Regulatory Note REG2004-03

Trifloxystrobin

The active ingredient trifloxystrobin and associated end-use products (EPs) Compass 50 WG, Flint 50 WG and Stratego 250 EC (containing the fungicides trifloxystrobin and propiconazole) have been granted temporary registration under Section 17 of the Pest Control Products (PCP) Regulations for the control of selected diseases caused by fungal pathogens on turfgrass, ornamentals, grapes, pome fruit group (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince), wheat (winter, spring, hard red, durum, Canada prairie, soft white), spring barley and oats. The food residue data, submitted to support registration of the technical grade active ingredient (TGAI) and its associated EPs related to food uses, are in addition to the residue chemistry data previously submitted to support the recommendation of maximum residue limits (MRLs) in/on imported almonds, cucurbit vegetable group [balsam apple, balsam pear, cantaloupe, chayote, cucumber, cucumber (Chinese), gherkin (West Indian), gourd (edible), melon, melon (citron), muskmelon, pumpkin, squash, squash (summer, winter), watermelon and waxgourd (Chinese)], fruiting vegetable group (chili, eggplant, groundcherry, pepino, pepper, pepper [bell, non-bell, non-bell (sweet)], tomatillo and tomato), grapes, hops, pome fruit group (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince), potatoes, sugar beets and wheat.

This Regulatory Note provides a summary of data reviewed and the rationale for the regulatory decision for these products.

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Foreword

Health Canada's Pest Management Regulatory Agency (PMRA) has issued a temporary registration for trifloxystrobin and the associated end-use products Compass 50 WG, Flint 50 WG and Stratego 250 EC (containing the fungicides trifloxystrobin and propiconazole), for the control of selected diseases caused by fungal pathogens on turfgrass, ornamentals, grapes, pome fruit group (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince), wheat (winter, spring, hard red, durum, Canada prairie, soft white), spring barley and oats. The food residue data, submitted to support registration of the TGAI and its associated EPs related to food uses, are in addition to the residue chemistry data previously submitted under submission 1999-1220 to support the recommendation of MRLs in/on imported almonds, cucurbit vegetable group [balsam apple, balsam pear, cantaloupe, chayote, cucumber, cucumber (Chinese), gherkin (West Indian), gourd (edible), melon, melon (citron), muskmelon, pumpkin, squash, squash (summer, winter), watermelon and waxgourd (Chinese)], fruiting vegetable group (chili, eggplant, groundcherry, pepino, pepper, pepper [bell, non-bell, non-bell (sweet)], tomatillo and tomato), grapes, hops, pome fruit group (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince), potatoes, sugar beets and wheat.

Methods for analysing trifloxystrobin environmental media are available to research and monitoring agencies upon request to the PMRA.

Bayer CropScience Inc. will be carrying out additional supervised residue trials, environmental toxicity, chemistry and fate studies and efficacy trials as a condition of temporary registration. Following the review of this information, the PMRA will publish a proposed registration decision document (PRDD) and request comments from interested parties before proceeding with a final regulatory decision.

A summary of the Agency's findings in support of this decision is found in this Regulatory Note.

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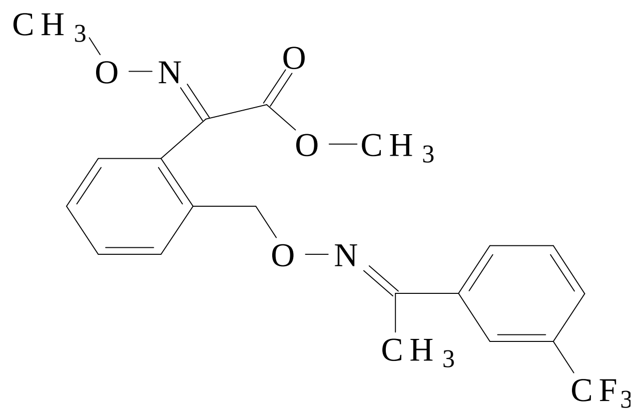
1.0 The active substance, its properties and uses

1.1 Identity of the active substance and impurities

Active substance	Trifloxystrobin
Function	Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	methyl (*E*)-methyoxyimino-{(*E*)-α-[1-(α,α,α-trifluoro-m-tolyl)ethylideneaminooxy]-o-tolyl}acetate
2. Chemical Abstracts Service (CAS)	methyl (*E*,*E*)-α-(methoxyimino)-2-[[[[1-[3-(trifluoromethyl)phenyl]ethylidene]amino]oxy]methyl] benzeneacetate
CAS number	141517-21-7
Molecular formula	$C_{20}H_{19}F_3N_2O_4$
Molecular weight	408.38
Structural formula	
Nominal purity of active	98.0% (Limits 96.0%, 100%)
Identity of relevant impurities of toxicological, environmental or other significance	The technical grade trifloxystrobin does not contain any impurities or microcontaminants known to be Toxic Substances Management Policy (TSMP) Track 1 substances

1.2 Physical and chemical properties of active substances and end-use products

Technical product: Trifloxystrobin

Property	Result	Comment
Colour and physical state	White to off-white solid (powder)	
Odour	Odourless to slightly sweet	
Melting point or range	72.9°C	
Boiling point or range	Approximately 312°C. Thermal decomposition begins about 285°C	
Density	1.36 g/mL	
Vapour pressure at 25°C	3.4×10^{-6} Pa by extrapolation	Relatively non-volatile.
Henry's Law constant at 20°C	$K = 2.25 \times 10^{-8}$ atm m^3/mol $1/H = 1.09 \times 10^{6}$	Non-volatile under field conditions from water and moist soil surfaces.
Ultraviolet (UV)–visible spectrum	λmax ϵ Methanol: 250 17 500 90% MeOH: +10% HCl 250 17 300 +10% NaOH 252 15 800 No absorption between 340 and 750 nm.	Minimal phototransformation is expected under natural environment.
Solubility in water at 25°C	0.61 mg/L	Low solubility.

Property	Result	Comment
Solubility in organic solvents at 25°C	Solvent — g/L methanol 76 acetone > 500 ethyl acetate > 500 n-hexane 11 dichloromethane > 500 toluene 500 n-octanol 18	
Octanol–water partition coefficient (K_{ow})	log K_{ow} = 4.5 at 25°C	Potential to bioaccumulate
Dissociation constant (pK_a)	No dissociation constant in the pH range 2–12.	
Stability (temperature, metal)	No thermal effect observed between room temperature and the melting point. The product is compatible with stainless steel, galvanized sheet metal, tin plate and polyethylene. Iron steel shows a slight corrosion but no weight loss.	

End-use products: Flint 50 WG and Compass 50 WG (Identical Products), Stratego 250 EC

Property	Flint 50 WG and Compass 50 WG	Stratego 250 EC
Colour	Gray to beige	Yellow
Odour	Weak, indeterminate	Moderately sweet
Physical state	Solid	Liquid
Formulation type	Wettable granule	Emulsifiable concentrate
Guarantee	Trifloxystrobin 50% (limits 48.5–51.5%)	Trifloxystrobin 125 g/L (limits: 118–132 g/L) Propiconazole 125 g/L (limits: 118–132 g/L)

Property	Flint 50 WG and Compass 50 WG	Stratego 250 EC
Formulants	The product does not contain any USEPA List 1 or List 2 formulants or formulants known to be TSMP Track 1 substances.	The product does not contain any USEPA List 1 or List 2 formulants or formulants known to be TSMP Track 1 substances.
Container material and description	Polyethylene bottle	Plastic 5L, 10L and 20L jugs
Bulk density	0.597 g/cc	1.098 g/cc
pH of 1% dispersion in water	9.7	4.2
Oxidizing or reducing action	Does not contain any oxidizing or reducing substances.	Does not contain any oxidizing or reducing substances.
Storage stability	No change after 2 years storage at 20°C.	No change after 2 years storage at 20°C in commercial packing.
Explodability	Not explosive	Not explosive

1.3 Details of uses

Trifloxystrobin is a new active ingredient in the strobilurin class of fungicides, which acts by obstructing electron transfer in mitochondria of fungal cells. This obstruction will inhibit spore germination and germ tube extension, preventing infection. Trifloxystrobin is to be formulated as three fungicide end-use products.

Compass 50 WG (50% trifloxystrobin) is to be used for control of brown patch, leaf spot and gray leaf spot on turf, as a drench for Rhizoctonia root rot of various container ornamentals, both indoor and outdoor, and as a foliar spray to control powdery mildew and scab on outdoor ornamental trees. Flint 50 WG (50% trifloxystrobin) is to be applied as a foliar spray to control powdery mildew and black rot of grapes, scab, sooty blotch, fly speck, powdery mildew and cedar apple rust of pome fruit (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince) as well as rust, powdery mildew, Septoria leaf blight and tan spot of wheat (including winter, spring, hard red, durum, Canada prairie and soft white). Stratego 250 EC (125 g/L trifloxystrobin plus 125 g/L propiconazole) is for foliar application to cereals to control Septoria leaf blotch, tan spot, powdery mildew, leaf rust, stem rust and stripe rust of wheat (including winter, spring, hard red, durum, Canada prairie and soft white), net blotch, scald and Septoria leaf blotch of spring barley as well as Septoria leaf blotch and crown rust of oats.

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

Product	Analyte	Method type	Linearity range	Recovery (%)	RSD (%)	LOQ (%)	Method
Technical	Trifloxystrobin	GC-FID	50–150%	100	0.225	Waived	Accepted
Technical	Major impurities	HPLC	0.1–1.0%	69–115	0.3–13.3	< 0.1	Accepted

2.2 Analytical methods for formulation analysis

Product	Analyte	Method ID	Method type	Linearity range	Mean recovery (%) (n)	RSD (%) (n)	Method
Flint 50 WG and Compass 50 WG	Trifloxystrobin	AF-1185/1	GC-FID	50–150%	101.1% (6)	0.156 (10)	Accepted
Stratego 250 EC	Trifloxystrobin	AF-1225/1	GC-FID	1.0–3.0 mg/mL	98.2 (3)	0.67 (5)	Accepted
	Propiconazole				99.3 (3)	0.73 (5)	Accepted

2.3 Methods for environmental residue analysis

Matrix	Method code	Method type	Analyte	LOQ	Mean % recovery	Mean % RSD	Method
Soil	AG-683	HPLC-MS	CGA-373466	10 ppb	88–110	4.2	Accepted
			CGA-321113		94–107	3.3	
			CGA-357261		90–103	3.8	
			CGA-279202		87–101	4.7	
			CGA-357262		84–103	6.1	
			CGA-331409		80–102	6.1	
Sediment	AG-688	HPLC-MS	CGA-373466	2 ppb	96–114	3.7	Accepted
			CGA-321113		92–113	2.9	
			CGA-357261		102–112	2.5	
			CGA-279202		92–104	3.9	
			CGA-357262		97–104	4.1	
			CGA-331409		98–105	4.9	

Matrix	Method code	Method type	Analyte	LOQ	Mean % recovery	Mean % RSD	Method
Water	AG-688	HPLC-MS	CGA-373466	0.1 ppb	82–112	3.1	Accepted
			CGA-321113		80–110	3.2	
			CGA-357261		96–117	4.4	
			CGA-279202		88–116	4.8	
			CGA-357262		91–115	4.8	
			CGA-331409		97–120	5	
Biota	The information submitted under section 2.4 addresses the analytical methodology requirements for biota (plant and animal matrices).						Accepted

2.4 Methods for residue analysis

Based on the plant (apple, cucumber and wheat) and animal (lactating goat and laying hen) metabolism studies, the residue of concern (ROC) for enforcement purposes was defined as the parent, trifloxystrobin, and the free form of its acetic acid metabolite, CGA-321113.

The analytical method AG-659A, proposed for data gathering and enforcement purposes, involves extraction with ACN:water (80:20, v:v) followed by a three-layer liquid-liquid partition with a saturated aqueous sodium chloride solution, toluene and hexane. The toluene layer is collected, partitioned with hexane and evaporated. Residues are reconstituted in 0.085% phosphoric acid:acetone (95:5, v:v) and cleaned up on a C-18 solid phase extraction column eluted with 0.085% phosphoric acid:acetone (30:70, v:v). Acetone is removed by evaporation and the eluate is partitioned into methyl tert-butyl ether (MTBE):hexane (1:1, v:v). The eluate is concentrated and residues are redissolved in 0.1% polyethylene glycol in acetone prior to analysis and quantitation by gas chromatography with nitrogen phosphorous detector (GC/NPD). The method limit of detection (LOD) for each of the analytes, trifloxystrobin and CGA-321113, was 0.08 ng injected on column. The reported limit of quantitation (LOQ) is 0.02 ppm for each analyte in all matrices except milk (0.01 ppm) and peanut hay (0.05 ppm). Procedural method validation indicated that, at spiking levels of 0.02–1.0 ppm, this method was found to give good mean recoveries of 72–112% with standard deviations ranging from 6 to 20% for trifloxystrobin and mean recoveries of 70–128% with standard deviations ranging from 6 to 20% for CGA-321113 in animal matrices. For plant commodities, mean recoveries were good, ranging from 83 to 108% with standard deviations of 2–23% for trifloxystrobin and 71–110% with standard deviations of 3–20% for CGA-321113, when spiked at 0.02–10.0 ppm. Good linearity was observed for trifloxystrobin (correlation coefficient, r = 0.99788) and CGA-321113 (correlation coefficient, r = 0.99996), in the range of 0.04–0.5 ng/µL. The control chromatograms generally had no peaks above the chromatographic background and the spike sample chromatograms contained only the analyte peaks. The peaks appeared well defined and symmetrical with no apparent carryover to the following chromatograms.

An independent laboratory method validation (ILV) was conducted to verify the reliability and reproducibility of Method AG-659, for the determination of trifloxystrobin and the acid metabolite in various plant and animal matrices. When incorporating the conditioning of the GC column with control matrix, the method trials for the determination of the two analytes were successful.

While the ILV was conducted on method AG-659, the method recommended for enforcement of trifloxystrobin per se in all subject plant or animal commodities is method AG-659A, which supercedes AG-659. Compared to AG-659, AG-659A also includes extractability and accountability results from the radiovalidation study using animal matrices as well as minor changes and ILV study suggestions to improve the ruggedness of the method.

According to the extraction efficiency data provided, the analytical method AG-659A was not successfully validated for meat as it was not capable of extracting all the radioactivity. As indicated in the lactating goat metabolism study, the extraction of liver with ACN and ACN:water released an average of 68%; however, microwave assisted extraction released an additional 29% of the total radioactive residues (TRRs). Based on the results of the radiovalidation study and the ruminant metabolism study, a microwave extraction step should be included in the enforcement analytical method AG-659A for animal matrices to ensure that the majority of the residues are extracted. Subsequently, validation of the microwave extraction step, at spiking levels equivalent to the LOQs of 0.01 ppm (milk), 0.02 ppm (all other animal matrices), 0.04 ppm (2 × 0.02 ppm), 0.10 ppm (5 × 0.02 ppm) and 0.20 ppm (10 × 0.02 ppm) should be conducted. Nevertheless, accountability results appeared consistent with the results obtained in the metabolism studies for apples and cucumbers.

This GC/NPD analytical method AG-659A was determined to be acceptable for the quantitation of the combined residues of trifloxystrobin and CGA-321113 and therefore can be supported as a data gathering and enforcement method for plant matrices only. The expansion of this analytical method to animal matrices will require the inclusion of a microwave extraction step to ensure adequate extraction of the residues.

3.0 Impact on human and animal health

3.1 Integrated toxicological summary

A detailed review of the toxicology database available for trifloxystrobin has been completed. Data submitted were, for the most part, complete and comprehensive, and included the full battery of studies currently required for registration purposes. Studies were conducted in conformance with currently acceptable international testing protocols. The scientific and regulatory quality of the toxicology database is considered sufficient to generally define the toxicity of this chemical.

Trifloxystrobin was moderately absorbed from the gastrointestinal tract and rapidly distributed. In the low-dose group, approximately 56% and 65% administered dose (AD) was absorbed in males and females respectively (based on the total recovery from urine, feces, bile and tissues), with 41 and 47% being in bile of males and females, respectively. In the high-dose, group, the degree of absorption was 41 and 27%, while the bile content was 35% and 19%, respectively for males and females. The blood kinetics revealed a moderate absorption rate in both sexes with two peaks (after 0.5 and 12 hours at the low dose and 12 and 24 hours at the high dose). The highest residues were found in blood, kidneys, spleen and liver and were comparable between sexes.

Excretion of the radioactivity was rapid. Approximately 85–96% of the dose was excreted within 48 hours. The route of elimination was influenced by the sex of the animals, females eliminated twice the amount with the urine than males, accounting for 27–42% and 12–19% of the dose, respectively. The amounts excreted via feces were 79–82% and 56–64% of the dose in males and females, respectively. In both sexes biliary excretion was the major route of elimination. The involvement of an enterohepatic shunt mechanism in the elimination process is indicated.

About 35 metabolites were isolated from urine, feces and bile and identified. The major route in the metabolic pathway is hydrolysis of the methyl ester to the acid, O-demethylation of the methoxyimino group yielding a hydroxyimino compound and oxidation of the methyl side chain to a primary alcohol followed by partial oxidation to the respective carboxylic acid. The oxidation of the methyl side chain to a primary alcohol was more pronounced in female rats resulting in sex-specific major metabolites. About 4–7% and 31–47% of the low and high dose respectively were eliminated in the feces as unchanged parent compound. This reflected the different extent of absorption at the two dose levels. Overall, the major metabolic pathways were significantly influenced by the sex of the animals but not by the dose level and pretreatment.

