(7)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Date: 15-July-2004

Subject: Carfentrazone-ethyl. Petition for Tolerances on Fish and Shellfish. Summary of Analytical Chemistry and Residue Data.

DP Barcodes:	D294823	Registration:	3F6587
PC Code:	128712	Decision #:	329605
MRID No:	46253902		

From: Tom Bloem, Chemist
Registration Action Branch 1, Health Effects Division (RAB1/HED; 7509C)

Through: PV Shah, Ph.D., Branch Senior Scientist
RAB1/HED (7509C)

To: Dianne Morgan/Joanne Miller; RM 23
Registration Division (7505C)

FMC Coporation proposed the establishment of permanent tolerances for the combined residues of carfentrzone-ethyl (ethyl-α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl)-4-fluorobenzenepropanoate) and carfentrazone-ethyl chloropropionic acid (α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoic acid) in/on the following raw agricultural commodities (RACs; see attachment 1 for structures):

fish ..... 0.2 ppm
shellfish ..... 0.2 ppm

AUG 24 2004

Executive Summary

Background: Carfentrazone-ethyl is a post-emergence herbicide of the phenyl triazolinone group used for control of broad leaf weeds. It acts as an inhibitor of protoporphyrinogen oxidase which results in disruption of the cell membrane and dessication of susceptible plant species. Section 3 registrations have been established for application of carfentrazone-ethyl to cereal grain group, the caneberry subgroup, cotton, and soybean (tolerances of 0.10-10 ppm; 40 CFR 180.515). Section 18 registrations have also been established for application of carfentrazone-ethyl to hops and fruiting vegetables (tolerances of 0.10-0.60 ppm). HED as also reviewed petitions pertaining to the application of carfentrazone-ethyl to numerous vegetable and fruit crop groups (D303030, T. Bloem, 30-Jun-2004; D293779, T. Bloem, 14-Jul-2004). The proposed use is for aquatic application. Therefore, portions of the OPPTS GLN 860 guidelines which do not pertain to aquatic application were not included.

Application Scenarios: The petitioner is requesting registration for application of Stingray™ (emulsifiable concentrate (EC); 1.9 lbs ai/gallon) to aquatic areas for the control of floating weeds. The maximum single application rate is 0.2 lbs ai/surface acre. The label indicates that retreatment may be necessary and recommends a 14-day retreatment interval (RTI; maximum seasonal application rate is not specified). The label includes the following restrictions: **(1)** do not apply within 1/4 mile upstream of a potable water intake in flowing or standing water body; **(2)** to make applications within a 1/4 mile potable water intake, the water intake must be turned off for 24 hours after the application (water may be turned on prior to 24 hours if the carfentrazone-ethyl level in the water intake is below 0.2 ppm); **(3)** do not use treated water for irrigation in commercial nurseries or greenhouse; and **(4)** for crops, do not use treated water for irrigation purposes until 14 days after treatment or until analysis indicates a concentration of carfentrazone ethyl and it major metabolite is <5 ppb.

The HED Metabolism Assessment Review Committee (MARC) has determined that the residues of concern in drinking water are carfentrazone-ethyl, F8426-ClPAc and F8426-CAc (MARC decision memoranda, J. Stokes, 19-Jun-1998). **The potable water and irrigation restrictions on the label concern the concentration of carfentrazone-ethyl (potable water) or carfentrazone ethyl and its major metabolite (irrigation). These restrictions should be for the combined residues of carfentrazone-ethyl, F8426-ClPAc and F8426-CAc. In addition, HED requests that the petitioner consistently indicate application rates in lbs ai/surface acre and indicate that the water may not be used as a water source for livestock until the combined concentration of carfentrazone-ethyl, F8426-ClPAc and F8426-CAc has dropped to <0.2 ppm. A revised Section B is requested.**

Based on the application rate of 0.2 lbs ai/surface acre and assuming a depth of 3 feet, a water concentration immediately after application of 25 ppb is calculated. This concentration is lower than the 34 ppb acute surface water estimated drinking water concentration (EDWC; used for risk assessment) provided by the Environmental Fate and Effects Division (EFED). Based on this and assuming the petitioner makes the label changes recommended above, HED concludes that the potable water restriction of <0.2 ppm is acceptable (0.2 ppm yields exposures ≤1% chronic population adjusted dose (cPAD) and aPAD).

Currently, HED has preliminary data concerning the foliar application of carfentrazone-ethyl to cereal grains at 0.031 lb ai/acre (preharvest interval (PHI) of 3-4 days). The spray volumes used in these studies were ~10 gallons/acre which leads to a concentration of carfentrazone-ethyl in the spray water of ~370 ppm. These studies resulted in residues of concern in the harvested field corn grain, forage, and stover of ≤0.82 ppm. Based on these data and since the petitioner has requested tolerances in/on all crop groups which include crops consumed by humans, HED concludes that the proposed irrigation water restriction (do not use treated water for irrigation purposes until concentration has dropped to <5 ppb or 14 days have passed) is acceptable.

Water and Irrigated Crops: As previously indicated, the MARC has concluded that the residues of concern in drinking water are carfentrazone-ethyl, F8426-ClPAc, and F8426-CAc (MARC decision memoranda, J. Stokes, 19-Jun-1998). As part of the rice registration, HED requested that the petitioner include holding times for the treated rice paddy water of 69 days (0.3 lbs ai/acre/season). This holding time was based on an aquatic dissipation study conducted on flooded rice fields (0.3 lbs ai/acre; 3-4 inch water depth; MRID 44654701) and the EC_{50} for green algae of 5.9 ppb. This study demonstrated a half-life for the combined residues of carfentrazone-ethyl, F8426-ClPAc, F8426-PAc, F8426-CAc, F8426-BAc, and 3-OH-F8426-BAc in water of 10 days. Based on this study, and the requested/proposed label restrictions for potable water, livestock water, and irrigation water, HED concludes that the petitioner has adequately addressed issues concerning the presence of carfentrazone-ethyl in water.

