United States
Environmental Protection
Agency

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

Pesticide Fact Sheet

Name of Chemical: Trifloxystrobin
Reason for Issuance: New Chemical Registration
Date Issued: September 20, 1999

DESCRIPTION OF CHEMICAL

CAS Name:	Benzeneacetic acid, (E,E)-alpha-(methoxyimino)-2-[[[[1-[3-(trifluoromethyl)phenyl]ethylidene]amino]oxy]methyl]-,methylester
CAS Registry No.:	141517-21-7
Chemical Class:	Beta-methoxyacryl ester(new)
Chemical Type:	Fungicide
Common Name:	Trifloxystrobin(ISO-proposed)
Other Names:	CGA-279202
Trade Names:	Trifloxystrobin Technical™; Flint™; Stratego™; Compass™
PC Code No.:	129112
Year of Initial Registration:	1999
U.S. and Foreign Producers:	Novartis Crop Protection, Inc.

TARGET PESTS

Trifloxystrobin works by interfering with respiration in plant pathogenic fungi. The site of action of strobilurin compounds is located in the mitochondrial respiration pathway. As a result of this mode of action, trifloxystrobin is a potent inhibitor of

fungal spore germination and mycelial growth. Trifloxystrobin is a broad-spectrum foliar fungicide that has high levels of activity against many fungal pathogens within the Ascomycete, Deuteromycete, Basidiomycete, and Oomycete classes. Pests controlled by this active ingredient include grape and cucurbit powdery mildew, apple scab and powdery mildew, peanut leafspot, and brown patch of turfgrasses.

USE PATTERNS AND FORMULATIONS

A water dispersible granular formulation is proposed for the three end-use products (Flint®, Compass® and Stratego®). All formulations will contain 50% active ingredient. Flint® is used on cucurbit vegetables, pome fruits and grapes (other than concord grapes). Stratego® is to be used on peanuts, (in a twin-pack with propiconozole). Compass® is intended for use on turfgrass (including residential sites), woody and herbaceous ornamentals.

SCIENCE FINDINGS

Summary Science Statements

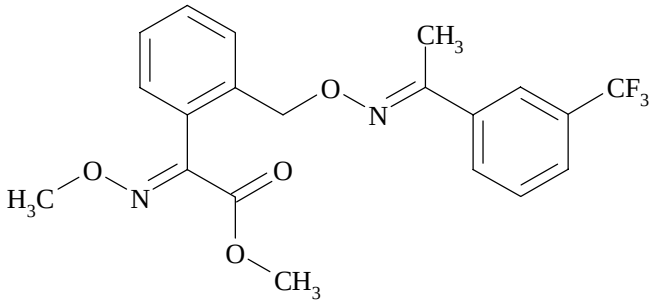
EPA finds that acute and chronic (non-cancer) aggregate risk and short- and intermediate-term occupational worker risk estimates for trifloxystrobin do not exceed EPA'S level of concern. EPA has concluded that there is a reasonable certainty that no harm will result to infants, children or adults from the use of trifloxystrobin on cucurbit vegetables, grapes, peanuts, pome fruits, turf, ornamentals, and imported bananas. EPA has established tolerances for residues of trifloxystrobin and its primary metabolite, CGA-321113 on these crops. A 12-hour REI is required to comply with the Agency's Worker Protection Standard, since the technical material is in acute Toxicity Category 3 and 4 and is a strong dermal sensitizer.

Chemical Characteristics

Mode of Action:	Interferes with respiration in plant pathogenic fungi.
Molecular Wt:	408.4
Appearance:	White, off-white powder
Melting Point:	72.9° C (pure active ingredient, PAI)
Boiling Point:	Not applicable; TGAI is a solid at room

	temperature
Vapor Pressure:	3.4×10^{-6} Torr (at 25° C, PAI)
Partition Coefficient:	log P_{ow} = 4.5 n-octanol/water at 25° C, PAI)log K_{oc} = 2709 (soil/water; "relatively immobile")
Solubility in Water:	0.610 mg/L (at 25° C, PAI)
pH:	7.7 at 25° C (1% w/w, aqueous dispersion)
Density:	1.36 g/ml(at 21° C, PAI)
Half-life:	Trifloxystrobin degrades rapidly with short half-life values (hours to days) in water and soils by mechanisms including metabolism, photolysis and hydrolysis

