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MEMORANDUM

SUBJECT: **Carbofuran.** Magnitude of the Residue and Processing Studies with Coffee.
GDLNs 860.1500, 860.1520
DP Barcode: D233094; CBRS No. 17769; MRID Nos.: 441868-01, 441868-02, and 441868-03; Case No. 0101.

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CBRS has been asked to review a magnitude of the residue and processing study submission on coffee. The study was submitted by FMC as part of the requirements for reregistration of carbofuran insecticide.

The qualitative nature of carbofuran residues in plants is not adequately understood; additional data regarding the components in an extract of soybean hay are required. CBRS tentatively concluded, pending receipt of the outstanding plant metabolism data, that the residues of concern

in plant and animal commodities are the residues which are currently regulated, i.e., parent carbofuran and its metabolites 3-hydroxy-carbofuran, 7-phenol-carbofuran, 3-hydroxy-7-phenol carbofuran, and 3-keto-7-phenol-carbofuran. The HED Metabolism Committee has concluded that field trials must include analysis for the regulated metabolites as well as the metabolite 3-ketocarbofuran.

CONCLUSIONS AND RECOMMENDATIONS

1. CBRS previously concluded that carbofuran and its carbamate metabolites are stable in the acid hydrolysates of a variety of commodities for up to 8 months of refrigerated storage and that carbofuran phenol metabolites are stable in acid hydrolysates for up to 6 months of refrigerated storage. Since refrigerated storage intervals did not exceed 7 months during the present study, CBRS has no storage stability concerns with the submitted data.

2. The submitted data are adequate to fulfill reregistration data requirements for carbofuran on coffee. The submitted data indicate that the combined carbofuran residues of concern were <0.05- 2.55 ppm [including up to 1.0 ppm carbamates] in/on coffee green beans harvested 29-30 days following the last of two applications at 1.5 g ai/bush/application (3.0 g ai/bush total), with a 5-6 month retreatment interval. The submitted data indicate that the existing tolerance for carbofuran on coffee of 0.1 ppm (based on the carbamate residues only) is too low and needs to be increased to 3 ppm (with up to 2 ppm carbamates).

3. The submitted coffee processing data indicate that individual residues of carbofuran metabolites of concern do not concentrate significantly in either ground roast or instant coffee processed from green coffee beans bearing detectable residues of 3-OH carbofuran and all three phenol metabolites. CBRS concludes that separate tolerances are not required for either beans beans or instant coffee and the recommended tolerance for green coffee beans will adequately cover expected residues in coffee processed commodities.

4. Per a REFs search conducted on 3/6/97, The Furadan 5G product used in these trials is NOT registered for use on coffee. Nevertheless, the Furadan 5G used in the experimental field trials and the Furadan 79 Puerto Rico 10G product registered for use on coffee differ only in the percent of active ingredient and CBRS will therefore translate this data between formulations. No maximum number of applications, minimum PHI, or minimum retreatment interval is specified on the Furadan 79 Puerto Rico SLN label. CBRS will require that these SLN labels be revised to reflect a maximum of two applications per year, a minimum PHI of 30 days, and minimum retreatment interval of 5 months.

DETAILED CONSIDERATIONS

Residue Analytical Methods

The raw agricultural and processed commodity samples from the current submissions were analyzed by FMC Corporation (Princeton, NJ) for residues of carbofuran (3-hydroxy-carbofuran (3-OH), and 3-keto-carbofuran (3-keto) using an HPLC method with fluorescence detection, and for residues of 7-phenol-carbofuran (7-Ph), 3-hydroxy-7-phenol-carbofuran (3-OH-7-Ph), and 3-keto-7-phenol-carbofuran (3-keto-7-Ph) using a GC method with mass selective detection.

