United States Environmental Protection Agency

Office of Prevention, Pesticides and Toxic Substances (7501C)

Pesticide Fact Sheet

Name of Chemical: Carfentrazone-ethyl
Reason for Issuance:New Chemical Registration
Date Issued: September 30, 1998

DESCRIPTION OF CHEMICAL

Generic Name: Ethyl 2-chloro-3-[2-chloro-4-fluoro-5-[4-(difluoromethyl)-4,5-diydro-3-methyl-5-oxo-1H-1,2,4-trizol-1-yl)phenyl]propanoate

Common Name: Carfentrazone-ethyl

Trade Name: Aim

EPA Shaughnessy Code: 128712

Chemical Abstracts Service (CAS) Number: 128639-02-1

Year of Initial Registration: 1998

Chemical Family: Aryl Triazolinone

U.S. Producer: FMC Corporation

USE PATTERNS AND FORMULATIONS

Application sites: Carfentrazone-ethyl is registered for use on wheat, corn and soybeans.

Types of Formulations: 90.0% technical
40.0% water-dispersable/dry flowable
50.0% water-dispersable/dry flowable

Types and Methods of Application: Ground application using boom sprayers

Application Rates: Application rates for wheat, corn, and soybeans range from 0.004 to 0.031 pounds of active ingredient per acre (post-emergence application).

Carrier: Water, Crop Oil, Nonionic Surfactant

3. Science Findings

Summary Science Statements

Based upon a battery of acute toxicity studies, Carfentrazone-ethyl is classified as Toxicity Categories III and IV (CAUTION). Carfentrazone-ethyl is not carcinogenic, neurotoxic, mutagenic and is not a developmental or reproductive toxicant. Carfentrazone-ethyl breaks down rapidly in the environment. While low levels of chemical residue may occur in surface and groundwater, risk concerns to non-target plants or animals are not expected. Carfentrazone-ethyl is considered to be practically non-toxic to birds on an acute and sub-acute basis. The chemical is moderately toxic to aquatic animals.

Chemical Characteristics - Technical Grade

Physical State - Viscous Liquid

Color - Yellow - Orange. Gardner No. 12

Odor - Faint petroleum odor

Melting Point - -22.1 C (onset of glass/liquid transition)

Density - 1.423 g/cm at 20 C

Solubility - water: 12 ug/ml(20C), 22 ug/ml(25C), 23ug/ml(30C); toulene: 0.9g/ml(20C),1.06 g/ml(25C), 1.2g/ml(30C); hexane: 0.03 g/ml(20C),0.05g/ml(25C),0.05g/ml (30C); miscible in all proportions with acetone, ethanol, ethyl acetate, methylene chloride

Vapor Pressure - 1.2 X 10^{-7} mmHg at 25 C
5.4 x 10^{-8} mmHg at 20 C

Dissociation Constant - Not Applicable

Octanol/Water Partition Coefficient - K_{ow} = 3.36

pH - 1% aqueous: 5.8, hydrolyzes

Toxicology Characteristics

Acute Toxicity - Carfentrazone-ethyl Technical

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
81-1	Acute Oral- Rats	43189027	LD_{50} >5000 mg/kg	4
81-2	Acute Dermal- Rats	43189209	LD_{50} >4000 mg/kg	3
81-3	Acute Inhalation- Rats	43189211	LC_{50} >5.09 mg/L	4
81-4	Primary Eye Irritation- Rabbits	43189214	Minimum eye irritant	3
81-5	Primary Skin Irritation- Rabbits	43189215	Non-irritant	4
81-6	Dermal Sensitization- Guinea pigs	43189217	Not a skin sensitizer	N/A