Fish: The petitioner has submitted and EFED has reviewed a fish metabolism study. Based on these data, HED concludes that the residues of concern in fish, for purposes of tolerance enforcement and risk assessment, are carfentrazone-ethyl and F8426-ClPAc. The petitioner has submitted a fish, crayfish, and shellfish magnitude of the residue study conducted at 1.5x the maximum single application rate. **Based on these data, HED concludes that a tolerances in/on fish and shellfish, for the combined residues of carfentrazone-ethyl and F8426-ClPAc, of 0.30 ppm are appropriate. A revised Section F is requested.**

Livestock: Tolerances for the combined residues of carfentrazone and F8426-ClPAc are currently established on the following commodities (established as part of D293779, T. Bloem, 14-Jul-2004): meat byproducts (cattle, goat, horse, and sheep) - 0.10 ppm; meat (cattle, goat, horse, and sheep) - 0.10 ppm; fat (cattle, goat, horse, and sheep) - 0.10 ppm; milk - 0.05 ppm. Based on the current and proposed tolerances and the proposed restriction concerning consumption of treated water by livestock (residues must be <0.2 ppm), HED concludes that the currently established cattle tolerances are appropriate and that tolerances for poultry and hog are unnecessary (180.6(a)(3)).

Analytical Enforcement Method - Fish/Shellfish: A livestock method P-315M is available for collecting data on residues of carfentrazone-ethyl, F8426-ClPAc, and F8426-PAc in livestock commodities (D233587, J. Stokes, 18-Jun-1998). This method has been radiovalidated using samples from the ruminant metabolism study and undergone a successful independent laboratory validation trial using milk. HED has forwarded this method to the Analytical Chemistry Laboratory (ACL) for a petition method validation (PMV; D305152, T. Bloem, 12-Jul-2004). Provided this method is validated by the ACL, HED concludes that this method is sufficient for enforcement of the tolerances associated with this petition.

Recommendations: Provided the petitioner submits revised Sections B and F and the analytical laboratory is able to validated the proposed fish/shellfish enforcement method, HED concludes that the residue chemistry database supports the establishment of the following tolerances for the combined residues of carfentrazone-ethyl and F8426-ClPAc (a human health risk assessment will prepared as a separate document):

fish ..... 0.30 ppm
shellfish ..... 0.30 ppm

Summary of Residue Chemistry Deficiencies:

- Revised Section B
- Revised Section F
- PMV of the fish/shellfish proposed enforcement method

Detailed Considerations

Background

Carfentrazone-ethyl is a post-emergence herbicide of the phenyl triazolinone group used for control of broad leaf weeds. It acts as an inhibitor of protoporphyrinogen oxidase which results in disruption of the cell membrane and dessication of susceptible plant species. The proposed use is for aquatic application. Therefore, portions of the OPPTS GLN 860 guidelines which do not pertain to aquatic application were not included.

Table 2 Carfentrazone-Ethyl Nomenclature

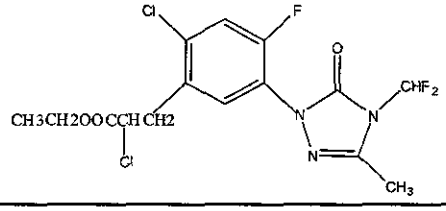
Chemical Structure	
Common name	carfentrazone-ethyl
Company experimental name	F8426
IUPAC name	(RS)-2-chloro-3-{2-chloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorophenyl}propionic acid
CAS name	α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoic acid
CAS #	128621-72-7
End-Use Product	Aim™ Herbicide (EPA Reg. No. 279-3194; water dispersable granule; 40% by weight)

Table 3 Physicochemical Properties of the Technical Grade Test Compound

Melting point/range	-22.1° C
pH	not available
Density	1.46 at 20° C
Water solubility (20°C)	12 µg/ml
Solvent solubility (g/L at 20°C)	acetone - >2000; acetonitrile - >2000; toluene - 900; dichloromethane - >2000; hexane - 30; ethanol - >2000; ethyl acetate - >2000
Vapour pressure	1.2×10^{-7} mm Hg (25° C); 5.4×10^{-8} mm Hg (20° C)
Dissociation constant (pK_a)	no dissociation constant
Octanol/water partition coefficient Log(K_{OW})	log K_{ow} = 3.36
UV/visible absorption spectrum	not available

860.1200 Directions for Use

The petitioner is requesting registration for application of Stingray™ (emulsifiable concentrate; 1.9 lbs ai/gallon) to aquatic areas for the control of floating weeds. The maximum single application rate is 0.2 lbs ai/surface acre. The label indicates that retreatment may be necessary and recommends a 14-day RTI (maximum seasonal application rate is not specified). The label includes the following restrictions: **(1)** do not apply within 1/4 mile upstream of a potable water intake in flowing or standing water body; **(2)** to make applications within a 1/4 mile potable water intake, the water intake must be turned off for 24 hours after the application (water may be turned on prior to 24 hours if the carfentrazone-ethyl level in the water intake is below 0.2 ppm); **(3)** do not use treated water for irrigation in commercial nurseries or greenhouse; and **(4)** for crops, do not use treated water for irrigation purposes until 14 days after treatment or until analysis indicates a concentration of carfentrazone ethyl and it major metabolite is <5 ppb.

