A (3X the proposed rate) was processed. Grain from CA was shipped unfrozen to TX for dry milling. Grain from MD was shipped frozen to TX for wet milling. Samples were stored at -20 °C until analysis. The analytical method was ACR 91.6.S1, with slight modifications to allow use of a laboratory robot. The grain and processing fractions were analyzed within 5 months of sampling. (Corn grain from CA was sampled on 9/14/92. Corn grain from MD was sampled 9/23/92 or 10/16/92. The grain was processed between 10/22/92 and 11/9/92. Crude and refined oil was analyzed on 11/25/92. The other processing fraction (grits, meal, flour, and starch) were analyzed on 2/3/93.) Recoveries were 82 and 91% for grain, 105% for crude and refined oil, 81% for grits, 86% for flour, 108% for meal, and 101% for starch. Representative chromatograms (for DE-498 standard and for controls, spikes, and samples of dry and wet milled crude and refined oil, grits, meal, flour, and starch) were submitted. (Representative chromatograms for grain were submitted in MRID #426778-03.) A calibration curve for DE-498 and sample calculations for determination of DE-498 in corn samples were also submitted. EPA has validated the method at 0.05 ppm. Although the petitioner indicates that the limit of detection of the method is 2 ppb, residues in grain were reported as 0.001 ppm in CA and 0.000 ppm in MD before correction for recovery and as not detectable

(<0.002 ppm) after correction for recovery. Residues in processing fractions (grits, meal, flour, refined oil, or crude oil from dry milling and starch, refined oil, or crude oil from wet milling) were reported as 0.000 or 0.001 before correction for recovery and as not detectable (<0.002 ppm) after correction for recovery.

The processing was done at Texas A&M University. Texas A&M's small-scale procedures for dry and wet processing (submitted in MRID #426778-02) were intended to produce commercially representative fractions.

Since flumetsulam is not known to be volatile or labile, storage stability data are not required for samples stored frozen for <30 days ("Pesticide Reregistration Rejection Rate Analysis, Residue Chemistry", EPA 737-R-93-001, February 1993).

Storage stability data on processing fractions were not provided. Based on available data, processing fractions could have been stored for periods of 2 weeks to 3 1/2 months. Oil was stored for only about 2-4 weeks. Storage stability data are normally required for processing fractions stored frozen for ≥30 days. However, in this case, only the solid by-products (grits, meal, flour, and starch), which more closely resemble grain, were stored for ≥30 days. The stability in grain for 555 days can cover storage of these fractions for roughly 3 1/2 months.

Unless the 3X application rate was chosen because of phytotoxicity, the application rate for the processing study normally should have been 5X or higher (as discussed in Deficiency #22b above). However, in this instance, considering the absence of detectable residues in all the processed fractions and properties of flumetsulam (low octanol-water partition coefficient [log P=0.21] and greater solubility in water than in hexane), CBTS concludes that concentration of residues in oil is highly unlikely. Therefore, the study is adequate to show that food or feed additive tolerances are unnecessary.

CBTS's Conclusion #22b

The processing study was conducted on corn which contained essentially no residues (reported as 0.000 or 0.001 ppm before correction for recovery and as not detectable [<0.002 ppm] after correction for recovery). Unless the 3X application rate was chosen because of phytotoxicity, the application rate for the processing study normally should have been 5X or higher. However, based on the results of this processing study and the properties of flumetsulam, CBTS can conclude that food or feed additive tolerances are not necessary.

Deficiency #26

For the purposes of the permanent tolerances on soybeans and corn, CBTS must reserve its conclusion regarding the need for animal feeding studies until questions regarding the nature of the residue, analytical methods, storage stability, and residue data are resolved. If no detectable residues are found in feed items, no animal feeding studies and no tolerances for animal commodities will be required.

Petitioner's Response to Deficiency #26

None. However, the questions regarding nature of the residue, analytical methods, storage stability, and residue data have been addressed.

CBTS's Conclusion #26

Deficiency #26 has been resolved. Since residues in feed items as a result of the proposed use on field corn will be <0.05 ppm and animal metabolism data show little transfer of residues, animal feeding studies and tolerances on animal commodities will not be required.

cc: RF, SF, Circu., N. Dodd (CBTS), E. Haeberer (CBTS), PP#3F4185, PM#23, A. Kocialski (CCB)

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