Acute Toxicity

- 50 DF Formulation

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
81-1	Acute Oral- Rats	43189208	LD_{50} >5000 mg/kg	4
81-2	Acute Dermal- Rats	43189210	LD_{50} >4000 mg/kg	4
81-3	Acute Inhalation- **Rats**	**43189212**	**LC_{50} >5.09 mg/L**	**3**
81-4	Primary Eye Irritation- Rabbits	43189214	Minimum eye irritant	3
81-5	Primary Skin Irritation- Rabbits	43189216	Slightly irritating	4
81-6	Dermal Sensitization- Guinea pigs	43189218	Not a skin sensitizer	N/A

- 40 DF Formulation

Guideline No.	**Study Type**	**MRIDs #**	**Results**	**Toxicity Category**
81-1	Acute Oral- Rats	44419010	LD_{50} >5000 mg/kg	4
81-2	Acute Dermal- Rats	44419011	LD_{50} >5000 mg/kg	4
81-3	Acute Inhalation- Rats	44419012	LC_{50} >5.72 mg/L	4
81-4	Primary Eye Irritation- Rabbits	44419013	Minimum eye irritant	3
81-5	Primary Skin Irritation- Rabbits	44419014	Slightly irritating	3
81-6	Dermal Sensitization- Guinea pigs	44419015	Not a skin sensitizer	N/A

Subchronic Toxicity

A 90-day subchronic feeding study was conducted in rats at intake levels of 0, 58, 226, 470, 831 and 1197 mg/kg/day for males and 0, 72, 284, 578, 1008 and 1427 mg/kg/day in females, respectively. The NOEL was 226 mg/kg/day in males and 284 mg/kg/day in females. The LOEL was 470 mg/kg/day in males and 578 mg/kg/day in females based on decreases in body weight, reductions in food consumption and histopathological lesions.

A 90-day subchronic feeding study was conducted in mice at dietary intake doses of 0, 143, 571, 1143, 2000 and 1857 mg/kg/day. The LOEL was 1143 mg/kg/day based on findings in the liver pathology. The NOEL was 571 mg/kg/day.

A 90-day subchronic feeding study in dogs administered by dietary admix doses of 0, 50, 150, 500 and 1000 mg/kg/day. The NOEL was 50 mg/kg/day and the LOEL was 150 mg/kg/day based on systemic toxicity (decrease in the rate of weight gain in females and an increase in porphyrin levels in both sexes).

Chronic Toxicity

A 1-year feeding study in dogs dosed at levels of 0, 50, 150, 500 and 1000 mg/kg/day in both sexes with a NOEL of 50 mg/kg/day and a LOEL of 150 mg/kg/day, based on an increase mean total urinary porphyrins.

An 18-month mouse carcinogenicity study was conducted in mice at dietary intake doses of 0, 10, 110 and 1090 mg/kg/day for males and 0, 12, 119 and 1296 mg/kg/day for females). The study found the compound to be noncarcinogenic to mice under the conditions of the study. The systemic NOEL was 70 ppm (equivalent to 10 mg/kg/day for males and 12 mg/kg/day for females), and the systemic LOEL was 700 ppm (equivalent to 110 mg/kg/day for males and 119 mg/kg/day for females) based on increased mortality and microscopic signs of hepatotoxicity.

A 2-year rat chronic toxicity/carcinogenicity study was conducted in rats at intake levels of 0, 2, 9, 37 and 188 mg/kg/day for males and 0, 3, 12, 49 and 242 mg/kg/day for females. The study found the compound to be noncarcinogenic to rats under the conditions of the study. The no-observed-effect level (NOEL) was 200 ppm (9 mg/kg/day) for males and 50 ppm (3 mg/kg/day) for females respectively and the lowest-observed-effect-level (LOEL) was 800 ppm (37 mg/kg/day) for males and 200 ppm (12 mg/kg/day) for females, based on liver histopathology and total urinary porphyrin

There was no evidence of carcinogenicity in this study.

Reproductive/Developmental Toxicity

A developmental toxicity study in rats was conducted in rats at dose levels of 0, 100, 600, and 1250 mg/kg/day in females, with a maternal LOEL of 600 mg/kg/day based on staining of the abdominogenital area and maternal NOEL of 100 mg/kg/day, and a developmental LOEL of 1250 mg/kg/day based upon a significant increase in the litter incidences of wavy and thickened ribs; and a developmental NOEL of 600 mg/kg/day.