The MARC has determined that the residues of concern in drinking water are carfentrazone-ethyl, F8426-ClPAc and F8426-CAc (MARC decision memoranda, J. Stokes, 19-Jun-1998). **The potable water and irrigation restrictions on the label concern the concentration of carfentrazone-ethyl (potable water) or carfentrazone ethyl and it major metabolite (irrigation). These restrictions should be for the combined residues of carfentrazone-ethyl, F8426-ClPAc and F8426-CAc. In addition, HED requests that the petitioner consistently indicate application rates in lbs ai/surface acre and indicate that the water may not be used as a water source for livestock until the combined concentration of carfentrazone-ethyl, F8426-ClPAc and F8426-CAc has dropped to <0.2 ppm. A revised Section B is requested.**

Based on the application rate of 0.2 lbs ai/surface acre and assuming a depth of 3 feet, a water concentration immediately after application of 25 ppb is calculated. This concentration is lower than the 34 ppb acute surface water EDWC (used for risk assessment) provided by EFED. Based on this and assuming the petitioner makes the label changes recommended above, HED concludes that the potable water restriction of <0.2 ppm is acceptable (0.2 ppm yields exposures ≤1% cPAD and aPAD). Currently, HED has preliminary data concerning the foliar application of carfentrazone-ethyl to cereal grains at 0.031 lb ai/acre (PHI of 3-4 days). The spray volumes used in these studies were ~10 gallons/acre which leads to a concentration of carfentrazone-ethyl in the spray water of ~370 ppm. These studies resulted in residues of concern in the harvested field corn grain, forage, and stover of ≤0.82 ppm. Based on these data and since the petitioner has requested tolerances in/on all crop groups which include crops consumed by humans, HED concludes that the proposed irrigation water restriction (do not use treated water for irrigation purposes until concentration has dropped to <5 ppb or 14 days have passed) is acceptable.

860.1340 Residue Analytical Methods

A livestock method P-315M is available for collecting data on residues of carfentrazone-ethyl, F8426-ClPAc, and F8426-PAc in livestock commodities (D233587, J. Stokes, 18-Jun-1998; limit of quantitation (LOQ) of 0.05 ppm (tissue) and 0.025 ppm (milk)). This method has been radiovalidated using samples from the ruminant metabolism study and undergone a successful independent laboratory validation trial using milk. HED has forwarded this method to the ACL for a PMV (D305152, T. Bloem, 12-Jul-2004). Provided this method is validated by the ACL, HED concludes that this method is sufficient for enforcement of the tolerances associated with this petition.

860.1360 Multiresidue Methods

The petitioner has submitted data pertaining to the multiresidue methods testing of carfentrazone-ethyl (D233587, J. Stokes, 18-June-1998). According to the petitioner's summary, carfentrazone-ethyl was detected under Protocol C using either the ECD or the nitrogen/phosphorous detector (NPD); better sensitivity was achieved with ECD. Complete recovery of carfentrazone-ethyl was achieved using Protocols D and F, except from the Florisil column when cleanup module C1 was used. Metabolites, F8426-ClPAc, 3-DM-F8426-ClPAc, and 3-OH-F8426-ClPAc were tested using PAM Protocols B and C. The metabolites could not be chromatographed without methylation, but with methylation the metabolites were recovered using Protocols B and C; ECD provided better sensitivity with Protocol C. These data have been forwarded to FDA to be included in PAM I, Appendix I (D235540, J. Stokes, 16-May-1997).

860.1480 Meat, Milk, Poultry, and Eggs

Tolerances for the combined residues of carfentrazone and F8426-ClPAc are currently established on the following commodities (established as part of D293779, T. Bloem, 14-Jul-2004): meat byproducts (cattle, goat, horse, and sheep) - 0.10 ppm; meat (cattle, goat, horse, and sheep) - 0.10 ppm; fat (cattle, goat, horse, and sheep) - 0.10 ppm; and milk - 0.05 ppm.

Based on the current and proposed tolerances and the proposed restriction concerning consumption of treated water by livestock (residues must be <0.2 ppm), the theoretical dietary burdens for beef and diary cattle, poultry, and hog are 10.46 ppm, 0.48 ppm, and 1.04 ppm, respectively. Table 5 is a summary of the livestock theoretical dietary burdens.

Table 5. Calculation of Maximum Dietary Burdens of Carfentrazone-ethyl Residue to Livestock.

Feed Commodity	% Dry Matter[1]	% Diet[1]	Recommended/Established Tolerance (ppm)	Dietary Contribution (ppm)[2]
Beef and Dairy Cattle				
Grass forage	25	40	5.0	8
Corn grain	88	40	0.10	0.05
Cottonseed meal	88	15	0.35	0.06
Cotton gin by-products	90	5	10	0.56
Water[3]	(0.2 x 135) ÷ 15 = 1.80 ppm			1.80
TOTAL BURDEN	--	100	--	**10.46**
Poultry				
Corn grain	88	80	0.1	0.08
Soybean	89	20	0.35	0.07
Water[4]	(0.2 x 0.23) ÷ 0.14 = 0.33			0.33
TOTAL BURDEN	--	100	--	**0.48**
Hog				
Corn grain	88	80	0.1	0.08
Soybean seed	89	5	0.1	0.01
Cottonseed meal	89	15	0.35	0.05
Water[5]	(0.2 x 9) ÷ 2= 0.9			0.90
TOTAL BURDEN	--	100	--	**1.04**

1 OPPTS 860.100 Table 1

2 Contribution = (tolerance ÷ % DM (if cattle)) x % diet

3 restriction on using treated water as a water source for livestock until concentration has dropped below 0.2 ppm; assumes 135 kg of water consumed per day and 15 kg feed intake per day (taken from PP# 1F3991, G. Otakie, 4-Aug-1992)

4 restriction on using treated water as a water source for livestock until concentration has dropped below 0.2 ppm; assumes 0.23 kg of water consumed per day and 0.14 kg feed intake per day (taken from PP# 1F3991, G. Otakie, 4-Aug-1992)

5 restriction on using treated water as a water source for livestock until concentration has dropped below 0.2 ppm; assumes 9 kg of water consumed per day and 2 kg feed intake per day (taken from http://www.ofac.org/factsheets/fact13.html)

Ruminant: A feeding study on dairy cows is available and has been reviewed (D233587, J. Stokes, 18-Jun-1998). In this study, dairy cows were fed a diet fortified with carfentrazone-ethyl at 1 ppm (0.1x), 3 ppm (0.3x), and 10 ppm (1.2x) (dry weight basis). Milk, cream, and fat samples were analyzed for residues of carfentrazone-ethyl, F8426-ClPAc, and F8426-PAc. Tissue samples were analyzed for F8426-ClPAc, and F8426-PAc. The compounds monitored in the various matrices were based on the result of a lactating goat metabolism study. The Method LOQ and limit of detection (LOD) were 0.025 and 0.005 ppm, respectively, for milk and 0.05 and 0.01 ppm, respectively, for tissues and cream.