Briefly, bean samples were chopped/macerated with liquid nitrogen, acid hydrolyzed, and stored under refrigeration for separate analysis for carbamates and phenols. For the determination of carbamates, the hydrolysate was applied to a C_{18} solid phase extraction (SPE) column coupled to an amino-propyl SPE cartridge. Residues were eluted with 1% methanol in dichloromethane (DCM), evaporated to dryness, and redissolved in acetonitrile (ACN) for analysis by HPLC using a C-18 column, a gradient mobile phase of ACN and water, a postcolumn reactor specific for carbamates, and a fluorescence detector. The limits of quantitation (LOQ) for carbamates were 0.05 ppm with a limit of detection (LOD) for carbamates of 0.01 ppm.

For the determination of phenolic metabolites, the hydrolysate was applied to a tandem SCX-C_{18} SPE cartridge. Residues were eluted with 5% ethanol (EtOH) in DCM and partitioned twice with 0.25 N sodium hydroxide. Residues were then derivatized with pentafluorobenzyl bromide (PFBB) in isopropanol and partitioned twice with hexane. EtOH was added, and the hexane was evaporated. The EtOH was acidified with concentrated HCl to ethylate the 3-hydroxy-7-phenol PFB derivative. After the addition of water, the ethylated mixture was repartitioned with hexane. Residues were further concentrated and cleaned up on a silica gel solid phase cartridge. The analytes were eluted from the cartridge with 5% EtOAc in hexane, the elution solvent was concentrated, and the final extract brought to volume with hexane for GC/MSD using a DB-5 fused silica capillary column. The limit of quantitation (LOQ) for phenols was 0.05 ppm, with a corresponding limit of detection (LOD) of 0.01 ppm.

For concurrent method recovery analyses untreated samples of RACs from the field trials and processed fractions from the processing studies were separately fortified with carbamates and phenols at various levels. Residues of carbofuran and its carbamate and phenolic metabolites were either nondetectable or at very low levels in/on samples of untreated RACs and processed fractions. Representative chromatograms, sample calculations, and standard curves were provided. The recovery data are summarized in Table 1.

These data indicate that the methods are adequate for data collection for carbofuran and its carbamate and phenolic metabolite residues in/on coffee.

Table 1. Concurrent method recoveries of carbofuran and its carbamate and phenol metabolites from fortified samples of coffee[a]

MRID (location) Commodity	Fortification Level (ppm)		Percent Recovery					
			Carbamates			Phenols		
	Carbamates	Phenols	Carbofuran	3-keto	3-OH	7-Ph	3-keto-7-Ph	3-OH-7-Ph
441868-01 (HI) green beans	0.05	--	72-98 (7), 68, 124	90-116 (7), 132	70-104 (9), 122	--	--	--
	0.5	--	91	68,98	89, 104	--	--	--
	2.0	--	76, 78	89,95	89-94	--	--	--
	--	0.05	--	--	--	52, 52, 62, 64, 82, 72	74-112 (6)	54, 64, 66, 72-88 (3)
	--	0.5	--	--	--	57, 126	84, 122	61, 118
		2.0	--	--	--	89	77	90
441868-02 (HI) green beans	0.05	--	74, 94	58, 68	76, 86	--	--	--
	0.5	--	79, 77	76, 69	83, 77	--	--	--
	--	0.05	--	--	--	74, 104	120, 108	96, 80
	--	0.5	--	--	--	67, 70	80, 88	55, 61
441868-03 (BR) green beans	0.05	--	72	64	92	--	--	--
	0.5	--	78	70	85	--	--	--
	--	0.05	--	--	--	91	138	64
	--	0.5	--	--	--	89	124	56
441868-03 (BR) Roast Beans	0.05	--	84	82	96	--	--	--
	0.5	--	59	57	75	--	--	--
	--	0.05	--	--	--	106	106	82
	--	0.5	--	--	--	77	103	72
441868-03 (BR) Instant Coffee	0.05	--	94	97	94	--	--	--
	0.5	--	78	63	77	--	--	--
	--	0.05	--	--	--	128	114	NA, 52
	--	0.5	--	--	--	92	116	NA, 52

[a] Value represents one sample unless otherwise indicated in parentheses; recovery values outside the acceptable 70-120% range are listed separately.