Technical trifloxystrobin was considered to be of low acute toxicity by the oral route in mice and rats, by the dermal route in rabbits and inhalation route in rats. It was mildly irritating to the skin and the eyes of rabbits. Results of skin sensitization testing using guinea pigs, employing the Buehler method were negative, but the test compound was a potential skin sensitizer by the Maximization test.

Acute oral toxicity studies with 2 metabolites (CGA-373466 and NOA 414412) and with the isomer (Z,E) indicated the low acute toxicity of these compounds.

Stratego 250 EC appeared to be of low acute oral, dermal and inhalation toxicity. The product is severely irritating to eyes and slightly irritating to skin. The test material is a skin sensitizer.

Flint 50 WG appeared to be of low acute oral, dermal and inhalation toxicity. The product is mildly irritating to eyes and slightly irritating to skin. The test material is a skin sensitizer.

Compass 50 WG appeared to be of low acute oral, dermal and inhalation toxicity. The product is mildly irritating to eyes and slightly irritating to skin. The test material is a skin sensitizer.

In subchronic repeat dosing studies in mice, rats and dogs, the most common indicators of toxicity were reduced body-weight gain and food consumption (associated with vomiting and diarrhea in dogs), increased liver weight and altered clinical chemistry parameters indicative of an effect on the liver which was identified as a target organ for trifloxystrobin. The effects on the liver included single cell necrosis (mice only) and hepatocellular hypertrophy. In addition, mice had extramedullary hematopoiesis and hemosiderosis in the spleen. The male rats were more sensitive to the toxic effect of trifloxystrobin than females.

Repeated dermal administration to rats over 28 days was tolerated by females without any local or systemic reactions at a limit dose of 1000 mg/kg bw/day. Increased liver and kidney weights were observed in males of the high-dose group.

In chronic toxicity studies, the liver appears to be the primary target organ in dogs and mice, but not in rats. This was indicated by increased liver weights, hepatocellular hypertrophy and single cell necrosis (mice).

In the one-year dog study, the no observed adverse effect level (NOAEL) of 5.0 mg/kg bw/day was set based on the clinical signs (vomiting, diarrhea), reduced body-weight gain and food consumption, increased relative liver weights, hepatocellular hypertrophy and the changes in blood chemistry parameters (decreased plasma albumin, increased alkaline phosphatase) indicating affected liver function.

In the mouse carcinogenicity study, the NOAEL was set at 36 mg/kg bw/day, based on increased liver weight, single cell necrosis and/or necrosis in the liver and increased incidence of hepatocellular hypertrophy.

In the rat chronic/carcinogenicity study, the NOAEL of 11.0 mg/kg bw/day was set based on the reduction in body-weight gain in both sexes, decreased food consumption and slightly increased incidence of developmental cyst in pituitary gland and angiomatous hyperplasia of the mesenteric node in males. An effect on the liver (increased relative weight) was seen only in females at the highest dose level of 73 mg/kg bw/day.

Genotoxicity studies indicated that trifloxystrobin is not mutagenic in both in vitro (reverse mutation assay, cytogenic and clastogenic assays) and in vivo assay (mice micronucleus test).

Trifloxystrobin was not a reproductive toxicant. The NOAEL for reproductive effects was set at the highest dose level of 110 mg/kg bw/day. The parental NOAEL was 3.8 mg/kg bw/day, based on decreased body weight, food consumption, histopathological changes in liver (hepatocellular hypertrophy) and kidneys (slightly increased incidence of minimal pigmentation of renal tubules) observed at 55 mg/kg bw/day. The offspring NOAEL was also 3.8 mg/kg bw/day, based on decreased body weight of F_{1a}, F_{1b} and F_2 pups during lactation days 7, 14 and 21 at 55 mg/kg bw/day. An increase in time of eye opening was seen at dose level of 110 mg/kg bw/day.

No teratogenic effects were observed in either rats or rabbits exposed to trifloxystrobin via oral gavage. The NOAEL for maternal toxicity was 10 mg/kg bw/day either for rats and rabbits, based on decreased body weight and food consumption. The NOAEL for developmental toxicity in rats was 100 mg/kg bw/day, based on increased incidence of enlarged thymus. The NOAEL for developmental toxicity in rabbits was 250 mg/kg bw/day based on increased incidence of skeletal abnormalities (fused sternebrae 3 and 4) at 500 mg/kg bw/day.

There was no evidence of increased sensitivity to trifloxystrobin in young animals in a rat reproduction study and in rat or rabbit developmental studies. The adverse effects in the pups or fetuses were observed at maternally toxic doses.

Trifloxystrobin was not selectively neurotoxic following acute gavage or subchronic dietary administration in rats. The acute NOAEL for neurotoxicity is 2000 mg/kg bw/day, and the subchronic NOAEL is 127 mg/kg bw/day. No clinical signs, neurobehavioural effects or pathology of neurological tissues were observed at an acute limit dose of 2000 mg/kg bw/day or following subchronic dietary administration up to and including 127 mg/kg bw/day.

3.2 Toxicological endpoint for assessment of risk following long-term exposure—ADI

The recommended acceptable daily intake (ADI) for trifloxystrobin is 0.038 mg/kg bw/day. The most appropriate study for selection of toxicity endpoints for chronic dietary exposure was a two-generation reproduction study in rats with a NOAEL of 3.8 mg/kg bw/day for both parental and offspring toxicity. This was based on treatment-related reduced body weight/body-weight gain and food consumption, and increased incidence of liver and kidney effects observed in parental animals, and decreased pup body weight during lactation. A total uncertainty factor (UF) of 100 is required to account for standard uncertainty factors of 10× for interspecies extrapolation and 10× for intraspecies variation.

$$\mathbf{ADI = \frac{NOAEL}{UF} = \frac{3.8\ mg/kg\ bw/day}{100} = 0.038\ mg/kg\ bw/day}$$

This ADI provides a margin of safety (MOS) equal to 6579-fold the NOAEL of 250 mg/kg bw/day for developmental study in rabbits.

3.3 Toxicological endpoint for assessment of risk following acute dietary exposure—acute reference dose (ARfD)

No toxicological endpoint attributable to a single oral dose was identified in the available toxicity studies on trifloxystrobin that would be attributable to females (13–50 years) or to general population (including infants and children).

3.4 Toxicological endpoint for assessment of occupational, residential and bystander risks

Farmers, custom applicators, lawn care operators, golf course and sod farm workers, and nursery and greenhouse operators have potential for exposure during application of end-use products containing trifloxystrobin over a short- to long-term duration via the dermal and inhalation routes. Following application, agricultural, golf course, sod farm, nursery and greenhouse workers and adults and children in residential and recreational settings have potential for short- to long-term exposure to trifloxystrobin residues from entering treated areas via the dermal and oral route. Duration and route-specific toxicological endpoints selected for the risk assessments are outlined below:

Short-term oral exposure, 1–30 days (children)
The endpoint for short-term oral exposure in children is based on a NOAEL of 16.5 mg/kg bw/day observed in a 28-day oral study in rats. At the higher dose level of 84.4 mg/kg bw/day a significant decrease in body-weight gain was observed. The target MOE for this scenario is 100 (10× for intraspecies extrapolation and 10× for intraspecies variation).

Short-term dermal exposure, 1–30 days (adults and children)
The endpoint for short-term dermal exposure is based on a NOAEL of 100 mg/kg bw/day established in the 28-day dermal study in rats. At the next highest dose, 1000 mg/kg bw/day, treatment-related increases in absolute and relative liver and kidney weights were observed. The target MOE for this scenario is 100 (10× for intraspecies extrapolation and 10× for intraspecies variation).

Intermediate-term and long-term dermal exposure, 1–>6 months (adults)
Two-generation reproduction study in rats was selected for the endpoint for intermediate- and long-term dermal exposure. The NOAEL of 3.8 mg/kg bw/day based on treatment-related reduction in body weight/body weight gain, food consumption and increased incidence of liver (hepatocellular hypertrophy) and kidney (pigmentation of renal tubule) effects observed in parental animals and decreased body weight in pups during the lactation periods (both generations). The target MOE is 100 (10× for intraspecies extrapolation, 10× for intraspecies variation).

Dermal absorption

An appropriate dermal toxicity study for intermediate and long-term dermal absorption is not available for use in the risk assessment, nor was a dermal absorption study submitted. A default dermal absorption value of 50% was selected for use in the risk assessment based on a comparison of dermal and oral toxicity and physical–chemical properties of trifloxystrobin. An increase in liver weights of male rats was observed at 337 mg/kg/day in the 28-day oral rat study and at 1000 mg/kg/day in 28-day dermal rat study. By dividing the effect level from the oral study by the dermal one, an apparent dermal absorption value of 33% is obtained. This is a crude estimate of dermal absorption potential and thus cannot be used quantitatively. Based on the K_{ow} of 4.5, trifloxystrobin should migrate easily into the lipophilic stratum corneum. However, movement into hydrophilic systemic component should be inhibited by its highly lipophilic properties.

Short-term inhalation exposure, 1–30 days (adults)

The endpoint for short-term inhalation exposure is based on a NOAEL of 16.5 mg/kg bw/day observed in a 28-day oral study in rats. At the higher dose level of 84.4 mg/kg bw/day a significant decrease in body-weight gain was observed. The target MOE for this scenario is 100 (10× for intraspecies extrapolation and 10× for intraspecies variation).

Intermediate-term and long-term inhalation exposure, 1–>6 months (adults)

Two-generation reproduction study in rats was selected for the endpoint for intermediate-term inhalation exposure. The NOAEL of 3.8 mg/kg bw/day based on treatment-related reduction in body weight/body-weight gain, food consumption and increased incidence of liver (hepatocellular hypertrophy) and kidney (pigmentation of renal tubule) effects observed in parental animals. The target MOE is 100 (10× for intraspecies extrapolation, 10× for intraspecies variation).

In the short-term risk assessments, oral and inhalation route-specific MOEs were not combined with the dermal route-specific MOEs as the NOAELs are based on different toxicological endpoints. The oral and inhalation short-term NOAEL is based on a decrease in body-weight gain while the dermal short-term NOAEL is based on an increase in liver and kidney weight. In the intermediate- and long-term risk assessments, route-specific MOEs were combined as the NOAEL of 3.8 mg/kg/day from the two-generation reproduction study in rats was selected as the endpoint for the dermal and inhalation routes of exposure.

Aggregate short-term oral and dermal exposure, 1–30 days (adults and children)
A short-term aggregate exposure assessment is required for adults and children because there is potential for concurrent exposure to trifloxystrobin from food, drinking water, residential and recreational sources. Similar endpoints (increased relative liver and kidney weights) were identified for 28-day oral study in rats and 28-day dermal study in rats. The NOAEL for the organ weights in the 28-day oral study in rats is 84.4 mg/kg bw/day. The target MOE is 100 (10× for intraspecies extrapolation, 10× for intraspecies variation). The NOAEL for the organ weights in the 28-day dermal study in rats is 100 mg/kg bw/day. The target MOE is 100 (10× for intraspecies extrapolation, 10× for intraspecies variation).

3.5 Impact on human or animal health arising from exposure to the active substance or to impurities contained in it

3.5.1 Occupational exposure and risk

3.5.1.1 Handler exposure and risk

Trifloxystrobin is a new fungicide with three proposed commercial end-use products, Compass 50 WG, Stratego 250 EC and Flint 50 WG. Lawn care operators (LCOs), golf course and sod farm workers, and nursery and greenhouse operators have potential for exposure to Compass 50 WG during mixing/loading and applying to turf and ornamentals. The proposed turf uses include golf courses, institutional, commercial and residential lawns, sod farms, sports fields, parks, municipal grounds and cemeteries. The proposed ornamental uses include non-bearing fruit trees, plants, flowers and flowering bushes in interiorscapes, field nursery plantings, residential and commercial landscapes, greenhouses, lath and shade houses, containers and other enclosed structures. Ground application is proposed. Compass is applied at 305 g a.i./ha on turf and up to 105 g a.i./1000 L on ornamentals. The typical area treated per day ranges from 0.4 to 30 ha or 150 to 16 000 L/day depending on the type of application equipment.

LCOs mixing/loading and applying Compass 50 WG to lawns, sports fields, parks and municipal grounds and outdoor ornamentals could be exposed throughout the growing season. Exposure would probably be intermittent over an intermediate-term duration. Workers mixing/loading and applying Compass 50 WG to golf course and sod farm turf would typically be exposed every 14–21 days up to 8 times per season which would result in intermittent short-term exposure. Field nursery workers mixing, loading and applying Compass 50 WG to plantings would typically be exposed once every 7–14 days up to 4 times per crop cycle which would result in short-term exposure. In greenhouses and interiorscapes, Compass 50 WG could be applied all year, resulting in long-term exposure potential for handlers.

Farmers and custom applicators have potential for exposure to trifloxystrobin during application of Stratego 250 EC and Flint 50 WG to wheat, barley, oats, grapes and pome fruits. Ground and aerial methods of application are proposed. Stratego 250 EC is co-formulated with propiconazole. Typical areas treated per day range from 16 to 100 ha for farmers and up to 400 ha for custom applicators. Maximum rates of application range from 63 to 123 g a.i./ha. Farmers mixing/loading and applying Stratego 250 EC and Flint 50 WG would typically be exposed once every 7–21 days, 2 to 4 times during the growing season which would result in short-term exposure intermittently throughout the growing season. Custom cereal applicators may be exposed intermittently over a 4- to 6-week period due to disease pressure and the duration of exposure would be short-term.

Exposure estimates for mixers, loaders, applicators (M/L/A) are based on data from the Pesticide Handlers Exposure Database (PHED) v.1.1 and the studies by the Outdoor Residential Exposure Task Force (ORETF), of which Bayer CropScience is a member. PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates. With a few exceptions, the PHED estimates meet the criteria for data quality, specificity and quantity outlined under the North American Free Trade Agreement NAFTA) Technical Working Group on Pesticides. To estimate exposure for each use scenario, appropriate subsets of A and B (and C grade for handheld equipment) were created from the dry flowable and liquid mixer/loader; aerial, airblast and groundboom applicator; and backpack, low and high pressure mixer/loader/applicator database files of PHED. All data were normalized for kg of active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e., summing the measure of central tendency for each body part which is most appropriate to the distribution of data for that body part.

The ORETF generated several exposure studies that monitored exposure of lawn care technicians and homeowners mixing, loading and applying pest control products to turf and ornamentals. These studies are considered appropriate for use as surrogate data to estimate exposure during mixing, loading and applying Compass 50 WG to turf and ornamentals. Exposure was monitored using cotton dosimeters, hand washes, face/neck wipes and personal air samplers. Exposure estimates are normalized for kg of active ingredient handled and presented on the median measure of central tendency.

The exposure estimates are based on mixer/loaders wearing long pants, long-sleeved shirts as well as gloves and applicators wearing long pants and long-sleeved shirts. For handheld application equipment, gloves are included for applicators. For the short-term risk assessments, route-specific estimates were generated based on the dermal NOAEL of 100 mg/kg/day and the oral NOAEL for the inhalation route of 16.5 mg/kg/day. As dermal and inhalation MOEs are based on different toxicological endpoints (increased liver and kidney weights and decreased body weights respectively), they were not combined. All short-term MOEs exceed the target of 100 and are considered acceptable. For the intermediate and long-term risk assessments, the NOAEL of 3.8 mg/kg/day from the two-generation rat reproduction study was selected for both dermal and inhalation exposure. Thus, the dermal and inhalation risk estimates were combined. A default dermal absorption value of 50% was incorporated into the systemic estimates of exposure. All intermediate and long-term MOEs exceed the target of 100 and are considered acceptable.

Table 3.5.1 Trifloxystrobin handler short-term exposure estimates and margins of exposure

Scenario [a]	Equipment	Dermal exposure [b] mg/kg/day	Inhalation exposure [b] mg/kg/day	Dermal MOE [c]	Inhalation MOE [c]
Compass 50 WG					
M/L/A golf course and sod farm turf	handheld and ground sprayers	0.0095–0.0257	0.00011–0.00042	3890–10 540	39 610–152 450
M/L/A nursery ornamentals	handheld and ground sprayers	0.00004–0.0318	0.000002–0.00086	3140–2 604 000	19 170–8 966 000
Stratego 250 EC					
M/L/A Farmer	ground boom	0.0075	0.00023	13 310	72 190
M/L/A Custom	ground boom	0.0225	0.00069	4440	24 060
M/L Custom	aerial	0.0183	0.00057	5470	28 870
A custom	aerial	0.0035	0.0003	28 990	660 000
Flint 50 WG					
M/L/A Farmer	airblast	0.0159–0.0238	0.00011–0.00016	4200–6300	100 800–151 210
M/L/A Farmer	ground boom	0.0346	0.00035	2890	47 420
M/L/A Custom	ground boom	0.1037	0.00104	960	15 810

[a] M/L/A = mixer, loader, applicator. M/L = mixer, loader. A = applicator

[b] Range of exposures are based on crop application rate, area treated per day and application equipment. Exposure mg/kg/day = PHED unit exposure × application rate × area treated per day × conversion factor (1 mg/1000 µg)/70 kg bw.

[c] MOE = NOAEL (mg/kg/day)/exposure (mg/kg/day) based on the NOAELs of 100 and 16.5 mg/kg/day for dermal and inhalation routes respectively. The target MOE is 100.