Residues of each analyte were <LOD in all cream, fat, liver, muscle (<0.01 ppm), and skim milk (≤0.005 ppm) samples collected from the 3 ppm and 10 ppm dosing groups (1 ppm samples were not analyzed). For the 10 ppm dose group, residues of F8426-ClPAc were detected in one sample of milk (0.008 ppm) and in kidney (0.013 ppm). Based on the current dietary burden for cattle, HED concludes that an increase in the established livestock tolerances is unnecessary.

Poultry and Hog: Based on the current dietary burden for poultry and hog and either the poultry metabolism study (conducted at 21x poultry dietary burden; TRR ≤0.055 ppm) or the ruminant feeding study (residues <LOQ at 10x the hog dietary burden), HED concludes that poultry and hog tolerances are unnecessary (180.6(a)(3)).

860.1400 Water, Fish, and Irrigated Crops

46253902.der.wpd

Water and Irrigated Crops: As previously indicated, the MARC has concluded that the residues of concern in drinking water are carfentrazone-ethyl, F8426-ClPAc, and F8426-CAc (MARC decision memoranda, J. Stokes, 19-Jun-1998). As part of the rice registration, HED requested that the petitioner include holding times for the treated rice paddy water of 69 days (0.3 lbs ai/acre/season). This holding time was based on an aquatic dissipation study conducted on flooded rice fields (0.3 lbs ai/acre; 3-4 inch water depth; MRID 44654701) and the EC_{50} for green algae of 5.9 ppb. This study demonstrated a half-life for the combined residues of carfentrazone-ethyl, F8426-ClPAc, F8426-PAc, F8426-CAc, F8426-BAc, and 3-OH-F8426-BAc in water of 10 days. Based on this study, and the requested/proposed label restrictions for potable water, livestock water, and irrigation water, HED concludes that the petitioner has adequately addressed issues concerning the presence of carfentrazone-ethyl in water.

Fish: The petitioner has submitted and EFED has reviewed a fish metabolism/bioconcentration study (MRID 44165042). Rainbow trout were exposed continuously to [C-phenyl-U-^{14}C]carfentrazone-ethyl at 16 ppb (41 days) and 160 ppb (28 days). Fish samples were collected after 1, 3, 7, 10, 14, 21, 28, 31 (16 ppb only) , 34 (16 ppb only), 37 (16 ppb only), and 41 (16 ppb only) days of exposure. The remaining fish were removed to untreated water and sampled 1, 3, 7, 10, and 14 days to determine the elimination rate.

After 41 days of exposure to water fortified with carfentrazone-ethyl at 16 ppb, residues in edible tissue, viscera, carcass, and whole body fish tissue were 0.26 ppm, 17.9 ppm, 0.32 ppm, and 2.48 ppm, respectively. The major compound identified was F8426-ClPAc (viscera - 92% total radioactive residue (TRR); edible 80% TRR). The conjugated metabolite 3-OH-F8426-ClPAc was also identified at ≤4% TRR (1 (edible) or 2 (nonedible) polar unknowns were also identified at ≤8% TRR). Carfentrazone-ethyl was not identified. The depuration portion of the study indicated that 98-99% of the TRR was eliminated 14 days after exposure. Based on these data, HED concludes that the residues of concern in fish, for purposes of tolerance enforcement and risk assessment, are carfentrazone-ethyl and F8426-ClPAc (the MARC has determined that F8426-ClPAc is not likely to be more toxic than parent; MARC decision document, J. Stokes, 19-Jun-1998).

The petitioner has submitted a fish, crayfish, and shellfish magnitude of the residue study conducted at 1.5x the maximum single application rate (46253902.der.wpd; see below). **Based on these data, HED concludes that a tolerances in/on fish and shellfish, for the combined residues of carfentrazone-ethyl and F8426-ClPAc, of 0.30 ppm are appropriate. A revised Section F is requested.**

Fish Magnitude of the Residue Study (46253902.der.wpd): Seven cylindrical fiber glass pools (6 treated; 1 control) were filled with 2 cm of sandy loam soil and ~3 feet of water (~1060 liters). Each treatment and control pool received 4 channel catfish (*Ictalurus punctatus*), 6 bluegill fish (*Lepomis macrochirus*), 14 northern crayfish (*Orconectes virillis*), and 2 clams (*Anodonta grandis*). The test substance (F8426 2EW (emulsifiable concentrate)) was added to the treated pools at a rate of 0.30 lb ai/surface acre (yields a theoretical concentration in the pools of 38 ppb). Water samples were collected form the treated pools 1.5 hours after application indicated a water concentration 42-76% the theoretical concentration. Tissue samples were collected 1, 3, 7, 14, 21, and 30 days after application. Tissue samples were collected by draining one of the treated pools on a sampling day and removing all of the organisms from the pool. The control samples were collected on the final day of sampling. Edible tissue was separated from the non-edible tissue on the day the samples were collected and combined to form a single species sample. The entire soft tissue mass of the clams was separated form the shell and collected. The tail of the crayfish was broken off and the edible tissue collected (remaining crayfish was discarded). Head fins and viscera of the fish were removed to obtain the edible tissue (edible tissue includes skin and bone).