Chemical Structure:



Trifloxystrobin

Toxicology Characteristics

Trifloxystrobin has been classified as a "not likely human carcinogen". Subchronic and chronic toxicity studies demonstrated that the primary effects of trifloxystrobin occur in the liver and kidneys, at high doses. Prenatal developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility to in utero exposure to trifloxystrobin. There were no mutagenicity concerns from testing of trifloxystrobin.

Acute Toxicity Profile

(Trifloxystrobin Technical)

Acute Oral
Toxicity

(Rats):	LD_{50} > 5g/kg
Toxicity Category:	IV

Acute Dermal Toxicity (Rabbits):	LD_{50} > 2g/kg
Toxicity Category:	IV

Acute Inhalation Toxicity (Rats):	LC_{50} > 4.65 mg/L
Toxicity Category:	IV

Primary Eye Irritation Toxicity (Rabbits):	mild irritant
Toxicity Category:	III

Primary Skin Irritation Toxicity (Rabbits):	mild irritant
Toxicity Category:	IV

Dermal Sensitization Toxicity (Guinea pigs):	strong sensitizer

Toxicological Profile

EPA has evaluated the available toxicity data and considered its validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children. The results of

toxicity studies for trifloxystrobin are listed below:

1. Subchronic-Feeding study. Rat. The No Observed Adverse Effects Level (NOAEL) was 500 ppm (30.6-32.8 mg/kg/day). Decreased body weight, hypertrophy of hepatocytes and pancreatic atrophy were observed at the Lowest Observed Adverse Effects Level (LOAEL) of 2000 ppm (127-133 mg/kg/day).

2. Subchronic-Feeding study. Mouse. The NOAEL was 500 ppm (76.9-110 mg/kg/day). Increased liver weights and necrosis of hepatocytes were observed at the LOAEL of 2000 ppm (315-425 mg/kg/day).

3. Subchronic-Feeding study. Dog. The NOAEL was 30 mg/kg/day. Increased liver weight and hepatocyte hypertrophy in males were observed at the LOAEL of 150 mg/kg/day.

4. 28-Day Dermal Toxicity study. Rat. The NOAEL was 100 mg/kg/day. Increased liver and kidney weight were observed at the LOAEL of 1000 mg/kg/day.

5. Developmental Toxicity study. Rat. The maternal NOAEL was 10 mg/kg/day. Decreased body weight gain and food consumption were observed at the maternal LOAEL of 100 mg/kg/day. The developmental NOAEL was equal to or greater than 1000 mg/kg/day. No developmental effects were observed. The developmental LOAEL was equal to or greater than 1000 mg/kg/day.

6. Developmental Toxicity study. Rabbit. The maternal NOAEL was 10 mg/kg/day. Decreased body weights and body weight gain, food consumption and efficiency were observed at the maternal LOAEL of 50 mg/kg/day. The developmental NOAEL was 250 mg/kg/day. Skeletal anomolies were observed at the developmental LOAEL of 500 mg/kg/day.

7. Reproductive Toxicity study. Rat. The parental NOAEL was 50 ppm (3.8 mg/kg/day). Decreased body weight and weight gain, decreased food consumption, liver, kidney and spleen effects were observed at the parental LOAEL of 750 ppm (55.3 mg/kg/day). The reproductive NOAEL was 1500 ppm (110.6 mg/kg/day). The reproductive LOAEL was greater than 1500 ppm (110.6 mg/kg/day).

8. Chronic-Feeding study. Dog. The NOAEL was 5 mg/kg/day.

Increased clinical signs, increased liver weight and hepatocellular hypertrophy were observed at the LOAEL of 50 mg/kg/day.

9. Carcinogenicity study. Mouse. The NOAEL was 300 ppm (39.4 mg/kg/day). Liver effects were observed at the LOAEL of 1000 ppm (131.1 mg/kg/day).