Storage Stability Data

The RAC samples from the field trials were promptly frozen after harvest, shipped frozen to FMC Corporation (Princeton, NJ) where they were stored frozen for no more than 30 days prior to being homogenized and acid hydrolyzed. Following acid hydrolysis, hydrolysates were stored in a refrigerator (~5 C) for no longer than 4 months until residue analysis.

Samples collected for the processing studies were frozen after harvest and then shipped frozen to the processing facilities, where samples were stored frozen for 18 days prior to being acid hydrolyzed. Following hydrolysis, samples were stored in a refrigerator (~5 C) for no more than 7 months prior to residue analysis. Data pertaining to the stability of carbofuran and its metabolites in frozen plant commodities were discussed in the Carbofuran Update; these data

indicated that residues were generally stable for up to 11 months of *frozen* storage. Data presented by the registrant and previously reviewed by CBRS (see D. Miller, 2/03/97, DP Barcodes: D221465, D221469, D221473, D221476, D223210, CBRS Nos. 16638, 16694, 16695, 16914, and 17452) are sufficient to conclude that carbofuran and its carbamate metabolites are stable in the acid hydrolysates of plant commodities for up to 8 months of *refrigerated* storage and that carbofuran phenol metabolites are stable in acid hydrolysates of plant commodities for up to 6 months of *refrigerated* storage. Since hydrolysates were stored in the present study under refrigerated conditions for no longer than 7 months, CBRS has no storage stability concerns with this submission.

Magnitude of the Residue in Coffee

Registered use patterns: Per a REFs search conducted on 3/6/97, The Furadan 5G product used in these trials is NOT registered for use on coffee (it is only registered for use on rice). Specifically, EPA Reg. No. 279-2712 (as part of EPA SLN Nos. PR-850001 and PR-960003) is the only carbofuran product registered for use on coffee. Nevertheless, the Furadan 5G used in the experimental field trials and the Furadan 79 Puerto Rico 10G product registered for use on coffee differ only in the percent of active ingredient (10% vs. 5%) and CBRS will therefore translate this data between formulations.

Furadan 10G is registered for use on established plantings of coffee at up to two applications of 1.5 g ai/tree (3.0 g ai/tree total). No maximum number of applications, minimum PHI, or minimum retreatment interval is specified although two applications are recommended, one in early winter following harvest and the other in late June or July. These use directions were obtained from EPA SLN Nos. PR-850001 and PR-960003, with parent EPA Reg. No. 279-2712; the parent product is not registered for use on coffee. CBRS will require that the SLN labels be revised to reflect a maximum of two applications per year, a minimum PHI of 30 days, and minimum retreatment interval of 5 months.

Discussion of the data: FMC Corporation has submitted data (1996; MRIDs 438522-01 and 438522-02) from trials conducted in HI and Brazil depicting residues of carbofuran and its carbamate metabolites (3-keto and 3-OH), and its phenolic metabolites (7-Ph, 3-keto-7-Ph, and 3-OH-7-Ph) in/on coffee green beans.

The seven Hawaiian trials were conducted on the islands of Kauai (3 trials), Hawaii (2 trials), and Oahu (2 trials). Two applications of Furadan 5G each at a rate of 1.5 g ai/tree were applied to soil around the drip line, the first was applied post flowering while the second was applied 5-6 months later. A PHI of 28-29 days was observed with each trial. Coffee samples were harvested at normal maturity, with the cherries skinned, dried, and the green bean removed from the shell using a commercial wet method procedure. The beans were then shipped frozen to the Residue Chemistry Department of FMC.