Table 3.5.2 Trifloxystrobin handler intermediate and long-term exposure estimates and margins of exposure

Scenario [a]	Equipment	Systemic exposure [b] mg/kg/day	Margin of exposure [c]
Compass 50 WG			
M/L/A residential, recreational and commercial turf	handheld and ground sprayers	0.00485–0.01312	290–780
M/L/A greenhouse, indoor, residential outdoor ornamentals	handheld and ground sprayers	0.00002–0.01678	230–180 600

[a] M/L/A = mixer, loader, applicator

[b] Range of exposures are based on application rate, area treated per day and application equipment. Systemic exposure mg/kg/day = PHED unit exposure × application rate × area treated per day × conversion factor (1 mg/1000 µg)/70 kg bw. A 50% default dermal absorption value is incorporated into the systemic exposure assessment.

[c] MOE = NOAEL (mg/kg/day)/exposure (mg/kg/day) based on NOAEL of 3.8 mg/kg/day. The target MOE is 100.

3.5.1.2 Post-application exposure and risk

There is potential for post-application exposure to workers re-entering turf, ornamentals and crops treated with end-use products containing trifloxystrobin. The duration of exposure for workers is determined by the co-occurrence of re-entry activities with residues of trifloxystrobin. Foliar half-life data is not available for trifloxystrobin as studies on dislodgeable foliar residues (DFR) were not submitted. Data from environmental and apple metabolism studies suggest that the parent persists for greater than 14 days on plant foliage.

Golf course and sod farm workers may re-enter treated turf to aerate, irrigate, scout, mow and harvest. There are up to eight applications of Compass 50 WG per year on turf. The duration of exposure is considered to be short-term due to frequent mowing in these areas; residues are likely to be removed during mowing events. In ornamentals, the number of applications is up to four per crop cycle and re-entry activities such as pruning, pinching, harvesting, irrigating and scouting are ongoing. Post-application exposure following drench application at seeding is expected to be negligible. Following foliar applications, outdoor ornamental re-entry workers could be exposed intermittently throughout the growing season for an intermediate-term duration as there could be several applications per season. Greenhouse and indoor ornamental re-entry workers could be exposed long-term following foliar applications as applications can occur year round. There is no indoor persistence data.

There is potential for post-application exposure to workers re-entering crops treated with Stratego 250 EC and Flint 50 WG to perform activities such as irrigating, thinning, scouting, hand pruning, hand weeding and hand harvesting crops. The number of applications of Stratego 250 EC and Flint 50 WG ranges from two to four. Workers re-entering cereal crops treated with trifloxystrobin could be exposed to trifloxystrobin residues intermittently for a short-term duration. Workers re-entering grapes and pome fruits could be exposed intermittently throughout the growing season for a short- to intermediate-term duration as there are up to four proposed applications and re-entry activities are ongoing.

The primary route of exposure for re-entry workers is dermal through contact with foliar residues. Inhalation exposure is expected to be negligible as the vapour pressure of trifloxystrobin is very low at 3.4×10^{-6} Pa at 25°C. Dermal exposure to workers re-entering treated areas is calculated by coupling crop-specific DFR or turf transferrable residue (TTR) values with activity-specific transfer coefficients (TCs). Activity-specific transfer coefficients are based on published literature and Agricultural Re-entry Task Force (ARTF) data, of which Bayer CropScience is a member. Chemical-specific DFR or TTR data was not submitted. Default DFR and TTR values of 20% and 5% of the seasonal application rates and a default daily dissipation rate of 10% (outdoors only) was used in the exposure assessment. The exposure estimates generated represent re-entry on the day of the last application or on the day of the proposed re-entry interval (REI).

For the short-term risk estimates, exposure was coupled with the dermal NOAEL of 100 mg/kg/day. For the intermediate and long-term risk assessments, the NOAEL of 3.8 mg/kg/day from the two-generation rat reproduction study was selected. A default dermal absorption value of 50% was incorporated into the intermediate and long-term systemic estimates of exposure.

For the Compass 50 WG label, exposure to workers re-entering areas treated by soil drench is considered to be negligible and thus acceptable. MOEs for re-entry activities in turf and outdoor non-bearing trees are above the target MOE of 100 and are considered acceptable. MOEs for re-entry activities associated with outdoor plants, flowers and flowering bushes range from 50 to 140. An agronomically practical REI could not be established to mitigate exposure to workers performing these activities. MOEs for re-entry activities associated with all indoor ornamentals range from 20 to 80. An REI could not be established as indoor degradation data is not available.

All MOEs for the Stratego 250 EC label are above the target MOE of 100 and are considered acceptable. For the Flint 50 WG label, girdling table grapes; harvesting, pruning, thinning, training, tying and leaf pulling grapes; and thinning pome fruit MOEs are below the target MOE on the day of the last application. REIs were established based on a 10% dissipation rate. REIs are 12 days, 5 days and 4 days for girdling table grapes; pruning, thinning, training, tying and leaf pulling grapes; and thinning pome fruits respectively. An REI is not required for harvesting grapes as there is a preharvest interval of 14 days. All other MOEs are above the target of 100 and are considered acceptable.

Table 3.5.3 Re-entry exposure and risk estimates for trifloxystrobin

Crop	Re-entry activity	Duration	Exposure [a] (mg/kg/day)	MOE [b]	REI [c]
Compass 50 WG					
Turf: golf course, sod	mowing, harvest, transplant aerate, fertilize, scout, irrigate	short-term	0.011–0.145	690–9380	0
Outdoor ornamentals—plants	harvest, prune, pinch, thin, irrigate, scout, hand weed	intermediate-term	0.028–0.078	50–140	0
Outdoor ornamentals—trees	prune, prop, train, tie, irrigate, scout, weed	intermediate-term	0.016–0.023	160–250	0
Indoor ornamentals	harvest, prune, pinch, thin, prune, prop, train, tie, irrigate, scout, weed	long-term	0.048–0.240	20–80	0
Stratego 250 EC					
Wheat, barley, oats	irrigation, scouting, weeding	short-term	0.002–0.027	3770–56 520	0
Flint 50 WG					
Wheat	irrigation, scouting, weeding	short-term	0.003–0.052	1940–29 060	0
Grapes	girdling	intermediate-term	0.037	100	12
	train, tie, hand harvest, prune, thin, leaf pull		0.039	100	5
	scout, irrigate, weed, hedge		0.007–0.013	290–580	0
Pome fruits	thinning	intermediate-term	0.039	100	4
	hand harvest, prune, prop, train, tie, irrigate, scout, weed		0.020–0.030	130–190	0

[a] Exposure (mg/kg/day) = DFR or TTR (µg/cm^2) × TC (cm^2/h) × 8 h × 50% dermal absorption (for IT and LT estimates) × conversion factor (1 mg/1000 µg)/70 kg bw. Based on default dislodgeable foliar and transferable residue values. TCs are based on published literature and ARTF data. Range of exposure based on activity-specific TCs.

[b] MOE = NOAEL (mg/kg/day)/exposure (mg/kg/day), short-term NOAEL is 100 mg/kg/day from a dermal rat study. Intermediate and long-term NOAEL is 3.8 mg/kg/day based on a two-generation rat reproduction study.

[c] REI or re-entry interval is established on the day when residues dissipate to levels low enough to permit safe re-entry (MOEs > 100).

3.5.2 Residential exposure and risk

3.5.2.1 Handler exposure and risk

There are no domestic products; therefore, a residential handler assessment was not required.

3.5.2.2 Post-application exposure and risk

Stratego 250 EC and Flint 50 WG are not proposed for use in residential areas. Compass 50 WG is proposed for use on residential turf and ornamentals, thus adults, youth and toddlers have potential to post-application exposure following application of Compass 50 WG by commercial applicators. There is potential for dermal exposure for adults and youth re-entering treated turf and ornamentals. There is potential for dermal and non-dietary oral exposure for toddlers re-entering treated turf. Inhalation exposure is not considered to be a significant route for people re-entering treated areas due to the low vapour pressure of trifloxystrobin (3.4×10^{-6} Pa at 25°C). Up to eight applications are permitted on turf and ornamentals; however, survey data indicate that homeowners typically have one to two fungicide applications per year. Adults and children have the potential for short-term exposure to trifloxystrobin residues in residential settings.

Post-application exposure estimates for residential lawns and ornamentals were generated on the basis of assumptions in the United States Environmental Protection Agency (USEPA) *Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments.* The USEPA has generated standard default assumptions for developing residential exposure assessments for both handler and post-application exposures when chemical- and/or site-specific field data are limited. These assumptions may be used in the absence of, or as a supplement to, chemical- and/or site-specific data. Dermal exposure for people re-entering treated turf is calculated by coupling TTR values with activity-specific transfer coefficients (TCs). For ornamentals, DFR values are coupled with TCs. Non-dietary oral estimates of exposure for toddlers re-entering treated turf are calculated by coupling available residues with activity pattern data. The applicant did not submit any chemical-specific TTR or DFR data. Default TTR and DFR values of 5% and 20% of the seasonal application rate, assuming two applications, was used in the assessment.

Route-specific estimates were generated based on the dermal NOAEL of 100 mg/kg/day and the oral NOAEL of 16.5 mg/kg/day. As dermal and oral MOEs are based on different toxicological endpoints (increased liver and kidney weights and decreased body weights respectively), they were not combined. All short-term MOEs exceed the target of 100 and are considered acceptable.

Table 3.5.4 Short-term residential exposure and risk estimates

Scenario	Dermal exp. [a] mg/kg/d	Oral exposure [b] mg/kg/d	Dermal MOE [c]	Oral MOE [c]
Turf				
Adults	0.0764	N/A	1310	N/A
Toddlers (1–6 yrs)	0.0274	0.00553	3650	3040
Ornamentals				
Adults	0.0123	N/A	8100	N/A
Youth (10–12 yrs)	0.0222	N/A	4510	N/A

[a] Dermal exposure = TTR or DFR × TC × duration/bw. Exposure duration is 2 h on turf and 0.67 h on ornamentals. Includes conversation factor (1 mg/1000 µg).

[b] Oral exposure = hand to mouth exposure + turf mouthing exposure + ingestion of soil exposure. For turf only.

[c] MOE = NOAEL (mg/kg/day)/exposure (mg/kg/day), dermal NOAEL is 100 mg/kg/day from a 28-day dermal rat study, oral NOAEL is 16.5 mg/kg/day based on a 28-day oral rat study. The target MOE is 100.

An aggregate risk assessment is required as adults and children (includes youth and toddlers) have potential for exposure to trifloxystrobin residues from both dietary (food and drinking water) and residential sources via the oral and dermal routes. The aggregate risk assessment is presented in Section 4.1.

3.5.3 Bystander exposure and risk

There is limited potential for exposure to bystanders during application of Stratego 250 EC. For Flint 50 WG, adults and youth have potential for acute exposure during harvesting of pome fruits at pick-your-own operations as this activity is only expected to occur once per year. An acute reference dose was not selected for trifloxystrobin as it is not considered to be acutely toxic, thus an exposure assessment was not required for the pick-your-own scenario. For Compass 50 WG, there is potential for exposure to adults and children playing on recreational turf including parks and sport fields and during golfing on treated turf. Exposure from recreational turf is covered by the residential turf assessments. Golfers could be exposed intermittently throughout the growing season for a short-term duration. Exposure estimates were generated following the guidance in the USEPA *Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments*.

Exposure estimates and MOEs were derived based on the dermal NOAEL of 100 mg/kg/day. MOEs are above the target of 100 and are considered to be acceptable.

Table 3.5.5 Post-application exposure and MOEs for golfers

Population	Dermal Exposure [a] mg/kg/d	Dermal MOE [b]
Adults	0.0053	18 760
Youth (10–12 yrs)	0.0096	10 450

[a] Dermal exposure = TTR (μg/cm^2) × TC (500 cm^2/h) × 4 h × conversion factor of (1 mg/1000 μg)/bw (70 kg for adults, 39 kg for youths).

[b] MOE = NOAEL/exposure, based on a NOAEL of 100 mg/kg/day from a dermal rat study with a target of 100.

An aggregate risk assessment is required as adults and youth have potential for exposure to trifloxystrobin residues from both dietary (food and drinking water) and recreational sources via the oral and dermal routes. The aggregate risk assessment is presented in Section 4.1.

4.0 Residues

4.1 Residue summary

Nature of the residue in plants

Trifloxystrobin, uniformly labelled in the glyoxyl-phenyl ring [GP-^{14}C] and the trifluoromethyl-phenyl ring [TFMP-^{14}C] was applied, using foliar spray applications, to apple trees (after flowering up to 14 days prior to harvest) and cucumber plants (after flowering up to 7 days prior to harvest) maintained in a greenhouse as well as wheat plants (beginning of shooting up to 52 days prior to harvest) maintained in an outdoor plot. Seasonal application rates were 400 g a.i./ha, 940 g a.i./ha and 500 g a.i./ha, respectively. All three metabolism studies demonstrated that the majority of the residues were surface-related and that there was minimal transfer from the peel to the pulp and/or from the site of application to the raw agricultural commodity. The parent, trifloxystrobin, constituted the predominant residue in the apple, whole fruit (average of 82% TRR) and the cucumber, small and large fruit (average of 85% TRR). However, in wheat grain (TFMP-label), trifloxystrobin and its related isomers were not identified. The predominant metabolite, NOA 414412, resulting from the hydrolysis of the methyl ester followed by hydroxylation of the TFMP ring in position 3, accounted for 4.6% TRR. The results of a starch derivatization procedure in TFMP-label grain concluded that starch accounted for 47.9% of the TRR in grain at harvest. In the GP-labelled wheat grain, the parent compound and its isomer CGA-357261 were detected at very low levels (each accounting for 1.3% TRRs); the fraction, consisting of the metabolites NOA 413161 and NOA 413163, represented the majority of the grain radioactivity (10.1% TRRs). The ROC may be defined as the parent, trifloxystrobin and the acetic acid metabolite, CGA-321113. The metabolism of trifloxystrobin in plants is adequately understood.

Confined accumulation in rotational crops
Trifloxystrobin, uniformly labelled in the glyoxyl-phenyl ring [GP-^{14}C] and the trifluoromethyl-phenyl ring [TFMP-^{14}C], was formulated with a 250 EC formulation blank and applied to soil at an application rate of 2.24 kg a.i./ha. Winter wheat, turnips and spinach were planted 30 days and 120 days following application. TRRs at the 30-DAT interval ranged from 5 ppb (turnip roots) to 42 ppb (mature wheat straw). Residues in plant samples from the 120-DAT interval were slightly higher, ranging from 15 ppb (turnip roots) to 127 ppb (mature wheat straw). The predominant residue identified in soil was CGA-321113 while the predominant residues identified in the raw agricultural commodities of the rotational crops were CGA-321113 (≤17.6% TRR; 3 ppb) and trifluoroacetic acid (≤65.9% TRR; 11 ppb). In most cases, the maximum residues occurred at a plantback interval of 120 days. Based on the magnitude of the residues (MORs) in the rotational crops from the confined crop rotation study, the need for a field accumulation study was triggered.

Field accumulation in rotational crops
Trifloxystrobin was applied to primary crops (not specified in the study) by foliar spray application or to soil (loam) at a seasonal rate of 1140 g a.i./ha. Leaf lettuce, turnip and wheat were planted 30 days and 120 days post-treatment. There were no measurable residues of trifloxystrobin and CGA-321113 (< 0.04 ppm) in any of the soil and rotational crop samples. As such, no plantback restrictions will be required for any of the crops on the Flint 50 WG and Stratego 250 EC labels; however, a 30-day plantback interval will be required for all other crops.

Nature of the residue in animals
The metabolism of [trifluoromethyl-phenyl-(U)-^{14}C] trifloxystrobin and [glyoxyl-phenyl-(U)-^{14}C] trifloxystrobin in lactating goats dosed intraruminally and in laying hens dosed orally at an average rate of 100 mg/kg feed/day for four consecutive days demonstrated that there was minimal transfer and bioconcentration of the parent compound and the metabolites in milk, eggs, muscle, fat, liver and kidneys. Of the total dose applied to goats, an average of 0.07%, 18% and 40% was released in the milk, urine and feces, respectively, for both labels. Tissue residues accounted for an average of 0.66% of the administered dose. When including the radioactivity in blood, bile, GI tract and cage wash, 84% of the administered dose was recovered. Of the total dose applied to hens, an average of 0.14% and 79% was released in the eggs and excreta, respectively, for both labels. Tissue residues accounted for an average of 1.2% of the administered dose. When including the radioactivity in blood, bile, GI tract and cage wash, 87% of the administered dose was recovered. The characterization/identification of TRRs in goat excreta, tissues and milk indicated that the parent compound was the predominant residue in milk, fat and GP-labelled feces, while CGA-321113, was the predominant metabolite identified in muscle, kidney, urine, GP-labelled liver and TFMP-labelled feces. The taurine conjugate of CGA-321113 (metabolite L_{7a}) was the predominant metabolite in TFMP-labelled liver. For laying hens, the parent compound was the predominant residue in fat and skin, lean meat and excreta while 1U (resulting from the demethylation of the methoxyimino group of CGA-321113) and CGA-357276 (resulting from the elimination of water or a

conjugated moiety of 1U) were the predominant metabolites in egg whites, 2F (resulting from the demethylation of the methoxyimino group of the parent) in egg yolks and L_{13b} (resulting from the hydroxylation of the TFMP ring of the parent) in liver. Based on the structures identified, the metabolism of trifloxystrobin in goat, hen and rat appears to proceed via the same metabolic pathway: hydrolysis, demethylation, hydroxylation, oxidation and decarboxylation followed by conjugation with taurine, glycine or glucuronic acid. As such, a swine metabolism study was not required.