10. Chronic Toxicity/ Carcinogenicity study. Rat. The NOAEL was 250 ppm (9.81-11.37 mg/kg/day). Decreased body weight and body weight gain were observed at the LOAEL of 750 ppm (29.7-34.5 mg/kg/day).

11. Gene Mutation study. Salmonella. Negative.

12. Gene Mutation study. Chinese Hamster Cultured V-79. Positive.

13. Structural Chromosome Aberration -Micronucleus study. Mouse. Negative.

14. Structural Chromosome Aberration -Cytogenetics study. Chinese Hamster. Negative.

15. DNA Repair study-hepatocytes. Rat. Negative.

16. Acute Oral Neurotoxicity study. Rat. The NOAEL and LOAEL could not be determined.

17. Metabolism study. Rat. The tissue half-lives ranged from 13 to 42 hours. The highest residues were found in liver, kidneys, spleen and blood. The parent compound was extensively metabolized to approximately 35 metabolites.

FOOD QUALITY PROTECTION ACT (FQPA) CONSIDERATIONS

For food only, the theoretical maximum residue concentration (TMRC) occupied no more than 17% of the chronic population adjusted dose (PAD) and 1% of the acute PADs for any one population subgroup. For drinking water, the estimated

concentrations in water were far below the drinking water levels of comparison (DWLOC) for both acute and chronic risk. There are no uses of the chemical by homeowners, but there will be use of trifloxystrobin on residential lawns and ornamentals by professional applicators. This would result in short and intermediate term exposures for applicators and homeowners. The short and intermediate term post application residential risk estimates do not exceed EPA's level of concerns since margins of exposure (MOE) ranged from 430 to 15 million.

FQPA provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for pre-and post-natal toxicity and the completeness of the database unless EPA determines that a different margin of safety will be safe for infants and children. Based on developmental and reproductive data for trifloxystrobin, EPA determined that an additional 10x safety factor for the protection of infants and children (as required by FQPA) should be removed. The rationale for removing the 10x factor is as follows (1) The toxicology database is complete for FQPA assessment; (2) There is no indication of increased susceptibility of rat or rabbits to trifloxystrobin. In the developmental and reproductive toxicity studies, effects in the fetuses/offspring were observed only at or above treatment levels which resulted in evidence of parental toxicity; (3) It was determined that a developmental neurotoxicity study in rats is not required; (4) The exposure assessments will not underestimate the potential dietary (food and drinking water) or nondietary exposures for infants and children from the use of trifloxystrobin. It was concluded that the aggregate risk does not exceed EPAs level of concern.

FOOD TOLERANCES

Tolerances are recommended for the combined residues of the fungicide trifloxystrobin and its metabolite CGA-321113, in or on cucurbit vegetables at 0.50 parts per million (ppm), grapes at 2.0 ppm, raisins at 5.0 ppm, peanuts at 0.05 ppm, peanut hay at 4.0 ppm, pome fruit at 0.50 ppm, wet apple pomace at 5.0 ppm, milk at 0.02 ppm, meat, fat and meat by products of cattle, goats, hogs, horses and sheep at 0.05 ppm, and imported bananas at 0.10 ppm.

OCCUPATIONAL AND RESIDENTIAL EXPOSURE

A 12-hour REI is required to comply with the Agency's Worker Protection Standard, since the technical material is in acute Toxicity Category 3 and 4 and is a strong dermal sensitizer. Use of trifloxystrobin on residential lawns and ornamentals by professional applicators will result in short and intermediate term exposures. The short and intermediate term post application residential risk estimates do not exceed EPAs level of concerns since MOEs ranged from 430 to 15 million. Post application occupational risks range from 104-4,400. The Agency concluded that the aggregate risk does not exceed EPAs level of concern

ENVIRONMENTAL FATE CHARACTERISTICS

Trifloxystrobin is expected to degrade rapidly (hours to days) in most soil and aquatic environments. The free form of the acid metabolite, CGA-321113, appears to be a mobile and persistent metabolite that can be further degraded but at a slower rate than the parent compound.