The samples were analyzed for residues of carfentrazone-ethyl and F8426-ClPAc using an adequately validated GC/ECD (gas chromatograph/electron-capture detector) method (LOQ and LOD of 0.05 ppm and 0.01 ppm, respectively). The samples were stored frozen and analyzed within 13 days. The rainbow trout metabolism indicated that carfentrazone-ethyl did continue to breakdown to F8426-ClPAc in tissue samples when placed in frozen storage (D294823, T. Bloem, 15-Jul-2004). Since F8426-ClPAc was measured in the current study and since the samples were stored frozen and analyzed within 13 days of collection, HED concludes that the storage interval has been validated. Residues of carfentrzazone-ethyl were <LOD in/on all samples and residues of F8426-ClPAc were <LOD in/on all crayfish samples. Resides of F8426-ClPAc were 0.17 ppm, 0.12-0.13 ppm, 0.03 ppm, <LOD, and <LOD in bluegill samples collected 1, 3, 7, 14, and 21 days after treatment, respectively. Resides of F8426-ClPAc were 0.15-0.16 ppm, 0.15-0.16 ppm, <LOD, <LOD, and <LOD in clam samples collected 1, 3, 7, 14, and 21 days after treatment, respectively. Residues of F8426-ClPAc in were 0.08-0.09 ppm, 0.08-0.09 ppm, 0.02 ppm, <LOD, and <LOD in catfish samples collected 1, 3, 7, 14, and 21 days after treatment, respectively.

860.1650 Submittal of Analytical Reference Standards

The analytical reference standards for carfentrazone-ethyl have been submitted to the EPA National Pesticide Standards Repository.

860.1550 Proposed Tolerances

Table 6 is a summary of the proposed and recommended tolerances for the combined residues of carfentrazone-ethyl and carfentrazone-ethyl chloropropionic acid in fish and shellfish. A revised Section F is requested. There are currently no established Codex, Canadian, or Mexican MRLs for carfentrazone-ethyl in fish and shellfish; therefore, harmonization is not an issue for this petition.

Table 6. Tolerance Summary

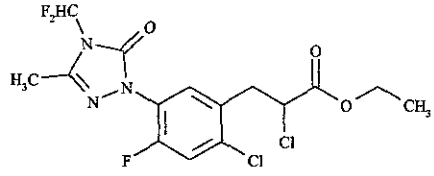
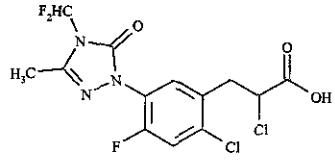
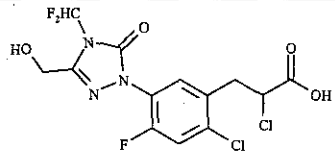
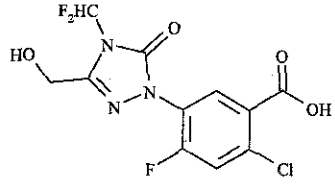
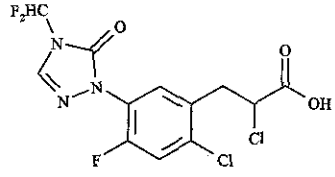
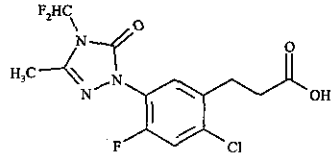
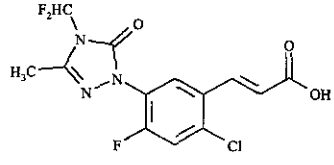
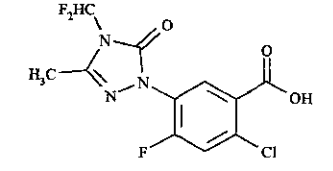
Proposed		Recommended	
Commodity Definition	**Tolerance (ppm)**	**Commodity Definition**	**Tolerance (ppm)**
fish	0.2	fish	0.30
shellfish	0.2	shellfish	0.30

RDI: RAB1 Chemists (14-Jul-2004)
T. Bloem:806R:CM#2:(703)605-0217:7590C
Template Version September 2003

Attachments

1. Chemical Structures
2. 46253902.der.wpd (magnitude of the residue in fish and shell fish)

Attachment 1: Chemical Names and Structures

Common name /code	Chemical name	Chemical structure
carfentrazone-ethyl F8426	ethyl-α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl)-4-fluorobenzenepropanoate	
carfentrazone-chloropropionic acid F8426-ClPAc	α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoic acid	
3-hydroxymethyl-carfentrazone-chloropropionic acid 3-OH-F8426-ClPAc	α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-hydroxymethyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoic acid	
3-hydroxymethyl-carfentrazone-benzoic acid 3-OH-F8426-BAc	2-chloro-5-[4-(difluoromethyl)-4,5-dihydro-3-hydroxymethyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzoic acid	
3-desmethyl-carfentrazone-chloropropionic acid 3-DM-F8426-ClPAc	α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoic acid	
F8426-propionic acid; F8426-PAc	2-chloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoic acid	
F8426-cinnamic acid; F8426-CAc	2-chloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropenoic acid	
F8426-benzoic acid; F8426-BAc	2-chloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzoic acid	

Carfentrazone-ethyl/F8426/128712/FMC Corporation
DACO 6.4, 7.4, 7.8/OPPTS 860.1400/OECD IIIA 8.4.3 and IIIA 8.3
Water, Fish, and Irrigated Crops - Fish, Crayfish, and Clam

Date	14-July-2004
Primary Evaluator	Tom Bloem, Chemist Registration Action Branch 1 (RAB1) Health Effects Division (HED; 7509C)
Approved by	George F. Kramer, Ph.D., Chemist RAB1/HED (7509C)

STUDY REPORTS:

MRID 46253902. Dow, K. (2004). Magnitude of the Residues of F8426Aquatic Herbicide in Sunfish/Catfish/Crayfish/Clams in a Static Aquatic System. Study Number 842FIS03R1. Unpublished study prepared by FMC Corporation. 89 pages.