A developmental toxicity study in rabbits was conducted at gavage dose levels of 0, 10, 40, 150 and 300 mg/kg/day. Evidence of treatment-related maternal toxicity consisted of unthriftiness and emaciation in tow does at 300 mg/kg/day. There were no treatment-related mortalities or gross pathological findings. No effects on body weight, body weight change, or organ weight data were identified at any treatment level. However, when considered in conjunction with the findings of the two pilot dose-setting studies, which were conducted at higher dose levels and which identified a steep dose-reponse curve with maternal mortality occuring at doses of 350 mg/kg/day and above, it was determined that 300 mg/kg/day provided an adequate high-dose assessment of maternal toxicity in rabbits. The maternal toxicity NOEL is greater than/equal to 150 mg/kg/day and maternal LOEL of 300 mg/kg/day. There was no evidence of treatment-related prenatal development toxicity, the developmental LOEL was not determined and the developmental NOEL is greater than/equal to 300 mg/kg/day.

A two-generation reproduction study in the rat at dietary levels of 0, 8.6, 42.4, 127, 343 mg/kg/day for males, and 0, 9.5, 47.8, 142, and 387 mg/kg/day for females established a parental NOEL for systemic and reproductive/developmental parameters of 127 mg/kg/day for males and 142 mg/kg/day for female. The parental LOEL for systemic and reproductive development parameters was 343 mg/kg/day for males and 387 mg/kg/day for females. There was no systemic toxicity demonstrated at dose levels of less than/equal to 1500 ppm. There were no treatment-related clinical signs of toxicity or increases in mortality at any dose levels. The offspring NOEL was 142 mg/kg/day and the LOEL was 387 mg/kg/day. The NOEL for reproductive toxicity was greater than/equal to 387 mg/kg/day; the highest dose tested. There were no clinical signs of toxicity reported for the pups of either generation.

Mutagenicity

Two reverse gene mutation assays (salmonella typhimurium) at dose yielded negative results, both with and without metabolic activation.

In vitro mammalian cell forward gene mutation assay in CHO cells yielded negative results both with and without activation.

In vitro chromosomal abberation assay yielded positive results under nonactivated conditions following doses of 3.75, 12.5, 37.5 and 125 ug/ml. There were consistent and statistically significant increased incidences of cells with aberrations at 125 ug/ml, the highest dose tested in the absence of metabolic activation.

In vivo mouse micronucleus cytogenic assay test was negative for clastogenic and/or aneugenic activity, following intraperitoneal injection doses of 600, 1200, and 2400 mg/kg . Dosed animals showed no reduction in the ratio of polychromatic erythrocytes to total erythrocytes. There was no evidence of polychromatic erythrocytes associated with exposure to the test material.

An unscheduled in vivo/in vitro DNA synthesis assay was negative following a single IP injection doses of 750, 1500, 3000 mg/kg. Slight lethargy was seen in the high dose animals. Higher levels (4000 mg/kg/) were lethal in a preliminary study. Cytotoxicity for the hepatocytes was not apparent at any dose. The results obtained with the positive controls confirmed the sensitivity of the test system to detect UDS. There was, however, no evidence that the test material induced agenotoxic response at any dose or sacrifice time.

Metabolism

A metabolism study in rats indicated that approximately 72.4 to 87% of the administered dose of carefentrazone-ethyl was rapidly absorbed and excreted in the urine within 24 hours after dosing. The major metabolites in both the urine and feces were F8426-chloropropionic acid (48.4 to 66.06%). The proposed metabolic pathway appeared to be the conversion of the parent compound by hydrolysis of the ester moiety to form F8426-chloropropionic acid, followed by oxidative hydroxylation of the methyl group to form 3-hydroxymethyl-F8426-chloropropionic acid, or dehydrochlorination to from F8426-cinnamic acid.