ECOLOGICAL EFFECTS

Avian Acute Oral and Dietary Toxicity

Species	% ai	Toxicity value	Toxicity category
Northern bobwhite	96.4	acute oral LD50 >2000[1] mg/kg body wt	practically nontoxic
		dietary LC50 >5050[2] ppm	practically nontoxic
Mallard	96.4	acute oral LD50 >2250[1] mg/kg body wt	practically nontoxic
		dietary LC50 >5050[1] ppm	practically nontoxic

[1] no mortality reported

[2] all birds found dead showed evidenced of pecking upon necropsy, and mortality was not considered to be treatment related

Avian Reproduction

Species	% ai	NOEC (ppm)	LOEC (ppm)	Affected endpoints
Northern bobwhite	96.4	320	>320 max. level tested	none
Mallard	96.0	500	>500 max. level tested	none

Nontarget Insect Acute Contact Toxicity

Species	% ai	LD50 (*u*g/bee)	Toxicity category
Honey bee	96.4	>200[1]	practically nontoxic

[1] no mortality reported

Freshwater Fish and Invertebrate Acute Toxicity Under Flow-through Conditions

Species	% ai	LC50 (ppm)	Toxicity category
Rainbow trout	96.4	0.014	very highly toxic
(degradate test)	97 (CGA-321113)	>106	practically nontoxic
Bluegill sunfish	96.4	0.054	very highly toxic
Water flea	96	0.025	very highly toxic
(degradate test)	97 (CGA-321113)	>95.3	practically nontoxic

[1] insufficient number of test organisms

Fish Early Life-Stage and Invertebrate Life-Cycle Toxicity Under Flow-through Conditions

Species	% ai	NOEC (ppb)	LOEC (ppb)	Affected endpoints
Rainbow trout	96.4	4.3	7.7	survival
Water flea	96.4	2.8	5.9	survival, reproduction

Estuarine/Marine Fish and Invertebrate Acute Toxicity Under Flow-through Condition

Species	% ai	LC50 or EC50 (ppb)	Toxicity category
Sheepshead minnow	96	78	very highly toxic
Mysid shrimp	96	8.62	very highly toxic
Eastern oyster (shell deposition)	96	29.3	very highly toxic

The above tests indicate that trifloxystrobin affects aquatic organisms at low concentrations. However, trifloxystrobin is not expected to occur in surface waters at concentrations high enough to be risky to aquatic organisms with the possible exception of estuarine invertebrates with similar sensitivity as mysid shrimp.

Nontarget Terrestrial Plant Seedling Emergence and Vegetative Vigor Toxicity (Tier I)[1]

Species	Seedling emergence		Vegetative vigor	
	Endpoint[2]	% inhibition	Endpoint[2]	% inhibition
Monocots:				
Corn	dry weight	6	none	0
Oat	dry weight	3	none	0
Onion	shoot length	3	none	0
Ryegrass	emergence	7	dry weight	9
Dicots:				
Cabbage	dry weight	13	dry weight	9
Soybean	shoot length	2	dry weight	1
Carrot	none	0	shoot length	4
Cucumber	shoot length	4	shoot length	7
Lettuce	none	0	none	0
Tomato	shoot length	3	dry weight	10

[1] MRID no. 444967-23 (supplemental); 50.3% ai; application rate = 0.249 lb ai/A
[2] only the most sensitive endpoint is tabulated

Nontarget Aquatic Plant Toxicity (Tier II)

Species	% ai	EC50 (ppb)	NOEC (ppb)
Vascular species:			
Duckweed	96	>1,930	410
Nonvascular species:			
Green algae	96	37	10
(degradate test)	98.2 (CGA-321113)	78,800	16,200

[1] the test solution was not renewed as it should have been for an unstable chemical
[2] a definite LC50 could not be determined

Trifloxystrobin is not considered to be a risk to birds, mammals, and honey bees, because of its low toxicity. There is no presumed risk for either terrestrial or aquatic plants. Trifloxystrobin has been classified as being highly toxic to fish and aquatic invertebrates; however, because of relatively low exposure concentrations in water, the risk to fish and invertebrates is

low. There is a possibility of some effects to estuarine invertebrates, but the exposure is uncertain and this risk is lower than the risk from registered alternatives.

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