EXECUTIVE SUMMARY:

Seven cylindrical fiber glass pools (6 treated; 1 control) were filled with 2 cm of sandy loam soil and ~3 feet of water (~1060 liters). Each treatment and control pool received 4 channel catfish (*Ictalurus punctatus*), 6 bluegill fish (*Lepomis macrochirus*), 14 northern crayfish (*Orconectes virillis*), and 2 clams (*Anodonta grandis*). The test substance (F8426 2EW (emulsifiable concentrate)) was added to the treated pools at a rate of 0.30 lb ai/surface acre (yields a theoretical concentration in the pools of 38 ppb). Water samples were collected form the treated pools 1.5 hours after application indicated a water concentration 42-76% the theoretical concentration. Tissue samples were collected 1, 3, 7, 14, 21, and 30 days after application. Tissue samples were collected by draining one of the treated pools on a sampling day and removing all of the organisms from the pool. The control samples were collected on the final day of sampling. Edible tissue was separated from the non-edible tissue on the day the samples were collected and combined to form a single species sample. The entire soft tissue mass of the clams was separated form the shell and collected. The tail of the crayfish was broken off and the edible tissue collected (remaining crayfish was discarded). Head fins and viscera of the fish were removed to obtain the edible tissue (edible tissue includes skin and bone).

The samples were analyzed for residues of carfentrazone-ethyl and F8426-ClPAc using an adequately validated GC/ECD (gas chromatograph/electron-capture detector) method (limit of quantitation (LOQ) and limit of detection (LOD) of 0.05 ppm and 0.01 ppm, respectively). The samples were stored frozen and analyzed within 13 days. The rainbow trout metabolism indicated that carfentrazone-ethyl did continue to breakdown to F8426-ClPAc in tissue samples when placed in frozen storage (D294823). Since F8426-ClPAc was measured in the current study and since the samples were stored frozen and analyzed within 13 days of collection, HED concludes that the storage interval has been validated. Residues of carfentrzazone-ethyl were <LOD in/on all samples and residues of F8426-ClPAc were <LOD in/on all crayfish samples. Resides of F8426-ClPAc were 0.17 ppm, 0.12-0.13 ppm, 0.03 ppm, <LOD, and <LOD in bluegill samples collected 1, 3, 7, 14, and 21 days after treatment, respectively. Resides of

F8426-ClPAc were 0.15-0.16 ppm, 0.15-0.16 ppm, <LOD, <LOD, and <LOD in clam samples collected 1, 3, 7, 14, and 21 days after treatment, respectively. Residues of F8426-ClPAc in were 0.08-0.09 ppm, 0.08-0.09 ppm, 0.02 ppm, <LOD, and <LOD in catfish samples collected 1, 3, 7, 14, and 21 days after treatment, respectively.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the fish, crayfish, and clam residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document (D294823).

COMPLIANCE:

The in-life phase of the study was conducted by Springborn Laboratories (Weraham, MA) and the analytical phase of the study was conducted by FMC Coporation (Princeton, NJ). Signed and dated Good Laboratory Practices (GLP), Quality Assurance, and Data Confidentiality statements were provided. No GLP deviations were reported which would impact the study results or their interpretation.

A. BACKGROUND INFORMATION

Carfentrazone-ethyl is a post-emergence herbicide of the phenyl triazolinone group used for control of broad leaf weeds. It acts as an inhibitor of protoporphyrinogen oxidase which results in disruption of the cell membrane and dessication of susceptible plant species.

Table A.1. Carfentrazone-Ethyl Nomenclature

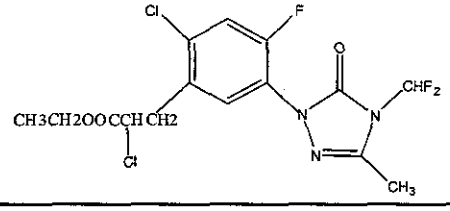
Chemical Structure	
Common name	carfentrazone-ethyl
Company experimental name	F8426
IUPAC name	(RS)-2-chloro-3-{2-chloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorophenyl}propionic acid
CAS name	α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoic acid
CAS #	128621-72-7
End-Use Product	Aim™ Herbicide (EPA Reg. No. 279-3194; water dispersable granule; 40% by weight)

Table A.2. Physicochemical Properties of the Technical Grade Test Compound	
Melting point/range	-22.1° C
pH	not available
Density	1.46 at 20° C
Water solubility (20°C)	12 µg/ml
Solvent solubility (g/L at 20°C)	acetone - >2000; acetonitrile - >2000; toluene - 900; dichloromethane - >2000; hexane - 30; ethanol - >2000; ethyl acetate - >2000
Vapour pressure	1.2 x 10^{-7} mm Hg (25° C); 5.4 x 10^{-8} mm Hg (20° C)
Dissociation constant (pK_a)	no dissociation constant
Octanol/water partition coefficient Log(K_{OW})	log K_{ow} = 3.36
UV/visible absorption spectrum	not available

B. EXPERIMENTAL DESIGN

B.1. Magnitude of the Residue

B.1.1. Study Site Information

The test system consisted of 6 replicate treatment systems and one control system each consisting of a cylindrical fiberglass pool (4 feet in diameter and 4 feet in depth). The pools contained approximately 2 cm layer of sandy loam soil (see below) and ~1060 liters of water. The water was unaltered well water obtained from a 100-meter bedrock well mixed with unchlorinated well water from the Town of Wareham, MA (see below). The water temperature was 17-20°C. A photoperiod of 16 hours of light (64 footcandles) and 8 hours of dark was employed.