The two Brazilian trials were conducted in representative coffee-growing regions of Brazil, South America. Two applications of Furadan 5G were applied at a rate of 1.5 g ai/tree to soil around the drip line. The first was applied approximately 1-2 months post-flowering, while the second was applied ca. 6 months later to allow for a 29 day PHI. Coffee cherries were harvested using normal agricultural practices; both control and treated cherry samples were dried in the sun and depulped to remove the dried husk using the commercial dry method procedure typical for coffee green bean production in Brazil. As with the Hawaiian samples, control and treated samples were shipped frozen to the Residue Chemistry Department at FMC.

One control and duplicate treated samples were collected from each test site. Residues of carbofuran and its carbamate and phenolic metabolites in/on treated and untreated green coffee beans were determined using the HPLC and GC/MS methods described above. Residues in/on treated samples are presented in Table 2.

Table 2. Residues of carbofuran and its carbamate and phenolic metabolites in/on coffee green beans harvested 28-29 days following two applications of Furadan 5G granular formulation at 1.5 g ai/bush/application (3.0 g/bush total).

	Residues (ppm) [a]								
	Carbamates				Phenols				
Test Location	Carbofuran	3-keto	3-OH	Total [b]	7-Ph	3-keto-7-Ph	3-OH-7-Ph	Total	Combined [b]
Kauai, HI Trial 1	ND ND	ND ND	(0.03) (0.02)	(0.03) (0.02)	0.16 0.16	(0.03) (0.03)	0.34 0.32	0.53 0.51	0.56 0.53
Kauai, HI Trial 2	ND ND	ND ND	0.24 0.26	0.24 0.26	0.24 0.24	0.08 0.11	0.60 0.68	0.92 1.03	1.16 1.29
Kauai, HI Trial 3	0.05 0.05	ND ND	0.63 0.95	0.68 1.00	0.33 0.30	0.20 0.19	1.09 1.06	1.62 1.55	2.30 2.55
Kauai, HI Trial 4	ND ND	ND ND	0.12 (0.04)	0.12 (0.04)	0.05 (0.02)	(0.03) (0.01)	0.27 0.17	0.35 0.20	0.47 0.24
Hawaii, HI Trial 5	ND ND	ND ND	0.16 0.07	0.16 0.07	(0.04) (0.03)	(0.02) (0.01)	0.33 0.24	0.39 0.28	0.55 0.35
Oahu, HI Trial 6	ND ND	ND ND	ND ND	ND ND	(0.01) (0.01)	ND ND	(0.02) (0.02)	(0.03) (0.03)	(0.03) (0.03)
Oahu, HI Trial 7	(0.01) ND	ND ND	0.07 0.09	0.08 0.09	0.13 0.13	(0.04) (0.03)	0.39 0.34	0.56 0.50	0.64 0.59
Sao Paulo, BR Trial 01	ND ND	ND ND	ND ND	ND ND	(0.03) (0.04)	(0.01) (0.01)	0.08 0.08	0.12 0.13	0.12 0.13
Minas Gerais, BR Trial 02	ND ND	ND ND	(0.03) (0.04)	(0.04) (0.04)	ND ND	0.16 0.13	0.20 0.15	0.20 0.15	0.23 0.19

[a] Residues in/on treated samples were not corrected for concurrent recovery. Residue values in parentheses are estimates; ≥ LOD (0.01 ppm) but ≤ LOQ (0.05 ppm).

[b] Total does not include residues of 3-keto-carbofuran which is not a residue of concern of carbofuran.

Geographic representation is adequate to support the registered uses (per a Greybeard decision dated 12/13/94 which responded to an FMC letter dated 11/23/94, studies in HI adequately support uses in both PR and HI). The submitted data indicate that the combined carbofuran residues of concern were <0.05- 2.55 ppm [including up to 1.0 ppm carbamates] in/on coffee

green beans harvested 29-30 days following the last of two applications at 1.5 g ai/bush/application (3.0 g ai/bush total), with a 5-6 month retreatment interval. The submitted data indicate that the existing tolerance for carbofuran on coffee of 0.1 ppm (based on only the carbamate residues) is too low and needs to be increased to 3 ppm (with up to 2 ppm carbamates).