Methods for residue analysis of plants and plant products and food of animal origin
The GC/NPD analytical method AG-659A was proposed for data gathering and enforcement purposes. The method limit of quantitation (LOQ) for trifloxystrobin and the acetic acid metabolite CGA-321113 was reported to be 0.02 ppm/analyte for most matrices, 0.01 ppm/analyte for milk and 0.05 ppm/analyte for peanut hay. Overall, this method was found to give acceptable mean recoveries of 72–112% (RSD≤20%) and 70–128% (RSD≤20%) for trifloxystrobin and CGA-321113, respectively, in animal matrices. Accordingly, for plant matrices, average recoveries of trifloxystrobin (83–108%; RSD ≤23%) and CGA-321113 (71–110%; RSD ≤20%) were good. The ILV did support the reliability and reproducibility of the GC/NPD method AG-659 for the determination of trifloxystrobin and CGA-321113 in plant and animal matrices. While the ILV was conducted on method AG-659, the method recommended for enforcement of trifloxystrobin per se in all subject plant and animal commodities is method AG-659A, which supercedes AG-659. Compared to AG-659, AG-659A also includes extractability and accountability results from ^{14}C-CGA-279202 animal validations as well as minor changes and ILV study suggestions (i.e., incorporation of a conditioning step of the GC column with control matrix) to improve the ruggedness of the method. The extraction efficiency data indicated that the analytical method AG-659A was not capable of extracting all the radioactivity in goat meat, therefore, a microwave extraction step should be included in the enforcement analytical method AG-659A for animal matrices to ensure that the majority of the residues are extracted.

Storage stability data—plant/animals
The storage stability data demonstrated that residues of trifloxystrobin and the acid metabolite, CGA-321113, were relatively stable in/on various raw agricultural and processed commodities and animal matrices stored at -18ºC. Spiked residues of trifloxystrobin and CGA-321113 (0.5–1.0 ppm) were stable for 24 months in/on grape, cucumber, potato, wheat (straw, grain and whole plant), 18 months in/on apple (whole fruit and wet pomace), grape juice, peanut (nutmeat, hay and oil), potato granules and 12–14 months in/on beef muscle, beef liver, milk and eggs. The half-life of trifloxystrobin and CGA-321113 could not be calculated as there was no noticeable evidence of degradation.

Crop field trials
To support the promulgation of MRLs in/on imported almonds, hops, potatoes, sugar beets, grapes, wheat and various crop groups (cucurbits, fruiting vegetables and pome fruits), several supervised crop field trials were conducted throughout the U.S., Europe and South Africa at rates equivalent to or greater than the registered label rates. Following a review of the submitted residue trial data, it was determined that MRLs could be established in/on all the above imported crops/crop groups with the exception of hops, due to unacceptable concurrent method validation data and a large variability in residue levels from one growing region to another. Subsequently, the registrant submitted additional supervised residue trials conducted in the representative NAFTA growing regions to support a petition for the domestic registration of Flint 50 WG on grapes, pome fruit group (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince) and wheat (winter, spring, hard red, durum, Canada prairie, soft white) and the domestic registration of Stratego 250 EC on wheat (winter, spring, hard red, durum, Canada prairie, soft white), spring barley and oats. Upon reviewing these residue trials, it was determined that the use of Flint 50 WG on wheat (winter, spring, hard red, durum, Canada prairie, soft white) and Stratego 250 EC on wheat (winter, spring, hard red, durum, Canada prairie, soft white), spring barley and oats can be supported provided the PHIs on the labels are amended to 45 days to ensure that the applications are made before the head is half emerged. However, the use of Flint 50 WG on pome fruit group (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince) and grapes can only be supported on a temporary basis pending additional data/trials conducted according to the proposed label and in the representative growing regions. Residue decline studies in cucumber, cantaloupe, summer squash, wheat, potato, almond, hops, sugar beet, apple, pear, grape, tomato and bell pepper demonstrated that, in most cases, residues of trifloxystrobin and CGA-321113 dissipated at a relatively slow rate over time. Therefore, the proposed MRLs will not be exceeded when the appropriate PHIs, recommended on the Flint 50 WG and Stratego 250 EC labels, are observed.

Processed food/feed
The processing studies, conducted on tomatoes, grapes, apples, potatoes, sugar beets and wheat, demonstrated that the combined residues of trifloxystrobin and the acid metabolite, CGA-321113, concentrated in raisins (1.84×). Since there exists a potential for the residues of trifloxystrobin and CGA-321113 to concentrate in raisins, a separate MRL will be established. As no concentration was observed in any other processed fraction used for human consumption, the residues in these processed commodities will be covered under the raw agricultural commodity (RAC) MRLs.

Meat/Milk/Poultry/Eggs
Trifloxystrobin was administered orally to lactating cattle [Holstein] and laying hens [Leghorn] at dosages equivalent to 2, 6 and 20 ppm and 1.5, 4.5 and 15 ppm, respectively, for a duration of 28 days. At the highest feeding level administered to dairy cattle (corresponding to ~2× the maximum anticipated dietary burden), maximum combined residues of trifloxystrobin and the acid metabolite CGA-321113 were < 0.02 ppm in milk, < 0.04 ppm in muscle (round and tenderloin), < 0.07 ppm in omental

fat, < 0.08 ppm perirenal fat, < 0.11 ppm in liver and < 0.04 ppm in kidney. Consequently, when exposed to feed treated according to the proposed Flint50 WG and Stratego 250 EC labels, total trifloxystrobin residues in tissues and organs are not expected to exceed 0.04 ppm while in milk, total residues will not exceed 0.02 ppm. Similarly, for hens administered the highest dosage of 15 ppm (equivalent to ~140× the maximum anticipated dietary burden), there were no measurable residues (< 0.04 ppm) of trifloxystrobin and the acid metabolite in eggs, skin with attached fat, breast and thigh muscle and liver. Hence, residues in poultry tissues and eggs are not expected to exceed the method LOQ (0.04 ppm) when exposed to wheat, barley and oat grain treated according to the proposed Flint 50 WG and Stratego 250 EC labels.

Dietary risk assessment

The proposed import of trifloxystrobin-treated almonds, potatoes, sugar beets, cucurbit vegetables, fruiting vegetables and pome fruits and the proposed domestic use of Flint 50 WG and Stratego 250 EC on pome fruits (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince), grapes, wheat (winter, spring, hard red, durum, Canada prairie, soft white), spring barley and oats does not pose an unacceptable chronic dietary (both food and water) risk to any segment of the population, including infants, children, adults and seniors.

Aggregate exposure and risk assessment

An aggregate risk assessment is required for trifloxystrobin as adults and children have potential for exposure to the active from dietary, residential and recreational sources via the oral and dermal routes. Acute dermal exposure from harvesting at pick-your-own facilities may also co-occur with acute dietary exposure. An acute reference dose was not selected for trifloxystrobin as it is not considered to be acutely toxic, thus an acute aggregate exposure assessment is not required. Short-term exposure from re-entering treated turf and ornamentals is considered to co-occur with chronic oral exposure from food and drinking water. All aggregate MOEs are above the target of 100 and are considered acceptable.

Table 4.1.1 Aggregate exposure and risk assessment

Scenario	Dietary exposure [a] mg/kg/d	Residential or recreational exposure [b] mg/kg/day		Aggregate MOE [c]
		Dermal	Oral	
Residential turf				
Adults	0.00934	0.0764	N/A	1143
Toddlers	0.02064	0.0274	0.00553	1713
Residential ornamentals				
Adults	0.00934	0.0123	N/A	4263
Youth	0.01029	0.0222	N/A	2907
Golfing				
Adults	0.00934	0.0053	N/A	6085
Youth	0.01029	0.0096	N/A	4587

[a] Includes food and drinking water. See Section 4, dietary risk assessment for further details.
[b] See section 3.5 for further details.
[c] Aggregate MOE = 1/[(1/oral MOE) + (1/dermal MOE)], where the oral MOE = oral NOAEL/dietary exposure, based on the NOAEL of 84.4 mg/kg/day for organ weights from the 28-day oral rat study and where the dermal MOE = dermal NOAEL/residential or recreational exposure, based on the NOAEL of 100 mg/kg/day from the 28-day dermal rat study. The target MOE is 100.

5.0 Fate and behaviour in the environment

For a summary, see Appendix III, tables 3, 4 and 5.

5.1 Physical and chemical properties relevant to the environment

Trifloxystrobin has low solubility in water. This is one of the indicators of a low potential for leaching. The vapour pressure of trifloxystrobin is 3.4×10^{-6} Pa at 25°C, and the calculated reciprocal of the Henry's Law constant is 1.09×10^{6} at 25°C. These values indicate that trifloxystrobin is non-volatile under field conditions from water and moist soil surfaces. The log K_{ow} is 4.5, indicating a potential for trifloxystrobin to bioaccumulate. The maximum light absorption is at 250–252 nm, indicating minimal phototransformation in the natural environment.

CGA-321113, a major transformation product, is soluble in water and very soluble in buffer solution at pH 5 and pH 6.6. This is one of the indicators of a potential for leaching to groundwater and movement in surface run-off water. The vapour pressure of CGA-321113 is $< 5.5 \times 10^{-6}$ Pa at 25°C, and the calculated reciprocal of the Henry's Law constant is 5.73×10^{7} at 25°C. These values indicate that CGA-321113 is non-volatile under field conditions from water and moist soil surfaces. The log K_{ow} is 0.34–2.2

(pH 5.5–9.0), indicating a low potential to bioaccumulate. The maximum light absorption is expected to be similar to that of trifloxystrobin, indicating minimal phototransformation in the natural environment.

5.2 Abiotic transformation

Hydrolysis of trifloxystrobin is an important route of transformation in alkaline pH conditions only and is not expected to be an important route under most environmentally relevant situations. Trifloxystrobin hydrolyses slightly at neutral pH and is hydrolytically stable at pH 5. The hydrolysis half-lives were 56 days and 20 hours in pH 7 and pH 9, respectively. The major transformation product formed under these pH conditions is CGA-321113.

Although the physicochemical properties indicate that trifloxystrobin does not absorb light between 340 and 750 nm, the laboratory studies indicated that trifloxystrobin is expected to isomerize in the photic zone of aquatic systems. Phototransformation in aqueous solution resulted in the isomerization of the parent compound to the CGA-357261 (Z,E) and CGA-357262 (Z,Z) transformation products. CGA-357261 was the only major transformation product identified in the irradiated solution.

Phototransformation of trifloxystrobin on soil is not expected to be a major route of transformation for trifloxystrobin but may promote isomerization of CGA-321113 to CGA-357261.

5.3 Biotransformation

Trifloxystrobin is non-persistent in soil and aquatic systems. The aerobic and anaerobic biotransformation dissipation time 50% (DT_{50}) values in soil were less than one day, with the formation of CGA-321113 as the major transformation product. Trifloxystrobin is also non-persistent in aquatic systems under aerobic conditions. Although an anaerobic aquatic biotransformation study was not submitted, the results of the anaerobic soil study indicated that trifloxystrobin is expected to be similarly non-persistent under anaerobic aquatic systems. The major transformation product in aquatic systems was CGA-321113.

CGA-321113 is persistent in aerobic soil, aerobic aquatic and anaerobic aquatic systems. The DT_{50} in aerobic soil is 250–350 days. The DT_{50} of CGA-321113 in the aerobic aquatic system and the anaerobic flooded soil system is 289 days and 1733 days, respectively.

5.4 Mobility

Based on the results of the batch equilibrium adsorption studies and the column leaching study, the mobility of trifloxystrobin in soil is classified as immobile to low. The CGA-321113 transformation product is classified to be of moderate to very high mobility in the soils tested. Based on batch equilibrium adsorption data the mobility of the transformation products, CGA-357261, CGA-373466 and CGA-357276 is classified as low to moderate, moderate to very high and immobile, respectively.

5.5 Dissipation and accumulation under field conditions

Terrestrial soil dissipation of Flint 50 WG was studied in a bare and cropped plot in ecozone 8.1 (mixed wood plains). The terrestrial soil dissipation of Stratego 250 EC (consisting of trifloxystrobin and propiconazole) was studied in bare plots in ecozone 8.1 (mixed wood plaines), 9.2 (temperate prairie), 9.3 (westcentral semi-arid prairies) and 5.3 (atlantic highlands).

The results of the field dissipation studies indicated that trifloxystrobin is non-persistent to slightly persistent and has a low potential to leach. DT_{50} values were 3–23 days and the parent compound was not detected in soil below the 15 cm depth. CGA-321113 and CGA-357261 were identified as major transformation products and CGA-373466 was identified as a minor transformation product. The majority of the field trials indicated that CGA-321113 is persistent (DT_{50} values 215–350 days). The results from ecozone 9.2 and 5.3, however, indicated that CGA-321113 is moderately to slightly persistent (DT_{50} values 36 to < 100 days). CGA-321113 was not detected below the 10 cm soil depth in any of the field studies conducted with Stratego 250 EC, but was detected throughout the soil profile up to a 45 cm depth in the field study conducted with Flint 50 WG.

Up to 23% of the total residues applied were found to carry over to the following growing season. All carryover residues were identified as CGA-321113. No residues of trifloxystrobin were found to carry over.

5.6 Bioaccumulation

Bioaccumulation of trifloxystrobin was studied in bluegill sunfish (*Lepomis macrochirus*) under flow-through conditions at nominal concentrations of 0 (solvent control), 0.16 and 1.6 mg/L for 28 days, followed by a 14-day depuration period.

Although the log K_{ow} of trifloxystrobin is high (4.5) and the maximum bioconcentration factor was calculated to be 130–1172× in fish tissues based on the results of the bioaccumulation study, it is unlikely that trifloxystrobin will bioconcentrate under environmentally relevant conditions, however, considering the rapid aquatic biotransformation and rapid depuration of the parent compound from fish.

5.7 Summary of fate and behaviour in the terrestrial environment

Trifloxystrobin is non-persistent in the terrestrial environment. Laboratory studies of transformation in soil indicated that biotransformation is an important route of trifloxystrobin transformation in aerobic soil. Hydrolysis was an important route of transformation only in alkaline conditions, with a half-life of 20 hours. The major transformation product, CGA-321113, was the only hydrolysis product. Soil phototransformation is not an important route of transformation for trifloxystrobin, but may promote the isomerization of CGA-321113 to CGA-357266. The aerobic and anaerobic biotransformation DT_{50} values in soil are less than one day, with the formation of CGA-321113 as the major transformation product. Based on the results of the batch equilibrium adsorption studies and the column leaching study, trifloxystrobin is expected to be immobile or have a low mobility in soils. The field dissipation studies indicated slower transformation than that observed in the laboratory with DT_{50} values between 3 and 23 days and indicated that trifloxystrobin did not leach beyond a 15 cm soil depth. The field studies indicated that trifloxystrobin is non-persistent to slightly persistent and has a low potential to leach under field conditions.

CGA-321113 was the major transformation product identified in all terrestrial transformation studies. The DT_{50} in aerobic soil is 250–350 days. The DT_{50} of CGA-321113 in the anaerobic flooded soil-water system was 1733 days. Based on the results of the batch equilibrium studies and a column leaching study, CGA-321113 is expected to have moderate to very high mobility in soils. The majority of the field trials indicated that CGA-321113 was persistent (DT_{50} values 215–350 days). The results from ecozone 9.2 and 5.3, however, indicated that CGA-321113 was moderately to slightly persistent (DT_{50} values 36 to < 100 days). CGA-321113 was not detected below 10 cm in any of the field studies conducted with Stratego 250 EC, but was detected throughout the soil profile up to a 45 cm depth in the field study conducted with Flint 50 WG (ecozone 8.1). The field studies indicated that CGA-321113 has the potential to leach under field conditions.

Up to 23% of the total residues applied were found to carry over to the following growing season. All carry over residues were identified as CGA-321113. No residues of trifloxystrobin were found to carry over.

5.8 Summary of fate and behaviour in the aquatic environment

Laboratory studies of transformation indicated that trifloxystrobin is not persistent in aquatic systems. Hydrolysis was an important route of transformation only in alkaline conditions, with a half-life of 20 hours. The major transformation product, CGA-321113, was the only transformation product formed as a result of hydrolysis. Trifloxystrobin is expected to isomerize in the photic zone of aquatic systems. Phototransformation is not an important route of transformation in aqueous solutions. Irradiation resulted in the isomerization of the parent compound to the CGA-357261 (Z,E) and CGA-357262 (Z,Z) transformation products. CGA-357261 was the only major transformation product identified in the irradiated solution. Trifloxystrobin is non-persistent in aquatic systems under aerobic conditions. Although an anaerobic aquatic biotransformation study was not submitted, the results of the anaerobic soil study indicated that trifloxystrobin is expected to be similarly non-persistent under anaerobic aquatic systems. The major transformation product in aquatic systems was CGA-321113. The mobility studies indicated that trifloxystrobin will probably partition into the sediment. Accumulation is unlikely, however, owing to the rapid transformation of the parent compound.

Although the log K_{ow} of trifloxystrobin is high (4.5) and the maximum bioconcentration factor was calculated to be 130–1172× in fish tissues based on the results of the fish bioaccumulation study, it is unlikely that trifloxystrobin will bioconcentrate under environmentally relevant conditions, considering the rapid aquatic biotransformation and rapid depuration of the parent compound from fish.

The major transformation product, CGA-321113, is persistent in aquatic systems. The DT_{50} in aerobic aquatic systems was 289 days. Although an anaerobic aquatic biotransformation study was not submitted, the results of the anaerobic soil study indicated that CGA-321113 is expected to be persistent under anaerobic aquatic systems. The mobility studies indicated that CGA-321113 is not likely to partition into the sediment and based on the log K_{ow} this compound is not expected to bioaccumulate.