Water was added to the soil filled test systems and allowed to equilibrate for 2 days before the test organisms were added (3' water depth). Each treatment and control pool received 4 channel catfish (*Ictalurus punctatus*), 6 bluegill fish (*Lepomis macrochirus*), 14 northern crayfish (*Orconectes virillis*), and 2 clams (*Anodonta grandis*). The test organisms were allowed to acclimate for 2 days prior to the addition of the test substance and were fed a diet of dry flaked fish food throughout the study. The test substance (F8426 2EW) was added to the treated pools at a rate of 0.30 lb ai/surface acre. To avoid initial patchy high concentrations, the measured test substance was added to a stainless steel bucket filled with the test water. This was then evenly distributed around the pool and the pool were mixed for five minutes using a hand-held paddle.

Water samples were collected form the control and treated pools 1.5 hours after application. Tissue and water samples were collected 1, 3, 7, 14, 21, and 30 days after application (only the day 0 and day 1 water samples were anlayzed). Tissue samples were collected by draining one of the treated pools on a sampling day and removing all of the organisms from the pool. The control samples were collected on the final day of sampling. Edible tissue was separated from the non-edible tissue on the day the samples were collected and combined to form a single species sample. The entire soft tissue mass of the clams was separated form the shell and collected. The tail of the crayfish was broken off and the edible tissue collected (remaining crayfish was discarded). Head fins and viscera of the fish were removed to obtain the edible tissue (edible tissue includes skin and bone).

Table B.1.1.1 Soil Characterization			
Type	%organic matter	pH	CEC meq/100g
sandy loam	2.2	5.8	7.7

Table B.1.1.2 Water Characterization.							
Study site	Water characteristics						
	Type	Hardness/Salinity (mg/liter $CaCO_3$)	pH	dissolved oxygen (mg/liter)	specific conductance (µmhos/cm)	Turbidity	Dissolved organic matter
4'x4' cylindrical fiberglass pools	well water	0-44	6.8-7.6	4.3-9.4	120	not provided	

B.2.2. Sample Handling and Preparation

All samples were frozen with 20 minutes of collections and remained frozen until analysis (tissue samples homogenized prior to being placed in frozen storage).

B.2.3. Analytical Methodology

The water and fish samples were analyzed by FMC Coporation (Princeton, NJ) for residues of carfentrazone-ethyl and F8426-ClPAc using the following methods.

Tissue: The homogenized tissue samples were extracted with acetone:water (7:3), reduced to the aqueous phase, and partitioned with hexane. The hexane extract (contains carfentrazone-ethyl) was cleaned up by eluting through a silica-gel solid-phase extraction (SPE) cartridge and analyzed via GC/ECD. The aqueous fraction from the hexane/aqueous partition (contains F8426-ClPAc) was acidified and refluxed for one hour. The hydrolysate was cleaned up by eluting through a C_8 SPE cartridge, methylated using a solution of BF_3 in methanol. After methylation the samples was cleaned up by passing through a silica gel SPE cartridge and analyzed via GC/ECD. The petitioner specified a LOQ of 0.05 ppm and a LOD of 0.01 ppm.

Water: The water samples were partitioned with hexane and the hexane phase directly analyzed via GC/ECD. The petitioner specified a LOQ of 0.005 ppm and a LOD of 0.001 ppm.

C. RESULTS AND DISCUSSION

The samples were analyzed for residues of carfentrazone-ethyl and F8426-ClPAc using an adequately validated GC/ECD method (see Table C.1; LOQ = 0.05 ppm; LOD = 0.01 ppm; residue in/on controls were <LOD). The samples were stored frozen and analyzed within 13 days. The rainbow trout metabolism indicated that carfentrazone-ethyl did continue to breakdown to F8426-ClPAc in tissue samples when placed in frozen storage (D294823). Since F8426-ClPAc was measured in the current study and since the samples were stored frozen and analyzed within 13 days of collection, HED concludes that the storage interval has been validated.

Seven cylindrical fiber glass pools (6 treated; 1 control) were filled with 2 cm of sandy loam soil and 3 feet of water (1068 liters). Each treatment and control pool received 4 channel catfish (*Ictalurus punctatus*), 6 bluegill fish (*Lepomis macrochirus*), 14 northern crayfish (*Orconectes virillis*), and 2 clams (*Anodonta grandis*). The test substance (F8426 2EW) was added to the treated pools at a rate of 0.30 lb ai/surface acre (yields a theoretical concentration in the pools of 38 ppb). Water samples were collected form the control and treated pools 1.5 hours after application. These samples indicated a water concentration 42-76% the theoretical concentration. Tissue samples were collected 1, 3, 7, 14, 21, and 30 days after application. Tissue samples were collected by draining one of the treated pools on a sampling day and removing all of the organisms from the pool. The control samples were collected on the final day of sampling. Edible tissue was separated from the non-edible tissue on the day the samples were collected and combined to form a single species sample. The entire soft tissue mass of the clams was separated form the shell and collected. The tail of the crayfish was broken off and the edible tissue collected (remaining crayfish was discarded). Head fins and viscera of the fish were removed to obtain the edible tissue (edible tissue includes skin and bone).

Residues of carfentrzazone-ethyl were <LOD in/on all samples and residues of F8426-ClPAc were <LOD in/on all crayfish samples. Resides of F8426-ClPAc were 0.17 ppm, 0.12-0.13 ppm, 0.03 ppm, <LOD, and <LOD in bluegill samples collected 1, 3, 7, 14, and 21 days after treatment, respectively. Resides of F8426-ClPAc were 0.0.15-0.16 ppm, 0.15-0.16 ppm, <LOD, <LOD, and <LOD in clam samples collected 1, 3, 7, 14, and 21 days after treatment, respectively. Residues of F8426-ClPAc in were 0.08-0.09 ppm, 0.08-0.09 ppm, 0.02 ppm, <LOD, and <LOD in catfish samples collected 1, 3, 7, 14, and 21 days after treatment, respectively (see Table C.3)

Table C.1. Summary of Concurrent Recoveries.