Magnitude of the Residue in Processed Coffee Commodities

Established tolerances: There are currently no tolerances for the carbofuran or its regulated metabolites on processed commodities of coffee.

Discussion of the data: FMC Corporation submitted data (1996; MRID 44186803) pertaining to the potential for concentration of residues of carbofuran and its carbamate and phenolic metabolites in the processed commodities of coffee. In two trials conducted in the states of Sao Paulo and Minas Gerais, Brazil, coffee was harvested 30 days following the last of two applications at 3.0 g ai/bush/application (or 6.0 g ai/bush total). Per the registrant, this represents 2x the maximum label application rate.

At crop maturity, the coffee cherries were harvested, dried, and depulped with the resulting green coffee beans processed into roast bean and instant coffee processed commodities according to simulated commercial procedures (only coffee samples from the Minas Gerais trial were used since samples from the Sao Paulo trial were exhausted before acceptable data was produced). Foreign matter was removed from the green coffee beans and the coffee roasted and cooled with ambient air. The roasted coffee was subsequently ground, extracted, brewed, and then frozen into trays. Following this, the coffee was freeze-dried. The registrant submitted adequate descriptions and material balance sheets for the processing procedures.

Residues of carbofuran and its carbamate and phenolic metabolites in/on treated and untreated coffee processed commodities were determined using the HPLC and GC/MS methods described above. The results of the coffee processing study are presented in Table 3.

Table 3. Residues of carbofuran and its carbamate and phenolic metabolites in/on **coffee processed from** green coffee beans treated with two applications of Furadan 5G at 3.0 g ai/bush/application. (6.0 g ai/bush total, 2x)[a]

Commodity	Carbamates				Phenols				Combined[a]
	Carbofuran	3-keto	3-OH	Total[a]	7-Ph	3-keto-7-Ph	3-OH-7-Ph	Total	
Residues (ppm)[b]									
Green bean Range Avg ± SD	ND ND	ND ND	0.20-.22 0.21±0.01	0.20-0.21 0.21 ± 0.01	0.13-0.14 0.14±0.01	(0.04)-0.07 0.06±0.02	0.24-0.28 0.26±0.02	0.43-0.48 0.45±0.03	0.64-0.70 0.66
Roast Bean Range Avg ± SD	ND ND	ND ND	ND ND	ND ND	0.14-0.17 0.16±0.02	0.06-0.08 0.07±0.01	0.34-0.45 0.40±0.06	0.54-0.70 0.62±0.08	0.54-0.70 0.62
Instant Coffee Range Avg ± SD	ND ND	ND ND	ND ND	ND ND	0.34-0.47 0.40 ± 0.07	0.18-0.21 0.19±0.02	0.38-0.43 0.41±0.03	0.95-1.06 1.00±0.06	0.95-1.06 1.00
Concentration Factors									
Roast Bean	--	--	--	--	1	1	1.5x	1.4x	<1x
Instant Coffee	--	--	--	--	2.9	3.2	1.6x	2.2x	1.3x

[a] Does not include residues of 3-keto-carbofuran which is not a residue of concern of carbofuran.
[b] Residue values in parentheses are estimates; ≥ LOD (0.01 ppm) but ≤ LOQ (0.05 ppm).
[c] Each block represents 3 duplicate analyses

The submitted coffee processing data indicate that total residues of carbofuran and its regulated metabolites of concern concentrate at <1x in roast beans but can concentrate at 1.3x in instant coffee processed from green coffee beans bearing detectable residues of 3-OH carbofuran and all three phenol metabolites following treatment at an exaggerated rate. Given that these concentration factors do not differ significantly from 1, CBRS conclude that separate tolerances are not required for either roast bean or instant coffee and the recommended tolerance for green coffee beans will adequately cover expected residues in coffee processed commodities.

RDI: Pilot Team:3/5/97; RPerfetti:3/6/97.
cc: RF, SF, List A Rereg. F. Circ. DJM.