5.9 Expected environmental concentrations

5.9.1 Soil

As the rates of application are different for Compass 50 WG, Stratego 250 EC and Flint 50 WG, the expected environmental concentration (EEC) of trifloxystrobin in soil was calculated separately, based on their respective maximum application rates, minimum intervals between applications and the maximum number of applications. The EEC of trifloxystrobin in soil was calculated assuming application to bare soil, soil bulk density of 1.5 g/cm^3, a soil depth of 15 cm and transformation between applications using the most conservative DT_{50} of 23 days (d) in soil. The soil EECs ranged from 0.046 to 0.321 mg trifloxystrobin/kg soil at a depth of 15 cm (Appendix III, Table 6).

EECs were also calculated for CGA-321113 using the most conservative scenario for Compass 50 WG and a DT_{50} value of 350 d and assuming 100% conversion from the parent compound.

5.9.2 Aquatic systems

Drinking water

Trifloxystrobin is slightly mobile to immobile in soils and transforms rapidly in soil and aquatic environments to a series of minor transformation products and the primary transformation product, CGA-321113. The CGA-321113 transformation product is formed at a high percentage of the parent and is persistent, soluble, mobile in the soil and stable to hydrolysis. The environmental fate characteristics of CGA-321113 indicate that this major transformation product can be expected to move into surface water sources as a result of surface run-off as well as leach to ground-water sources. For the purposes of the assessment, 100% conversion from the parent compound to the CGA-321113 transformation product was assumed.

Trifloxystrobin and CGA-321113 residues in potential drinking water sources (ground water and surface water) were modelled using the parameters provided in Appendix III, Table 7. The maximum drinking water concentrations of trifloxystrobin and CGA-321113 in ground-water sources as a result of leaching were estimated using the model LEACHM (maximum annual peak over 20 years; Appendix III, Table 8. Drinking water concentrations in surface water sources (reservoir and dugouts) as a result of surface run-off were estimated using the linked PRZM/EXAMS models (90^{th} percentile of the yearly peak and yearly average over 50–75 years; Appendix III, Table 8). These values are considered to be “upper bound” concentrations in a drinking water source.

Direct overspray in surface water
The maximum seasonal application rate is used to calculate the EEC of trifloxystrobin from direct overspray in surface waters at 30 cm water depth. The EEC of trifloxystrobin in water after the multiple applications of each of the three end-use products at the maximum application rate and assuming a half-life of 8 hours between applications ranged from 0.021 to 0.102 mg a.i./L (Appendix III, Table 6).

5.9.3 Vegetation and other food sources

The EECs of trifloxystrobin in vegetation and food sources are based on the maximum annual label rate of application of Flint 50 WG (50% trifloxystrobin), Stratego 250 EC (125 g/L trifloxystrobin, 125 g/L propiconazole) or Compass 50 WG (50% trifloxystrobin). This did not account for any transformation on the foliage (as data were not available). A direct over-spray scenario, using a nomogram developed by the USEPA from the data of Hoerger and Kenaga (1972), Kenaga (1973), and modified according to Fletcher et al. (1994) for use in ecological risk assessment (Urban and Cook 1986), was used (Appendix III, Table 9).

6.0 Effects on non-target species

6.1 Effects on terrestrial organisms

The toxicity of trifloxystrobin and its EPs, Stratego 312 EC (187.5 g/L trifloxystrobin and 125 g/L propiconazole) and Flint 50 WG (50.8% trifloxystrobin), was studied with three types of invertebrates: earthworms, honeybees, and beneficial predators and parasites. Trifloxystrobin, Stratego 312 EC and Flint 50 WG were considered to be non-toxic to earthworms up to a concentration of 1000 mg/kg soil dry weight (dw). Earthworms exposed to trifloxystrobin and Stratego 312 EC exhibited significant weight loss with NOECs of < 12.3 and 37 mg/kg soil, respectively. The sublethal NOEC for Flint 50 WG was 1000 mg/kg soil. Trifloxystrobin and its EPs were found to be relatively non-toxic to honeybees based on the acute contact (NOEL ≥ 100μg/bee) and acute oral (NOEC ≥ 10.7 μg/bee) studies. Both Stratego 312 EC and Flint 50 WG were found to be harmless to the ground beetle (*Poecilia cupreus*), failing to elicit mortality or sublethal effects at levels up to twice the field application rate (FAR: 1 L Stratego 312 EC/ha and 500 g Flint 50 WG/ha). Similarly, Stratego 312 EC was classified as harmless to the rove beetle (*Aleochara bilineata*) over an exposure period of 29 days, at concentrations up to 2 × FAR. Flint 50 WG was harmful to the beneficial aphid predator *Orius laevigatus* at both 1× and 2× FAR. At both treatment levels, mortality was 100% after 9 days, resulting in an estimated LC_{50} of < 250 g a.i./ha. Flint 50 WG is slightly harmful to the seven-spotted lady beetle (*Coccinella septempunctata*) at 1× FAR, exhibiting significant mortality at this level. Stratego 312 EC was also slightly harmful to *Coccinella septempunctata* at both 1× and 2× FAR, with significantly higher mortality rates and reduced larval pupation rates. The predaceous mite (*Typhlodrumus pyri*) was not susceptible to toxic effects from Flint 50 WG exposure up to 2× FAR (i.e., mortality or fecundity). However, Stratego 312 EC was found to be moderately harmful to *Typhlodrumus pyri* at both exposure levels, with the LC_{50} and the NOECs for mortality and egg production being less than 1× FAR. Stratego 312 EC was harmful to the parasitic wasp (*Aphidius colemani*), eliciting 100% mortality after 48 h exposure at both 1× and 2× FAR. In contrast, Flint 50 WG did not significantly reduce survival or fecundity rates in *Aphidius colemani* at concentrations up to 2× FAR.

Studies on the acute oral toxicity, acute dietary toxicity and reproductive toxicity to birds were reviewed. Trifloxystrobin is categorized as practically non-toxic to mallard ducks and bobwhite quail in acute oral exposure and short-term dietary studies. No treatment-related mortalities or sublethal effects were seen in any of the studies up to the highest doses tested. The acute oral toxicity NOECs for mallards and bobwhite quail were 2250 and 2000 mg a.i./kg bw, respectively, and the short-term dietary NOEC for both species was 5200 mg a.i./kg bw. The avian reproduction NOECs for mallards and bobwhite quail were 474 mg/kg diet and 323 mg/kg diet, respectively. An additional avian reproduction study was conducted by administering 1-methyl-2-pyrolidinone (MNP), a formulant in the Stratego formulation, to the Japanese quail. The NOEC was 403 mg/kg diet.

Following oral dosing in rats, trifloxystrobin was absorbed at a moderate pace, with the majority of the dose ending up in the bile. Tissue residue levels were very low, with the highest residues being found in the blood, kidneys, liver and spleen. Excretion was rapid, with 85–96% of the dose being excreted within 48 hours. Female rats eliminated twice as much in their urine as did males, however, biliary excretion was the major route of loss in both sexes, with the majority of trifloxystrobin excreted in the feces.

Trifloxystrobin was not acutely toxic to rats or mice following oral dosage. Oral LD_{50}s were > 5000 mg a.i./kg bw for both species. Oral LD_{50}s in rats were also > 2000 mg a.i./kg bw for the trifloxystrobin metabolites CGA-373466 and NOA-41442 and two EPs Stratego 250 EC and Flint 50 WG. Effects were seen at lower levels however, in the rat short-term (28-d) and mouse subchronic (90-d) oral dosing studies. NOAELs were 200 and 500 ppm, respectively under the prolonged exposure scenarios. Trifloxystrobin was not a reproductive toxicant. The NOAEL for reproductive effects was set at the highest dose level of 110 mg/kg bw/day.

The effect of Flint 50 WG was assessed on seedling emergence and vegetative vigour for six dicot species and four monocot species. In all species, no phytotoxic effects were seen over a 21-d period at the only dose tested, 113 g a.i./ha. The EC_{25} for Flint 50 WG is therefore > 113 g a.i./ha.

6.2 Effects on aquatic organisms

Studies on the toxicity of trifloxystrobin, CGA-321113, and two EPs, Stratego 312 EC and Flint 50 WG, were reviewed for a variety of freshwater and marine organisms. Trifloxystrobin was found to be either highly toxic or very highly toxic to all freshwater invertebrates tested. The most sensitive freshwater invertebrate tested was *Daphnia longispina* with a 48-h EC_{50} of 0.015 mg a.i./L and a NOEC below the lowest concentration tested, 0.0043 mg a.i./L. Chronic exposure of trifloxystrobin to *Daphnia magna* over 21 days significantly reduced daphnid length, weight and reproductive output at 0.0028 mg/L. CGA-321113 was not acutely toxic to *Daphnia magna*, with a 48-h EC_{50} > 95 mg/L. Chronic exposure to CGA-321113 over 21 days resulted in a NOEC of 3.2 mg/L based on immobilisation. The EPs, Stratego 312 EC and Flint 50 WG, were very highly toxic to *Daphnia magna* (48-h EC_{50}s: 0.071 and 0.010 mg EP/L, respectively). Chronic exposure to Flint 50 WG significantly reduced daphnid survival and reproductive capacity at 0.020 mg EP/L and above (NOEC = 0.011 mg EP/L).

Studies submitted for freshwater fish showed that trifloxystrobin and the EPs Stratego 312 EC and Flint 50 WG are highly toxic or very highly toxic to both cold- and warmwater fish, while the transformation product CGA-321113 is practically non-toxic. The most sensitive freshwater fish tested was rainbow trout (*Oncorhynchus mykiss*) with a 96-h LC_{50} of 0.012–0.041 mg a.i./L. Bluegill sunfish (*Lepomis macrochirus*) were similarly susceptible to trifloxystrobin (96-h LC_{50} = 0.046–0.135 mg a.i./L). Sublethal effects seen in fish included loss of equilibrium and changes in swimming behaviour (both species), decreased respiratory function and altered pigmentation. Acute exposure of rainbow trout to CGA-321113 failed to elicit mortality up to the highest tested concentrations (NOEC = 106 mg a.i./L). The EPs, Stratego 312 EC and Flint 50 WG, were both very highly toxic to rainbow trout under acute exposure (96-h LC_{50} ranges: 0.074–0.12 and 0.033–0.040 mg EP/L, respectively). Chronic exposure of trifloxystrobin to early-life stages of the rainbow trout over 95 days resulted in a significant reduction in the hatching rate of eggs at 0.015 mg a.i./L (the highest tested concentration). The mortality of hatchlings increased significantly at concentrations of 0.0077 mg a.i./L and above, resulting in a NOEC of 0.0043 mg a.i./L.

Trifloxystrobin exposure to three groups of freshwater algae (green algae, diatoms and blue-green algae) was reviewed. Trifloxystrobin significantly inhibited cellular growth in green algae (*Selenastrum capricornutum* [proposed *Pseudokirchneriella subcapitata*] and *Scenedesmus subspicatus)* and diatoms (*Navicula pelliculosa*). The lowest reported EC_{50}s (and the affected endpoint) for each of the above species were 0.0385 (cell density), 0.00682 (growth rate), < 0.006 (biomass) mg/L, respectively. Blue-green algae (*Anabaena flos-aquae*) did not appear to be affected by exposure to trifloxystrobin up to the highest tested concentration of 0.120 mg/L. Studies with *Selenastrum capricornutum* showed that CGA-321113 inhibited cell density at concentrations greater than 0.018 mg/L, but the EC_{50} was beyond the range tested (i.e., > 0.100 mg/L), and the EPs, Stratego 312 EC and Flint 50 WG, reduced cellular biomass (EC_{50}s: 0.0438 and 0.0193 mg EP/L, respectively). In a 14-day acute toxicity study, trifloxystrobin was found to inhibit frond production in the freshwater floating plants, duckweed (*Lemna gibba*), at test concentrations greater than 0.41 mg/L, however, the EC_{50} was beyond the range of concentrations used in this study (i.e., > 1.93 mg/L).

Two studies were reviewed on the effects of trifloxystrobin toxicity to marine invertebrates. Trifloxystrobin was very highly toxic to mysid shrimp (*Mysidopsis bahia*) with a 96-h LC_{50} of 0.00862 mg/L, and a NOEC based on mortality of 0.00360 mg a.i./L. Sublethal effects observed in mysids included erratic swimming behaviour and lethargy. Significant reductions in shell deposition were observed in the eastern oyster (*Crassostrea virginica*) following acute exposure to trifloxystrobin (96-h EC_{50} = 0.0293 mg/L). Because significant reductions in shell deposition were observed at the lowest trifloxystrobin test concentration of 0.0098 mg/L, a NOEC could not be established.

One study on trifloxystrobin toxicity to a marine fish, the sheepshead minnow (*Cyprinodon variegatus*), was reviewed. Trifloxystrobin was very highly toxic to sheepshead minnows (96-h LC_{50} = 0.078 mg/L; NOEC based on mortality = 0.0323 mg/L). At concentrations greater than 0.0987 mg a.i./L, some fish exhibited a loss of equilibrium, or lethargy.

6.3 Effects on biological methods of sewage treatment

No data were submitted.

6.4 Risk characterization

6.4.1 Environmental behaviour

Trifloxystrobin is non-persistent in soil and water. Laboratory studies of transformation in soil indicate that biotransformation is the important route of trifloxystrobin transformation. Hydrolysis is an important route in alkaline conditions only. Phototransformation appears to promote isomerization, but this is not expected to be an important route of transformation. Mobility studies indicated that trifloxystrobin is expected to be immobile to having a low mobility in soils. This was confirmed by the field studies that indicated that trifloxystrobin is non-persistent to slightly persistent and has a low potential to leach under field conditions.

CGA-321113 was the major transformation product identified in the terrestrial and aquatic transformation studies. The biotransformation and mobility studies indicated that this transformation product is persistent in soil and water and is expected to have a moderate to very high mobility in soils. These results were confirmed in the terrestrial field dissipation studies.

Compass 50 WG had the highest EEC value, the risk assessment for each type of non-target organism was initially performed exclusively for this end-use product. If a potential risk was determined for Compass 50 WG, risk assessments for Stratego 250 EC and Flint 50 WG were also conducted. If a negligible risk was determined, no further assessments were performed. The Flint 50 WG and the Compass 50 WG formulations are identical. They are reported separately in the risk assessment since the use pattern and EEC values differ for each product.

6.4.2 Terrestrial organisms

Earthworms: The estimated initial EEC for each end-use product was estimated using the maximum seasonal rate on each label (Appendix III, Table 6). The EEC for Compass 50 WG, Stratego 250 EC and Flint 50 WG were 0.321, 0.046 and 0.119 mg a.i./kg soil, respectively. Corresponding EECs calculated for each end-use product were 0.642, 0.404 and 0.238 mg EP/kg soil. The NOEC for the trifloxystrobin technical, the Stratego 312.5 EC formulation and the Flint/Compass 50 WG formulation were < 12.3 mg a.i./kg soil, 37 mg EP/kg soil and 1000 mg EP/kg soil, respectively. The risk quotients, RQ (EEC/NOEC), were calculated to be $\leq$0.03 for all end-used products. Trifloxystrobin, therefore, poses a negligible risk to earthworms at the proposed application rates.

Honeybees: In the acute contact toxicity studies, trifloxystrobin and the end-use products were considered to be relatively non-toxic to honeybees according to Atkins et al. (1981) (LD_{50} > 100 µg/bee). In the acute oral toxicity studies, trifloxystrobin and the end-use products were considered to be relatively non-toxic to honeybees. The LC_{50} values for trifloxystrobin, Flint/Compass 50 WG and Stratego 250 EC were > 200 µg a.i./bee, 136.7 µg/bee and > 186.7 µg/bee, respectively.

Predators and parasites: Studies on the contact toxicity of trifloxystrobin to beneficial predators and parasites were conducted with the end-use products. The toxicity of Compass/Flint 50 WG and Stratego was found to range from harmless to harmful to beneficial invertebrates (Appendix III, Table 11). Compass/Flint 50 WG was harmful to the aphid predator (*Orius laevigatus*) and slightly harmful to the seven-spotted lady beetle (*Coccinella septempunctata*). Stratego 321.5 EC was slightly harmful to the seven-spotted lady beetle *(Coccinella septempunctata*) moderately harmful to the predaceous mite (*Typholodromus pyri*) and harmful to the parasitic wasp (*Aphidius colemani*).

Birds: Wild birds, such as bobwhite quail (*Colinus virginianus*) and mallard duck (*Anas platyrhynhcos*), could be exposed to residues of trifloxystrobin as a result of the consumption of sprayed vegetation and/or contaminated prey. The EECs of trifloxystrobin in the diets of the bobwhite quail and mallard duck were 21.9–210.1 and 4.23–40.6 mg/kg dw, respectively (Appendix III, Table 10).

The acute oral risk to birds was assessed using the NOEL for each respective species, food consumption (bobwhite quail: 19.6 g/ind/day; mallard duck: 134g/ind/day) and body weight (bobwhite quail: 0.204 kg bw/ind; mallard duck: 1.14 kg bw/ind) estimates from their respective studies and the highest predicted EEC for all end-use products. Based on the predicted daily intake (DI = Food Consumption × EEC; bobwhite quail: 4.12 mg a.i./ind/d, mallard duck: 5.44 mg a.i./ind/d), the maximum number of days of intake of trifloxystrobin by a bobwhite quail and a mallard duck to reach their respective NOELs was 99 and 472 days, respectively. Therefore, the acute risk to birds is expected to be negligible for all proposed trifloxystrobin end-use products.

The acute dietary risk to birds was assessed using the NOEC for each respective species and the highest predicted EEC value. Based on the RQ values (EEC/NOEC) of 0.04 and < 0.01 for the bobwhite quail and mallard duck, respectively, the acute dietary risk to birds is expected to be negligible for all proposed trifloxystrobin end-use products.