Environmental Characteristics

PARENT CARFENTRAZONE-ETHYL

STUDY TYPE	HALF LIFE/OTHER
Hydrolysis	3.6 hrs at pH9 8.6 days at pH 7 Stable at pH 5
Photolysis in Water	8 days
Aerobic Soil Metabolism	1.3 days
Anaerobic Aquatic Metabolism	0.3-0.8 days
Mobility-Aged Leaching	Immobile in loamy sand, sandy clay loam and silt loam soils Rapid breakdown of the compound in the soil
Terrestrial Field Dissipation	2 to 5 days

Mechanism of Pesticidal Action

Carfentrazone-ethyl (F8426 technical) is a post-emergence herbicide. This chemical controls weeds through the process of membrane disruption which is initiated by the inhibition of the enzyme protoporphyrinogen oxidase. In plants, this inhibition interferes with the chlorophyll biosynthetic pathway. In mammals, this inhibition interferes with the heme biosynthetic pathway

and results in alterations in hematological profiles and/or in increased urinary porphyrin levels and hepatotoxicity following long-term dosing.

Potential to Contaminate Groundwater

Carfentrazone-ethyl breaks down rapidly in the environment, while its degradates are persistent in aquatic and terrestrial environments. Because of its low application rate, Carfentrazone-ethyl residues are expected to occur at low levels in surface water and groundwater. These residues are not expected to trigger acute or chronic risk for non-target plants or animals.

Ecological Characteristics

Terrestrial

Carfentrazone-ethyl is practically non-toxic to the mallard duck and the bobwhite quail on an acute basis (LD_{50} >2,250 mg/kg) and practially non-toxic to the mallard duck and bobwhite quail on a sub-acute basis (LC_{50} ppm).

Aquatic - Freshwater

Carfentrazone-ethyl is moderately toxic to the rainbow trout (96-hour LC_{50} = 16 ppm) and to the bluegill sunfish (96-hour LC_{50} = 2.0ppm).

Aquatic - Estuarine/Marine

Carfentrazone-ethyl is moderately toxic to the eastern oyster (96-hour LC_{50}/EC_{50} = 2.05 ppm), to mysid shrimp (96-hour LC_{50}/EC_{50} = 1.16ppm), and to the tidewater silverside fish (LC_{50}/EC_{50} = 1.14ppm).

Plants

In terrestrial plant testing, the onion is the most sensitive plant with regard to seedling emergence (EC_{25}0.009 lb/A a.i.) and the tomato is the most sensitive in regard to vegetative vigor (EC_{25} 0.0012 lb/a.i.). On the basis of the NOEL's the radish and lettuce were most sensitive; both had vegetative vigor NOEL's of 0.0004 pounds a.i./A. Carfentrazone-ethyl is highly toxic to aquatic plants.

Position and Rationale

Available data provide adequate information to support the conditional registration of Carfentrazone-ethyl herbicide as a technical product, Aim 40DF and Aim 50DF herbicide, for use on wheat, corn, and soybeans.

Use, Formulation, Manufacturing Process or Geographic Restrictions:

Environmental Hazards

For Manufacturing-use products the following language should be stated: “Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or public waters unless this product is specifically identified and addressed in an NPDES permit. Do not discharge effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional office of the EPA.”

For End-Use Products the following language should be stated: “Carfentrazone-ethyl is very toxic to aquatic plants and moderately toxic to fish. Do not apply directly to water, to areas where surface water is present or to intertidal areas below the high water mark, except as specified on this label. Do not contaminate water when disposing of equipment washwaters.”

Spray drift advisory language is required for aerial application.

A 30 day plant-back interval is required for crops other than small grains.

5. Summary of Data Gaps

Residue Chemistry:

A field rotational trial with a small grain other than wheat.

Environmental Fate:

Aqueous photolysis study.

Ecological Effects:

Early life stage fish study.

6. Contact Person at EPA

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