Matrix	Spike level (mg/kg)	Sample size (n)	Recoveries (%)	Mean ± std dev
carfentrazone-ethyl				
fish/clam/crayfish tissue	0.1	2	63, 97	80 ± 24
	0.55	1	65	--
	0.05	3	63, 81, 90	78 ± 14
water	0.05	1	113	--
	0.005	1	98	--
F8426-ClPAc				
fish/clam/crayfish tissue	0.1	2	68, 97	82 ± 21
	0.55	1	106	--
	0.05	3	118, 120, 129	122 ± 6
water	0.05	1	88	--
	0.005	1	104	--

Table C.2. Summary of Storage Conditions

Matrix	RAC or Extract	Storage Temp. (°C)	Maximum Storage Duration (days)[1]	Interval of Demonstrated Storage Stability (days or months)
tissue	RAC	frozen	13	The rainbow trout metabolism indicated that carfentrazone-ethyl did continue to breakdown to F8426-ClPAc in tissue samples when placed in frozen storage (D294823). Since F8426-ClPAc was measured in the current study and since the samples were stored frozen and analyzed within 13 days of collection, HED concludes that the storage interval has been validated.
water	RAC	frozen	20	

[1] from harvest to extraction; extracts were stored for ≤ 12 days; since fortified samples run concurrent to the treated samples resulted in acceptable % recoveries, HED concludes that the storage intervals for the extracts has been verified

Table C.3. Bluegill, Catfish, Crayfish, and Clam Residues in Edible Tissue

Application Scenario	Matrix	Residues (ppm)	
		Carfentrazone-ethyl	F8426-ClPAc
day 0			
F8426 2EW was added at a rate of 0.30 lb ai/surface acre	water[1]	0.021-0.029	0.002-0.003
1 day after treatment			
F8426 2EW was added at a rate of 0.30 lb ai/surface acre	water	0.011-0.019	0.011-0.022
	bluegill	<0.01, <0.01	0.17, 0.17
	clam	<0.01, <0.01	0.15, 0.16
	crayfish	<0.01, <0.01	<0.01, <0.01
	catfish	<0.01, <0.01	0.09, 0.08
3 days after treatment			
F8426 2EW was added at a rate of 0.30 lb ai/surface acre	bluegill	<0.01, <0.01	0.12, 0.13
	clam	<0.01, <0.01	0.15, 0.16
	crayfish	<0.01, <0.01	<0.01, <0.01
	catfish	<0.01, <0.01	0.08, 0.09

Table C.3. Bluegill, Catfish, Crayfish, and Clam Residues in Edible Tissue			
Application Scenario	Matrix	Residues (ppm)	
		Carfentrazone-ethyl	F8426-ClPAc
7 days after treatment			
F8426 2EW was added at a rate of 0.30 lb ai/surface acre	bluegill	<0.01, <0.01	0.03, 0.03
	clam	<0.01, <0.01	<0.01, <0.01
	crayfish	<0.01, <0.01	<0.01, <0.01
	catfish	<0.01, <0.01	0.02, 0.02
14 days after treatment			
F8426 2EW was added at a rate of 0.30 lb ai/surface acre	bluegill	<0.01, <0.01	<0.01, <0.01
	clam	<0.01, <0.01	<0.01, <0.01
	cryafish	<0.01, <0.01	<0.01, <0.01
	catfish	<0.01, <0.01	<0.01, <0.01
21 days after treatment			
F8426 2EW was added at a rate of 0.30 lb ai/surface acre	bluegill	<0.01, <0.01	<0.01, <0.01
	clam	<0.01, <0.01	<0.01, <0.01
	cryafish	<0.01, <0.01	<0.01, <0.01
	catfish	<0.01, <0.01	<0.01, <0.01

[1] target rate of 0.039 ppm (measured rate was 46-80% of the target rate)

D. CONCLUSION

The study adequately demonstrates the residues of carfentrazone-ethyl and F8426-ClPAc in fish crayfish, and clam following a single application of carfentrazone-ethyl to water at a theoretical concentration 38 ppb.

E. REFERENCES

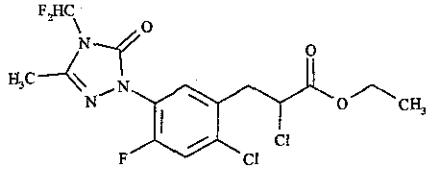
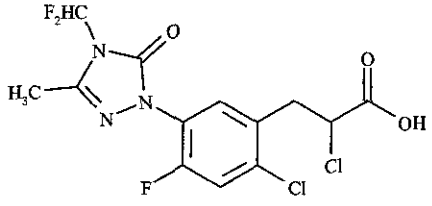
none

F. DOCUMENT TRACKING

RDI: RAB1 Chemists (14-July-2004)
T. Bloem:806R:CM#2:(703)605-0217:7590C
Template Version September 2003

Attachment 1: Chemical Structures

Attachment 1: Chemical Structures

Chemical Name	Structure
Carfentrazone-ethyl; F8426 ethyl α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoate	
F8426-chloropropionic acid; F8426-ClPAc α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoic acid	

13544

R100927

Chemical:	**Benzenepropanoic acid, .alpha.-2-dichlor**
PC Code:	**128712**
HED File Code	**11000 Chemistry Reviews**
Memo Date:	**07/15/2004**
File ID:	**DPD294823**
Accession Number:	**412-05-2000**

HED Records Reference Center
09/07/2004