The reproductive risk to birds was assessed using the NOEC for each respective species and the EEC value for each end-use product. For the bobwhite quail, the NOEC of 320 mg a.i./kg bw was the highest concentration tested. For the mallard duck, the NOEL of 474 mg a.i./kg bw was the highest dose tested. The RQ values for the bobwhite quail based on sublethal effects were 0.65, 0.07 and 0.21 for Compass 50 WG, Stratego 250 EC and Flint 50 WG, respectively. Corresponding RQ values for the mallard duck were 0.4, 0.009 and 0.02. Therefore, based on the most sensitive species tested, the reproductive risk to the birds is expected to be low for Compass 50 WG and Flint 50 WG and negligible for Stratego 250 EC.

Small wild mammals: Wild mammals could be exposed to residues of trifloxystrobin as a result of the consumption of sprayed vegetation and/or contaminated prey. From Appendix III, Table 10, the trifloxystrobin EECs at the Compass 50 WG application rate in the diets of rats and mice were 605.4 and 601.76 mg a.i./kg dw, respectively. Corresponding EECs at the Stratego application rate were 63.06 and 62.68 mg a.i./kg dw; and at the Flint 50 WG application rate were 194.23 and 193.06 mg a.i./kg dw.

In the assessment of the acute risk to rats, default values were used for food consumption (FC) (0.060 kg dw/ind/day) and body weight per individual (BWI) (0.350 kg bw/ind). The highest EEC was 605.4 mg a.i./kg dw for trifloxystrobin. The DI was calculated as 36.3 mg a.i./ind/day. The LD_{50} was > 5000 mg a.i./kg bw for trifloxystrobin. As a NOEL was not available, one-tenth of the LD_{50} was used. Based on the DI, the maximum number of days of intake of trifloxystrobin by a rat to reach the NOEL was 4.8 days.

In the assessment of the acute risk to mice, default values were used for FC (0.0060 kg dw/ind/day) and BWI (0.033 kg bw/ind). The highest EEC was 601.76 mg a.i./kg dw for trifloxystrobin. The DI was calculated as 3.61 mg a.i./ind/day. The LD_{50} was > 5000 mg a.i./kg bw for trifloxystrobin. As a NOEL was not available, one-tenth of the LD_{50} was used. Based on the DI, the maximum number of days of intake of trifloxystrobin by a rat to reach the NOEL was 4.57 days. Therefore the acute risk to rats and mice is expected to be negligible for all proposed trifloxystrobin end-use products.

Dietary studies were conducted with trifloxystrobin on both rats and mice. The most sensitive and appropriate NOELs were 200 mg/kg dw based on reduced body weights and 500 mg/kg dw based on increased liver weights and necrosis of hepatocytes and spleen. Using the EECs for each respective end-use product, the RQ values were calculated to be 0.32–3.03 and 0.12–1.20 for the rat and mouse, respectively. This indicated a low risk for both the rat and the mouse to Stratego 250 EC and Flint 50 WG EPs and a moderate risk for both species to Compass 50 WG.

A reproduction study was conducted with trifloxystrobin on rats. The most sensitive and appropriate NOEL was 1500 mg/kg dw based no effects at the highest dose tested. Using the EECs for each respective end-use product, the RQ values were calculated to be 0.04–0.40. This indicated negligible to low risk for the rat on a reproductive basis.

Non-target terrestrial plants: All the toxicity studies with non-target plants were conducted with Flint/Compass 50 WG. No effects were shown at the highest concentration tested (113 g a.i./ha), therefore the EC_{25} (seedling emergence and vegetative vigour) was determined to be > 113 g a.i./ha. The highest test concentrations were compared to the EEC resulting from one application of the Compass 50 WG (305 g a.i./ha) and Flint 50 WG (105 g a.i./ha). The corresponding RQ values were 2.70 and 0.93, indicating a low to moderate risk to terrestrial plants.

No studies were conducted with the Stratego 250 EC end-use product.

Summary of the risk to terrestrial organisms: An assessment of the environmental safety associated with the use of trifloxystrobin and its associated end-use products has identified negligible to low risk to birds on a reproductive basis. The risk to small mammals was determined to be negligible to moderate. The risk to vascular plants was low to moderate. The risks to earthworms, bees as well as birds on an acute and dietary basis are expected to be negligible.

6.4.3 Aquatic organisms

The following EECs were used to calculate the risks to aquatic organisms:
0.102 mg a.i./L and 0.203 mg EP/L for Compass 50 WG; 0.021 mg a.i./L and 0.183 mg EP/L for Stratego 250 EC; and 0.035 mg a.i./L and 0.070 mg EP/L for Flint 50 WG. For those risks calculated for the CGA-321113 transformation product an EEC of 0.387 mg/L was used (Appendix III, Table 6).

Non-target freshwater invertebrates: *Daphnia longispina* was the most sensitive species exposed to trifloxystrobin technical. Since a NOEC could not be determined from the study, 1/10 of the EC_{50} (0.0015 mg/L) was use as the most sensitive endpoint. From the acute toxicity studies conducted with the trifloxystrobin EPs, the most sensitive species tested was *Daphnia magna*. The NOECs were 0.006 mg EP/L for Compass/Flint 50 WG and 0.041 mg EP/L for Stratego 250 EC. The RQ values calculated for the end-use product using the toxicity data obtained from trifloxystrobin technical were 68.00, 14.00 and 23.33 for Compass 50 WG, Stratego 250 EC and Flint 50 WG, respectively. Corresponding RQ values using the end-use product toxicity data were 33.83, 4.46 and 11.67. Therefore the acute risk to aquatic invertebrates was determined to be high for Compass 50 WG and Flint 50 WG and moderate to high for Stratego 250 EC.

From the studies of chronic toxicity of trifloxystrobin and its end-use products to *Daphnia magna*, the NOECs were 0.0028 mg a.i./L for trifloxystrobin and 0.011 mg EP/L for Compass/Flint 50 WG. The RQ values calculated for the EP using the toxicity data obtained from trifloxystrobin technical were 36.96, 7.61 and 12.68 for Compass 50 WG, Stratego 250 EC and Flint 50 WG, respectively. RQ values using the end-use product toxicity data were 18.45 and 6.36 for Compass 50 WG and Flint 50 WG, respectively. Therefore the chronic risk to aquatic invertebrates was determined to be moderate to high for Compass 50 WG and Flint 50 WG and moderate for Stratego 250 EC.

Acute and chronic toxicity tests were also conducted with CGA-321113, the major transformation product. The NOECs were determined to be 95.3 mg a.i./L and 3.2 mg a.i./L based on the acute and chronic toxicity tests, respectively. Corresponding RQ values were calculated to be < 0.01 and 0.12, indicating a negligible risk to *Daphnia magna* on an acute basis and a low risk on a chronic basis.

Freshwater fish: From the acute toxicity studies of trifloxystrobin and its end-use products to rainbow trout, the NOECs were 0.0072 mg a.i./L for trifloxystrobin, 0.015 mg EP/L for Compass/Flint 50 WG and 0.074 mg EP/L for Stratego 250 EC. The acute NOEC for the bluegill sunfish was 0.028 mg a.i./L. The rainbow trout RQ values calculated for the end-use product using the toxicity data obtained from trifloxystrobin technical were 14.17, 2.92 and 4.86 for Compass 50 WG, Stratego 250 EC and Flint 50 WG, respectively. Corresponding RQ values using the end-use product toxicity data were 13.53, 2.47 and 4.67. The bluegill sunfish RQ values were 3.64, 0.75 and 1.25 for the Compass 50 WG, Stratego 250 EC and Flint 50 WG end-use products, respectively.

Therefore the acute risk to freshwater fish was determined to be low to high for all end-use products.

From the studies of chronic toxicity of trifloxystrobin technical to rainbow trout, the NOEC was determined to be 0.0043 mg/L. The rainbow trout RQ values calculated for the end-use products using the toxicity data obtained from trifloxystrobin technical were 23.72, 4.88 and 8.14 for Compass 50 WG, Stratego 250 EC and Flint 50 WG, respectively. Therefore the chronic risk to freshwater fish was determined to be high for Compass 50 WG and moderate for the Stratego and Flint 50 WG end-use products.

An acute toxicity test was also conducted with CGA-321113, the major transformation product. The NOEC was determined to be 106 mg a.i./L and the corresponding RQ value was calculated to be < 0.01, indicating a negligible risk to rainbow trout on an acute basis.

Freshwater algae: From the acute toxicity studies of trifloxystrobin and its EPs to freshwater alga, the most sensitive NOECs were 0.002 mg a.i./L (*Scenedesmus subspicatus*; reduced growth rate and biomass), 0.0056 mg EP/L (*Selenastrum capricornutum*; reduced growth rate and biomass), 0.0072 mg EP/L (*Selenastrum capricornutum*; reduced biomass and growth rate) for trifloxystrobin technical, Compass/Flint 50 WG and Stratego 250 EC, respectively. The RQ values calculated for the end-use product using the toxicity data obtained from trifloxystrobin technical were 51.00, 10.50 and 17.50 for Compass 50 WG, Stratego 250 EC and Flint 50 WG, respectively. Corresponding RQ values using the end-use product toxicity data were 36.25, 25.42 and 12.50. Therefore the acute risk to freshwater algal is moderate to high for all end-use products.

An acute toxicity test was also conducted with CGA-321113, the major transformation product. The NOEC was determined to be 0.018 mg a.i./L (cell density). The calculated RQ value was 21.50, indicating a high risk to freshwater alga on an acute basis.

Freshwater vascular plants: From the acute toxicity studies of trifloxystrobin technical to the *Lemna gibba*, the NOEC was 0.41 mg a.i./L. The RQ values calculated for the end-use product using the toxicity data obtained from trifloxystrobin technical were 0.25, 0.05 and 0.08 for Compass 50 WG, Stratego 250 EC and Flint 50 WG, respectively, indicating a negligible to low risk to non-target marine/estuartine fish for all end-use products.

Non-target marine/estuarine invertebrates: From the acute toxicity studies of trifloxystrobin technical to the mysid shrimp and the eastern oyster, the NOECs were 0.0036 mg/L (mortality) and < 0.0098 mg/L (mortality), respectively. Since the NOEC was lower than the lowest concentration tested, 1/10 of the EC_{50} (0.00293 mg/L) was used for the eastern oyster risk assessment. The mysid shrimp RQ values calculated for the end-use product using the toxicity data obtained from trifloxystrobin technical were 28.33, 5.83 and 9.72 for Compass 50 WG, Stratego 250 EC and Flint 50 WG, respectively. Corresponding RQ values for the eastern oyster were 34.81, 7.17 and 11.94.

Therefore the acute risk to non-target marine/estuartine invertebrates was determined to be high for Compass 50 WG, moderate to high for Flint 50 WG and moderate for Stratego 250 EC.

Non-target marine/estuarine fish: From the acute toxicity studies of trifloxystrobin technical to the sheepshead minnow, the NOEC was 0.0323 mg/L (mortality). The RQ values calculated for the end-use product using the toxicity data obtained from trifloxystrobin technical were 3.16, 0.65 and 1.08 for Compass 50 WG, Stratego 250 EC and Flint 50 WG, respectively, indicating a low to moderate risk to non-target marine/estuartine fish for Compass 50 WG and Flint 50 WG and a low risk for Stratego 250 EC.

Summary of the risk to aquatic organisms: An assessment of the environmental safety associated with the use of trifloxystrobin and its associated end-use products has identified risks to all aquatic species. The risk was determined to be moderate to high to freshwater and marine/estuarine invertebrates on an acute and chronic basis and a high to freshwater algae on an acute basis. A moderate to high risk to coldwater fish was determined on an acute and chronic basis, a low to moderate risk to warmwater fish was determined on an acute basis and a low to moderate risk was determined for marine and estuarine fish on an acute basis. The risk to vascular plants was determined to be negligible to low.

An assessment was also conducted on the CGA-321113 transformation product for several aquatic species. The risk was determined to be low to negligible for freshwater invertebrates on an acute and chronic basis, negligible for freshwater fish on an acute basis and high risk to freshwater algae on an acute basis.

No chronic fish study conducted with CGA-321113 was submitted. Due to its persistence and its environmental relevance, a chronic freshwater fish toxicity study should be conducted with CGA-321113.

6.5 Risk mitigation

Based on the data submitted and on the existing data requirements for use-site categories 6, 13, 14, 27, 28 and 30, an assessment of the environmental safety associated with the use of trifloxystrobin has been conducted. Application of the technical active ingredient trifloxystrobin and the formulated end-use products using a scenario of the maximum application rates of 2.4 kg a.i./ha for Compass 50 WG, 125 g a.i./ha for Stratego 250 EC and 770 g a.i./ha has identified areas of concern, particularly with aquatic invertebrates, freshwater alga and fish.

Compass 50 WG (end-use product) will pose a risk to the following organisms:

- aquatic invertebrates (e.g., *Daphnia magna, Daphnia longispina*, mysid shrimp, eastern oyster)
- fish (e.g., rainbow trout, sheepshead minnow)
- freshwater alga (e.g., *Navicula pelliculosa*)
- terrestrial vascular plants
- small mammals (e.g., rat and mouse)

Stratego 250 EC (end-use product) will pose a risk to the following organisms:

- aquatic invertebrates (e.g., *Daphnia magna, Daphnia longispina*, mysid shrimp, eastern oyster)
- freshwater fish (e.g., rainbow trout)
- freshwater alga (e.g., *Navicula pelliculosa*)

Flint 50 WG (end-use product) will pose a risk to the following organisms:

- aquatic invertebrates (e.g., *Daphnia magna, Daphnia longispina*, mysid shrimp, eastern oyster)
- fish (e.g., rainbow trout, sheepshead minnow)
- freshwater alga (e.g., *Navicula pelliculosa*)

Buffer zones: Based on the proposed application rates, the following buffer zones to protect sensitive terrestrial and aquatic habitats are recommended to mitigate risks.

Compass 50 WG

Method of application	**Buffer zone (metres) required for the protection of:**		
	Terrestrial habitat	**Freshwater habitat**	**Estuarine/marine habitat**
Field sprayer (without the use of shrouds and cones)	0	18	14
Field sprayer (with the use of shrouds)	0	6	5
Field sprayer (with the use of cones)	0	13	10
Airblast (early season)	2	21	17
Airblast (late season)	1	12	8

Stratego 250 EC

A buffer zone of **four metres** required between the downwind point of direct application and the closest edge of sensitive aquatic habitats (such as lakes, rivers, sloughs, ponds, coulees, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

Flint 50 WG

Method of application	Buffer zone (metres) required for the protection of:		
	Terrestrial habitat	Freshwater habitat	Estuarine/marine habitat
Field sprayer	0	10	6
Airblast (early season)	1	17	13
Airblast (late season)	1	9	6

7.0 Efficacy

7.1 Effectiveness

7.1.1 Intended uses

Compass 50 WG is proposed for foliar application to turfgrass, for drench application to growing medium of selected container ornamentals at seeding and transplant and for foliar spray application to selected ornamental container plants and trees grown both indoors and outdoors. Tankmix rates with Banner MAXX are also proposed to increase control of anthracnose and summer patch on turfgrass.

Flint 50 WG is proposed for airblast application to grapes and pome fruit (apple, pear, crabapple) and ground boom application to wheat.

Stratego 250 EC, containing 125 g each of trifloxystrobin and propiconazole, is proposed for ground boom and aerial spray application to wheat, barley and oats.

Table 7.1.1 Proposed uses of Compass 50 WG

Disease	Rate product	Application interval (days)	Comments
Turfgrass (g/100 m^2) golf course, institutional, commercial and residential lawns, sod farms, sports fields, parks, municipal grounds and cemetaries Do not apply more than 2 sequential applications for gray leaf spot control. Do not apply more than 3 sequential applications for all other diseases. Alternate with a fungicide having a different mode of action. Up to 2.4 kg can be applied per hectare per year.			
Brown patch	3.1–6.1 4.6–6.7	14–21	For curative applications, apply 6.1 g/100 m^2 and repeat applications on a 21-day interval.
Leaf spot	3.1–4.6 4.6–7.6	14–21	For curative applications, apply 4.6–7.6 g/100 m^2 and repeat applications according to the application interval timing.
Anthracnose	4.6–6.1	14–21	For curative applications, apply 6.1–7.6 g/100 m^2 and repeat applications according to the application interval timing.
Gray leaf spot	7.6	14–21	For curative applications, apply 6.1–7.6 g/100 m^2 and repeat applications according to the application interval timing.
Red thread	3.1–4.6	14–21	For curative applications, apply 6.1–7.6 g/100 m^2 and repeat applications according to the application interval timing.
Summer patch	6.1–7.6	14–21	Under heavy disease pressure or at sites with a history of summer patch infestation, refer to tank mix section in this label.
Pink snowmold Gray snowmold	7.6	late fall	Apply one application in late fall before snow cover. Do not apply on top of snow.
Fusarium patch	6.1–7.6	fall–early spring	Apply one application in late fall before snow cover or early spring after snow melts. Do not apply on top of snow.
Tankmixes			
Anthracnose	3.1–4.6 g + 16–32 mL	14–21	For longer and more broad-spectrum disease control mix Compass 50 WG with Banner MAXX.

Disease	Rate product	Application interval (days)	Comments
Summer patch	6.1–7.6 g + 64–127 mL	21–28	Under heavy disease pressure, apply Banner MAXX at 127 mL/100 m^2. After 21–28 days apply either Compass 50 WG at 6.1 g every 14 days or Banner MAXX at 64 mL and Compass 50 WG at 6.1–7.6 g every 21–28 days.
Ornamentals (g/100 L) For list of crops, see Section 7.1.4 For ornamentals grown in interiorscapes, field nursery plantings, forest nurseries, residential and commercial landscapes, greenhouses, lath and shadehouses, containers and other enclosed structures. For plants grown outdoors, up to 2.4 kg per hectare per year or crop cycle can be used. For seedlings and plants in enclosed structures, up to 8.4 kg per hectare per year or crop cycle can be used. Use no more than one or two applications of Compass 50 WG (depending on disease) before rotating to another product with non-strobilurin chemistry.			
Botrytis	15–30	7–14	Apply to point of drip when conditions are favourable for disease.
Myrothecium leaf spot	7.5–15	7–14	Apply to point of drip when conditions are favourable for disease.
Powdery mildew	7.5–15	7–14	Apply to point of drip when conditions are favourable for disease.
Scab	15–30	7–14	Apply to point of drip when conditions are favourable for disease
Rhizoctonia root rot	3.8	21–28	Apply as a drench to wet the upper 1/2 of the growing media. Start application at time of seeding, again at transplanting and at 21–28 day intervals thereafter.

Table 7.1.2 Proposed uses of Flint 50 WG

Disease	Rate product (g/ha)	Application interval (days)	Comments
Grapes Maximum 560 g/ha per season, PHI 14 days. Do not apply more than four applications of strobilurins per season for table or wine grapes and three applications for other grapes. For resistance management, alternate with non-strobilurin after three applications of this group. Do not apply Flint 50 WG to Concord grapes or crop injury may occur.			
Powdery mildew	105–140	14–21	Use shorter intervals when disease pressure is severe.
Black rot	140	7–14	Begin applications when shoots are 1–3 inch length and continue as needed on a 7–14 day interval. Use shorter intervals when disease pressure is severe.
Pome fruit: Apples, pears, crabapples Maximum 770 g/ha per season, PHI 14 days. Do not apply more than four applications of strobilurins per season. For resistance management, alternate with two sprays non-strobilurin after three applications of this group. To prevent crop injury to Concord grapes, avoid spray drift and rinse spray equipment after applying Flint 50 WG.			
Scab	140–175	7–10	Begin applications at green tip. Flint 50 WG will provide up to 100 hours post-infection activity.
Sooty blotch Fly speck	140–175	10–14	Begin applications preventatively. Use the higher rate and shorter interval when disease pressure is severe. Alternate with a sterol inhibitor.
Powdery mildew	140–210	10–14	Begin applications preventatively. Use the higher rate and shorter interval when disease pressure is severe. Alternate with a sterol inhibitor.
Cedar apple rust	140–210	10–14	Begin applications preventatively. Use the higher rate and shorter interval when disease pressure is severe. Alternate with a sterol inhibitor.
Wheat Maximum 490 g/ha (2 applications) per season, PHI 35 days. Grazing: For two sprays (490 g/ha)—do not allow grazing, do not harvest for forage or hay. For one spray (245 g/ha)—do not allow grazing within 30 days of treating, do not harvest for forage within 30 days or for hay within 45 days after application.			

Disease	Rate product (g/ha)	Application interval (days)	Comments
Rust Powdery mildew Leaf blight Tan spot	245 g/ha	> 14	Begin applications preventatively when conditions are favourable for disease development. A second application may be made if needed.
Glume blotch	245 g/ha	> 14	Make an application at early heading stage. Head disease control may be enhanced when preceded by a foliar application prior to heading.

Table 7.1.3 Proposed uses of Stratego 250 EC

Disease	Rate product (mL/ha)	Application interval (days)	Comments
Maximum two applications per season, PHI 35 days. Grazing: For two sprays—do not allow grazing, do not harvest treated crop for forage or hay For one spray—do not allow grazing within 30 days of application, do not harvest treated crop for forage within 30 days, 35 days for grain and straw, or for hay within 45 days after application.			
Wheat			
Septoria leaf blotch Septoria glume blotch Tan spot Powdery mildew Leaf and stem rust Stripe rust	500	> 14	Apply at the very early stages of disease development. This could occur anytime during tillering or stem elongation [this is BBCH Growth Stages 21–36]. Typically one application from the beginning of stem elongation up to flag leaf emergence is required. A second application may be made if needed. Single application: 4 leaf stage to full head emergence Two applications: First—4 leaf stage to flag leaf stage Second—up to full head emergence May be applied by ground in 100–200 L water/ha or by air in 50 L water/ha.
Barley			
Net blotch Spot blotch Scald Septoria leaf blotch Leaf and stem rust			
Oats			
Septoria leaf blotch Crown rust			

7.1.2 Mode of action

Trifloxystrobin is a new active ingredient belonging to the strobilurin class of fungicides. It acts by hydroquinone binding, thus obstructing electron transfer in mitochondria and inhibiting respiration in fungal cells. This results in inhibition of spore germination and germ tube extension, so that infection is prevented. Although it has some curative properties, trifloxystrobin is to be used primarily as a protectant, that is, first applied prior to spread of disease symptoms. Propiconazole, co-formulated in Stratego 250 EC, has a different mode of action. It has systemic activity and inhibits sterol biosynthesis.

7.1.3 Crops

Compass 50 WG is proposed for use on turfgrass and ornamentals. Flint 50 WG is proposed for use on grapes, pome fruit (apples, pears, crabapples) and wheat. Stratego 250 EC is proposed for use on wheat, barley and oats.

7.1.4 Effectiveness against pests

On turf and ornamentals, Compass 50 WG typically provided disease control equivalent to, or slightly less than, other strobilurins. For some claims there were insufficient trials or inadequate levels of control to support claims for control of the specified diseases. Accepted claims were control of brown patch, leaf spot and gray leaf spot on turf, Myrothecium leaf spot on ornamentals except crabapple and hawthorn, powdery mildew on container and tree ornamentals except rose and citrus, apple scab on crabapple and hawthorn, and Rhizoctonia root rot of ornamentals (for use as a drench at seeding only). Proposed tankmixes of Compass 50 WG with Banner MAXX were not accepted.

On grapes, apples, pears and wheat, Flint 50 WG typically provided disease control similar to other strobilurins, mancozeb or captan and slightly less than sterol inhibitors. In most cases there were sufficient trials and adequate levels of control to support claims for the proposed diseases and application rates. Accepted claims include control of powdery mildew and black rot on grapes; scab, sooty blotch, fly speck, powdery mildew and cedar apple rust on pome fruit (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince); and rust, powdery mildew, Septoria leaf blight and tan spot on wheat (winter, spring, hard red, durum, Canada prairie and soft white). Septoria glume blotch of wheat was not accepted due to insufficient data for the proposed use directions. Acceptance of the claim for black rot on grapes is conditional on submission of further trials to confirm that 140 g/ha is the lowest effective rate.

Stratego 250 EC, containing trifloxystrobin and propiconazole, is accepted for control of Septoria leaf blotch, tan spot, powdery mildew, leaf and stem rust, and stripe rust of wheat, net blotch, scald and Septoria leaf blotch of spring barley, and Septoria leaf blotch and crown rust of oats. Claims for control of Septoria glume blotch of wheat, spot blotch, leaf rust and stem rust of barley were not accepted due to insufficient supporting data. Accepted disease claims can be extended to all wheat types (winter wheat, spring wheat including hard red, durum, Canada prairie and soft white). Without the application for glume blotch, the product is to be applied as a foliar spray once or twice between cereal four-leaf stage and when the head is half-emerged, as indicated on other fungicide labels for propiconazole. A 45-day preharvest interval should not be necessary.

7.2 Phytotoxicity to target plants or to target plant products

For Compass 50 WG no crop tolerance trials were submitted to address phytotoxicity directly, however observations were noted in efficacy trials with a very limited number of ornamental and turf varieties. The corresponding U.S. label suggests that a larger number of ornamentals have been tested for phytoxicity in practice. A note on the proposed Canadian label indicates a few plants known to be injured by the product; however, it is prudent to add a more general statement as well, advising that the grower test the product on a small number of plants before using it for commercial scale production on any new variety.

Two trials tested Flint 50 WG on Concord grapes, and found rates as low as 35 g a.i./ha produced phytotoxic symptoms on leaves (burning, curling and crinkling). No other varieties showed crop injury as a result of Flint 50 WG applications. An advisory statement against application or drift to Concord grapes is already on the proposed label. Other strobilurin fungicides have shown adverse effects to certain apple varieties. Aside from slight russetting in one out of several apple trials on variety MacIntosh, no phytotoxicity was reported for Flint 50 WG on apples, pears or wheat.

Crop tolerance was assessed in terms of yield effect of Stratego 250 EC at sites with or without disease. Yields of cereal crops were typically improved by most treatments including Stratego 250 EC, compared with the untreated check. No yield suppression or other phytotoxic effects were noted in the efficacy trials.

7.3 Impact on succeeding crops, adjacent crops and on treated plants or plant products used for propagation

7.3.1 Impact on succeeding crops

Not assessed.

7.3.2 Impact on adjacent crops

The Flint 50 WG label includes recommendations to avoid spray equipment residues and spray drift that might affect Concord grapes grown adjacent to other varieties or to apple orchards.

7.4 Economics

Not assessed.

7.5 Sustainability

7.5.1 Survey of alternatives

7.5.1.1 Non-chemical control practices

The proposed control claims of Compass 50 WG, Flint 50 WG and Stratego 250 EC are for diseases affecting primarily the foliage of cereal crops, fruit crops, ornamentals and turf. Non-chemical control practices for these diseases may include use of resistant or tolerant varieties, disease avoidance by altering planting dates, rotation with non-host crops, removal of infested crop debris and sanitation of enclosed structures. Management of the crop canopy by planting, thinning, mowing, irrigation or pruning can also contribute by reducing leaf wetness or humidity that favour disease. A few biological control products have recently been registered but are limited to greenhouse use on ornamentals.

7.5.1.2 Chemical control practices

For a list of alternative products registered for the same crops and diseases as trifloxystrobin see Appendix IV, Table 1.

7.5.2 Compatibility with current management practices including integrated pest management

Trifloxystrobin products are generally compatible with current management practices. They will add to the limited options for ornamental and turf disease control. Flint 50 WG can be substituted for applications of older chemicals in disease control programs in orchards and vineyards. It will provide an alternative chemistry for cereals where few fungicide options are available and can contribute to resistance management. No adverse effects on beneficial insects (predators and parasites) were noted in trifloxystrobin efficacy trials; however, some species were shown to be affected in environmental toxicology studies (see Section 6.4.2), which should be considered if these species are important to the insect or arthropod control program.

7.5.3 Contribution to risk reduction

Not assessed.

7.5.4 Information on the occurrence or possible occurrence of the development of resistance

Trifloxystrobin belongs to the strobilurin class of fungicides [Group 11, Quinone Outside Inhibitors (QoIs)] that exhibit no known cross-resistance to fungicides in other chemical classes, i.e., sterol inhibitors, dicarboximides, benzimidazoles, anilinopyrimidines or phenylamides. Resistance to some fungicides within Group 11 has been reported, however. The North American Fungicide Resistance Action Committee (NAFRAC) has developed guidelines for management of the QoI group of fungicides, both general and crop-specific. Limitations on number of sequential and total applications of this group refer to foliar use only and do not include seed treatment or soil drench.

For turf resistance management, the NAFRAC recommended limit is two applications of a QoI fungicide followed by at least two applications of a fungicide from another (non-QoI) group (2:≥2 rotation) for control of most turf diseases. A rotation of 1 QoI:≥1 non-QoI is recommended for gray leaf spot, which is apparently more prone to resistance. Gray leaf spot is a new disease to Canada and there are no registered fungicides available for rotation at this time. For ornamental resistance management, general NAFRAC recommendations are a 1:≥1 rotation with non-QoI fungicides. On the Compass 50 WG label, all diseases, including higher risk pathogens, would be conservatively covered by this rotation sequence.

A maximum number of applications is not specified for turf and ornamentals but in general, QoI use without any tankmixed applications should not exceed 1/3 of the total number of fungicide applications. This is addressed by the label limitation of 2.4 kg/ha/year for turf and four applications per crop cycle or season for ornamentals.

The Flint 50 WG label proposes the following maximum number of applications: pome fruits four, wine or table grapes four, other grapes three and wheat two, which is consistent with NAFRAC recommendations on these crops. A rotation of two strobilurin to two non-strobilurin applications is also recommended for pome fruit and vine crops. There are no rotations identified yet for wheat, for which only two applications per season are proposed.

Stratego 250 EC contains fungicides with two complementary chemistries—strobilurin and sterol inhibitor. Its limited use on cereals (two applications per year) and the combination of these active ingredients is consistent with NAFRAC recommendations for management of both groups.

All trifloxystrobin product labels should include the proposed management strategies within the standard Resistance Management statements as per Regulatory Directive DIR99-06.

7.6 Conclusions

For details of accepted uses, see Appendix IV, Table 2.

Compass 50 WG is accepted for control of:
- brown patch, leaf spot and gray leaf spot on turf;
- Myrothecium leaf spot on ornamentals except crabapple and hawthorn;
- powdery mildew on ornamentals except rose and citrus;
- apple scab on crabapple and hawthorn; and
- Rhizoctonia root rot of ornamentals (for use as a drench at seeding only).

Tankmixes were not supported.

Flint 50 WG is accepted for control of:
- powdery mildew and black rot on grapes;
- scab, sooty blotch, fly speck, powdery mildew and cedar apple rust on pome fruit (apple, crabapple, loquat, mayhaw, pear, oriental pear and quince); and
- rust, powdery mildew, Septoria leaf blight and tan spot on wheat (including winter, spring, hard red, durum, Canada prairie and soft white).

Acceptance of the claim for black rot on grapes is conditional on submission of further trials to confirm that 140 g/ha is the lowest effective rate.

Stratego 250 EC, containing trifloxystrobin and propiconazole, is accepted for control of:
- Septoria leaf blotch, tan spot, powdery mildew, leaf and stem rust and stripe rust of wheat (including winter wheat, spring wheat including hard red, durum, Canada prairie and soft white);
- net blotch, scald and Septoria leaf blotch of spring barley; and
- Septoria leaf blotch and crown rust of oats;

Proposed resistance management statements on these product labels require some revision to be consistent with latest recommendations from NAFRAC.

8.0 Toxic Substances Management Policy considerations

During the review of Trifloxystrobin Technical Fungicide, Compass 50 WG, Stratego 250 EC and Flint 50 WG, the PMRA has taken into account the federal Toxic Substances Management Policy[1] and has followed its Regulatory Directive DIR99-03[2]. It has been determined that this product does not meet TSMP Track 1 criteria because:

- Trifloxystrobin does not meet the criteria for persistence. Its values for half-life in water (DT_{50} < 8 hours), soil (DT_{50} < 1 day) and sediment (DT_{50} < 1 day) are below the TSMP Track 1 cut-off criteria for water (≥ 182 days), soil (≥ 182 days) and sediment (≥ 365 days). Although data on the persistence in air were not available, the vapour pressure and Henry's Law constant indicate that trifloxystrobin will not volatilize from water or moist soil under field conditions, thus long-range atmospheric transport of trifloxystrobin is not likely to occur.

- Trifloxystrobin is not bioaccumulative. The octanol–water partition coefficient (log K_{ow}) is 4.5, which is below the TSMP Track 1 cut-off criterion of > 5.0.

- The toxicity of trifloxystrobin and its end-use products, Compass 50 WG, Stratego 250 EC and Flint 50 WG are summarized in sections 3.6, 4.7 and 6.4. The end-use products are predicted to pose a high to very high risk to aquatic organisms; however, their conditions of use can be adequately mitigated to minimize exposure of aquatic habitats.

- Trifloxystrobin does not form any major transformation products that meet the TSMP Track 1 criteria.

- Trifloxystrobin (technical grade) does not contain any by-products or microcontaminants that meet the TSMP Track 1 criteria. On the basis of its chemical structure, trifloxystrobin will not form chlorinated dioxins, dibenzofurans or hexachlorobenzene and none of the starting materials will contain or form these compounds. Impurities of toxicological concern are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process.

The formulated products do not contain any formulants that are known to contain TSMP Track 1 substances.

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1 The federal *Toxic Substances Management Policy* is available through Environment Canada's Web site at the following site: www.ec.gc.ca/toxics

2 The *Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, DIR99-03, is available through the PMRA's Information Service. Phone: 1-800-267-6315 within Canada or (613) 736-3799 outside Canada (long distance charges apply); Fax: (613) 736-3798; E-mail: pmra_infoserv@hc-sc.gc.ca or through our Web site at www.hc-sc.gc.ca/pmra-arla

9.0 Regulatory decision with additional data requirements

The PMRA has carried out an assessment of available information in accordance with Section 9 of the Pest Control Products (PCP) Regulations and has found it sufficient pursuant to Section 18(*b*), to allow a determination of the safety, merit and value of trifloxystrobin technical, Compass 50 WG, Flint 50 WG and Stratego 250 EC. The Agency has concluded that the use of trifloxystrobin and the associated end-use products in accordance with the enclosed annotated labels has merit and value consistent with Section 18(*c*) of the PCP Regulations and does not entail an unacceptable risk of harm pursuant to Section 18(*d*). The Agency has determined that these products are eligible for temporary registration pursuant to Section 17(*a*), subject to the Terms and Conditions outlined in the registration letter and summarized below:

- submission of an enforcement analytical method for animal matrices which includes a microwave assisted extraction step to release the majority of bound residues;

- submission of four supervised residue trials conducted on grapes grown in zone 5;

- submission of monitoring data of treated apple samples collected from zones 1A and 5B;

- submission of a long-term hydrolysis study conducted with CGA-321113 at a lower temperature (10°C) relevant to groundwater in Canada for one year or until a 50% decline is observed. Shorter-term hydrolysis studies should also be run concurrently at several elevated temperatures (20, 30, 40, 50°C) in order to determine if hydrolysis takes place at all, and to extrapolate to lower temperatures;

- submission of a chronic freshwater fish, early life cycle toxicity test with CGA-321113;

- submission of a dissipation/accumulation study on turf, since Compass 50 WG is to be applied to turf. The study should be conducted in compliance with the Agriculture Canada T-1-255 Guideline and should entail side-by-side turf and bare soil plots; and

- submission of grape efficacy trials in Canada or northern U.S. at sites with high disease pressure, comparing 105 and 140 g/ha Flint 50 WG applied every 7 to 14 days for control of black rot. Sufficient trials should be conducted to demonstrate whether 105 or 140 g/ha is the lowest effective rate for black rot control.

List of abbreviations

a.i.	active ingredient
ACN	acetonitrile
ADI	acceptable daily intake
AFC	antibody-forming cell
ALP	alkaline phosphatase
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
bw	body weight
bwg	body-weight gain
B	biomass
BWI	body weight per individual
B-cells	bursa derived lymphocytes
CAS	Chemical Abstracts Service
CD	cluster of differentiation (for naming cell surface molecules expressed on lymphocytes in immunology)
ConA	concavalin A
d	day(s)
DAT	days after treatment
DFR	dislodgeable foliar residues
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50%
EC	emulsifiable concentration
EEC	expected environmental concentration
EP	end-use product
FAR	field application rate
FC	food consumption
FID	flame ionized detection
FOB	functional observational battery
F_0	parental animals
F_1	1^{st} generation offspring
F_2	2^{nd} generation offspring
GC	gas chromatrography
GIT	gastrointestinal tract
GSD	geometric standard deviation
hL	hectolitre
ILV	independent laboratory method validation
IUPAC	International Union of Pure and Applied Chemistry
K_{ow}	octanol–water partition coefficient
K_d	adsorption quotient
K_{oc}	adsorption quotient normalized to organic carbon
LC_{50}	lethal concentration 50%
LCO	lawn care operator
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level

LOD	limit of detection
LOQ	limit of quantitation
LPS	lipopolysaccharide
MIS	maximum irritation score
MAS	maximum average score (at 24, 48 and 72 h)
M/L	mixers, loaders
M/L/A	mixers, loaders, applicators
MMAD	mass median aerodynamic diameter
MNP	1-methyl-2-pyrodidinone
MOE	margin of exposure
MOR	magnitude of residues
MOS	margin of safety
MRL	maximum residue limit
MTBE	methyl-tert-butyl ether
NAFRAC	North American Fungicide Resistance Action Committee
NAFTA	North American Free Trade Agreement
NK	natural killer cell
NOAEL	no observed adverse effect level
NPD	nitrogen phosphorous detector
ORETF	Outdoor Residential Exposure Task Force
PCP	pest control product
PFC	plaque-forming cell assay
PC	positive control
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
PRDD	Proposed Registration Decision Document
pK_a	dissociation constant
PMA	phorbol myristate acetate
ppb	parts per billion
ppm	parts per million
QoI	quinone outside inhibitor
REI	re-entry interval
RQ	risk quotient
RSD	relative standard deviation
sRBC	sheep red blood cell preparation (T-cell dependent antigen)
STMdR	supervised trial median residue
T-cells	thymic derived lymphocytes
T3	tri-iodothyronine
T4	thyroxine
TBC	thyroxine-binding capacity
TC	transfer coefficient
TGAI	technical grade active ingredient
TRR	total radioactive residue
TSH	thyroid stimulating hormone
TS	test substance
TSMP	Toxic Substances Management Policy

TTR	turf transferable residues
UDPGT	uridine 5'-diphosphatase-glucuronyl transferase
UDS	unscheduled deoxyribonucleic acid synthesis
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
µg	microgram
µL	microlitre

Appendix I Toxicology Summary Tables

Table 1 Toxicity summary table

METABOLISM—The fate of CGA-279202 (TRIFLOXYSTROBIN) was investigated in male and female rats after single oral administration of ^{14}C labelled compound at dose levels of 0.5 or 100 mg/kg bw or as a daily doses (0.5 mg/kg bw) of non-labelled test material following by one radiolabelled dose.			
The rate of absorption was moderate. The experiment with bile-canulated rats demonstrated that at low dose, (single or repeated), 56% and 65% administered dose was absorbed by males and females, respectively, with 41 and 47% being in bile of males and females, respectively. In the high dose group, the degree of absorption was 41 and 27%, while the bile content was 35% and 19%, respectively to males and females. The blood kinetics revealed a moderate absorption rate in both sexes with two peaks (after 0.5 and 12 hours at the low dose level and 12 and 24 hours after the high dose). The areas under the blood time curve (AUC) were similar for both sexes indicating a similar bioavailability. **Distribution:** Seven days either after a single or repeated oral administration of 0.5 mg/kg, the tissue residues were very low. The highest residues were found in blood, kidneys, liver, spleen, and were comparable between sexes. The radioactivity in the blood was associated mainly with the red blood cells. The radioactivity depleted from tissues and organs with half-lives of 13 to 33 hours independent of the dose and sex. The slowest depletion occurred in blood and spleen. **Excretion:** The excretion was rapid: 85–96% of the dose was excreted within 48 hours independent of the dose, pretreatment with non-labelled test material and sex of the animals. Seven days after administration the radioactivity was almost completely eliminated. The route of elimination was influenced by sex of the animals: females eliminated twice the amount with the urine than males, accounting for 27–42% and 12–19% of the dose, respectively. The amounts excreted via feces were 79–82% and 56–64% of the administered dose (AD) in males and females, respectively. In both sexes biliary excretion was the major route of elimination. The involvement of an enterohepatic shunt mechanism in the elimination process is indicated. **Metabolism:** About 35 metabolites were isolated from urine, feces and bile and identified. The major route in metabolic pathway is hydrolysis of the methyl ester to the acid, O-demethylation of the methoxyimino group yielding a hydroxyimino compound and oxidation of the methyl side chain to a primary alcohol followed by partial oxidation to the respective carboxylic acid. The major metabolic pathways postulated were significantly influenced by the sex of the animals but not by the dose level and pretreatment within the limits of this study.			
STUDY	**SPECIES/STRAIN AND DOSES**	**NOEL/NOAEL and LOEL mg/kg bw/day**	**TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS**
ACUTE STUDIES—Technical			
Oral	Rat—Tif:RAI; 5/sex; 5000 mg/kg bw	LD_{50} > 5000 mg/kg	Hypersensitivity to touch, red stained face, excessive salivation, soft/watery stool, darked stained urogenital areas up to day 12. **Low Toxicity**
Oral	Mouse—Tif:MAG; 5/sex; 5000 mg/kg	LD_{50} > 5000 mg/kg	Piloerection and hunched posture up to day 2 in males and females. **Low Toxicity**
Dermal	Rabbit—NZW, 5/sex; 2000 mg/kg	LD_{50} > 2000 mg/kg	**Low Toxicity**

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
Dermal	Rat—Tif:RAI; 5/sex; 2000 mg/kg	LD_{50} > 2000 mg/kg	**Low Toxicity**
Inhalation	Rat—SD, 5/sex/dose; 1.39 and 4.65 mg/L	LC_{50} > 4.65 mg/L MMAD = 2.6–4.9 µm GSD = 1.90–2.02 µm	Piloerection and ptosis up to day 4. Weight loss in two females at days 1 to 7. **Low Toxicity**
Skin Irritation	Rabbit—NZW, 3/sex; 0.5 g dose	MIS = 1.7 at 4 hours MAS = 0.3 (24, 48 and 72 h)	**Mildly Irritating**
Eye Irritation	Rabbit—NZW; 3/sex 0.047 g dose	MIS = 11.5 at 24 hours MAS = 8.6 (24, 48 and 72 h)	Conjunctival irritation in 4 rabbits up to and including 96 hours. **Mildly Irritating**
Skin Sensitization (Buehler method)	Guinea pig—HA; 10 males in the test group; 4 males for positive control. 0.4 g of test material for induction and challenge. Positive control, DNCB, 0.3% for induction, 0.1% for challenge.	Test material gave a negative sensitization response DNCB positive control gave a positive response showing the responsiveness of the assay	**Not a Skin Sensitizer**
Skin Sensitization (Maximization Test)	Guinea pig—Pirbright white, 10/sex; 5% and 50% of test material for intradermal and epidermal induction, respectively; 30% for challenge	No positive control group Test material gave a positive skin sensitization response	**Potential Skin Sensitizer**
SPECIAL ACUTE STUDIES—METABOLITES OF TRIFLOXYSTROBIN			
Oral (with CGA-373466, a metabolite of Trifloxystrobin)	Rat—Winstar, 5/sex; 2000 mg/kg bw	LD_{50} > 2000 mg/kg	**Low Toxicity**
Oral (with NOA-414412, a metabolite of trifloxystrobin)	Rat—Winstar, 5/sex; 2000 mg/kg bw	LD_{50} > 2000 mg/kg	Piloerection and hunched back in males with recovery within 1 day. **Low Toxicity**
Oral (with Z,E-isomer of trifloxystrobin)	Rat—Tif:RAI; 5/sex; 2000 mg/kg	LD_{50} > 2000 mg/kg	**Low Toxicity**
ACUTE STUDIES—FLINT 50 WG (EP)			
Oral	Rat—Sprague-Dawley, 5/sex, 5000 mg/kg bw/day	LD_{50} > 5000 mg/kg	**Low Toxicity** No signal words required

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
Oral	Rat—Tif:RAI f (SPF) 5/sex, 2000 mg/kg bw/day	LD_{50} > 2000 mg/kg	**Low Toxicity** No signal words required
Dermal	Rabbit NZW 5/sex, 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw	**Low Toxicity** No signal words required
Inhalation	Rat—Sprague-Dawley (5/sex)	LC_{50} > 2.74 mg/L	**Low Toxicity** No signal words required
Skin Irritation	Rabbit—NZW, 3/sex (0.5 g)	MIS = 1.5/8.0 at 1 hour	**Slightly Irritating** No signal words required
Eye Irritation	Rabbit—NZW, 3/sex (100 mg) unwashed and washed eye	MIS = 10.8/110 at 24 hours and persisted up to and including 72 hours (unwashed eye) MIS = 7.3/110 at 1 hour (washed eye)	**Mildly Irritating** **Caution Eye Irritant**
Dermal Sensitization (Buehler Test)	Guinea Pigs—Albino (10/sex) 50% induction 10% challenge	No Skin Sensitizer by the Buehler test. No maximization test was conducted, which is more sensitive than Buehler test.	**Potential Skin Sensitizer**
ACUTE STUDIES—STRATEGO 250 EC (EP)			
Oral	Rat—Tif:RAI f (SPF) 5/sex, 2000 mg/kg	LD_{50} > 2000 mg/kg	**Low Toxicity**
Dermal	Rat—Tif:RAI f (SPF) 5/sex, 4000 mg/kg bw	LD_{50} > 4000 mg/kg bw	**Low Toxicity**
Inhalation	Rat—HanImb:WWIST (SPF) (5/sex)	LC_{50} > 4.88 mg/L	**Low Toxicity**

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
Skin Irritation	Rabbit—NZW, 3 females (0.5 mL)	MIS = 1.0/8.0 at 24, 48 and 72 hours	**Slightly Irritating** No signal words required
Eye Irritation	Rabbit—NZW, (3 males) (0.1 mL) unwashed eye)	MIS = 14.7/110 at 24 and 48 hours (irreversible)	**Severely Irritating** **Danger Eye Irritant**
Dermal Sensitization (Buehler Test)	Guinea Pigs—Pirbright White (10/sex) 100% induction 30% challenge	Not Skin Sensitizer	**Not Skin Sensitizer**
Skin Sensitization (Maximization Test)	Guinea pig—Pirbright white, 10/sex; 5% and 50% of test material for intradermal and epidermal induction, respectively; 30% for challenge	No positive control group Test material gave a positive skin sensitization response	**Potential Skin Sensitizer**
ACUTE STUDIES—COMPASS 50 WG (EP)			
Oral	Rat—Tif:RAI f (SPF) 5/sex, 2000 mg/kg	LD_{50} > 2000 mg/kg	**Low Toxicity**
Dermal	Rat—Tif:RAI f (SPF) 5/sex, 4000 mg/kg bw	LD_{50} > 4000 mg/kg bw	**Low Toxicity**
Inhalation	Rat—HanImb:WWIST (SPF) (5/sex)	LC_{50} > 4.88 mg/L	**Low Toxicity**
Skin Irritation	Rabbit—NZW, 3 females (0.5 mL)	MIS = 1.0/8.0 at 24, 48 and 72 hours	**Slightly Irritating** No signal words required
Eye Irritation	Rabbit—NZW, (3 males) (0.1 mL)	MIS = 10.8/110 at 24 hours and persisted up to and including 72 hours (unwashed eye) MIS = 7.3/110 at 1 hour (washed eye)	**Mildly Irritating** **Caution Eye Irritant**
Dermal Sensitization (Buehler Test)	Guinea Pigs—Pirbright White (10/sex) 100% induction 30% challenge	No Skin Sensitizer by the Buehler test. No maximization test was conducted, which is more sensitive than Buehler test.	**Potential Skin Sensitizer**

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
SHORT-TERM AND SUBCHRONIC STUDIES			
28-day, capsules (dose range finding study)	Beagle dog 2/sex/dose 0 (empty capsule), 20, 50 or 150 mg/kg bw/day for 29 days. At day 29, dogs in control, 20 and 50 mg/kg bw/day, were sacrificed. Due to a lack of toxic effects the dosage level for dogs in the 150 mg/kg bw/day groups was increased to 500 mg/kg bw/day for an additional 21 days.	NOAEL = 20/50 mg/kg bw/day (M/F) LOAEL = 50 mg/kg bw/day (M) 150/500 mg/kg bw/day (F)	**50 mg/kg/d (M):** ↓body weight and food consumption. **150/500 mg/kg/d:**clinical signs [diarrhea, vomiting (M&F)], ↓body weight and food consumption (M), ↑relative liver and spleen weights (F)
28-day dermal, rat	Tif:RAIf (SPF)—rat 10/sex/dose 0, 10, 100 or 1000 mg/kg bw/day, 5 days/week (4 mL/kg bw)	Systemic toxicity NOAEL = 100/1000 mg/kg bw/day (M/F) LOAEL = 1000 mg/kg bw/day (M) Dermal toxicity NOAEL = 1000 mg/kg bw/day (M&F)	**1000 mg/kg/d (M) :** ↑ absolute and relative liver and kidney weights.
28-day oral, rat	Tif:RAIf (SPF)—rat 5/sex/dose 0, 200, 100, 4000, 12,000 ppm equal to 0, 16.5, 84.4, 337 or 1074 mg/kg bw (M); 0, 16.4, 84.1, 327 or 1005 mg/kg bw/day (F)	NOAEL = 200/400 ppm (M/F) (16.5/84/1 mg/kg bw/day M/F) LOAEL = 1000/4000 ppm (84.4/327 mg/kg bw/day, M/F)	≥ **84.4/327 mg/kg/d:** ↓body weight (M), body weights, alteration in blood chemistry (F) ≥ **337 mg/kg/d:** ↑relative liver weights (M) **1074/1005 mg/kg/d:** ↑ relative kidney weight (M), ↑ relative kidney and liver weight (F).
90-day dietary, mouse	Tif:MAGf (SPF) —mouse 10/sex/dose 0, 200, 2000 or 7000 ppm equal to 0, 76.9, 315 or 1275 mg/kg bw/day (M) and 0, 110, 425 or 1649 mg/kg (F)	NOAEL = 500 ppm (M/F) (77.9/110 mg/kg bw/day, M/F) LOAEL = 2000 ppm (M/F) (315/425 mg/kg bw/day, M/F)	**315/425 mg/kg/d:** ↑ absolute and relative liver weights (M&F), ↑ incidence of necrosis of hepatocytes (M&F), ↑ incidence of splenic extramedullary hematopoiesis (M). **1275/1649 mg/kg/d:** ↓body-weight gain (M), ↑ water consumption (F), ↑ in absolute and relative spleen weights, ↑ incidence hypertrophy of hepatocytes, and splenic extramedullary hematopoiesis and hemosiderosis (M&F)

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
90-day dietary, rat (4-week recovery)	Tif:MAGf (SPF)—rat 15/sex/dose 0, 100, 500, 2000 or 8000 (F only) ppm (equal to 0, 6.4, 30.6 or 127.3 mg/kg bw/day (M) 0, 6.8, 32.8, 132.5 or 618.3 mg/kg bw/day (F) 10/sex/dose dosed at 0, 2000 (M) and 8000 ppm (F)—treated for 90 days and 4-week recovery period (FOB and motor activity)	**Systemic toxicity** NOAEL = 100/500 ppm (M/F) (6.4/32.8 mg/kg bw/day, M/F) LOAEL = 500/2000 ppm (M/F) (30.6/132.5 mg/kg bw/day, M/F) **Neurotoxicity** NOAEL > 2000/8000 ppm (M/F) (127.3/613.8 mg/kg bw/day, M/F)	**30.6/132.5 mg/kg/d (M/F):** ↓ food consumption ↓ body-weight gains, ↑ relative liver and kidney weights (M&F), ↓ food and water intake, ↓ body-weight gains, ↓ total protein and globulin levels in plasma, atrophy of pancreatic parenchyma (F). **127.3/618.3 mg/kg/d (M/F):** ↓ body-weight gain (M&F), ↓ water intake (M&F),↓ total protein and globulin levels in plasma (F), ↑ cholesterol (M), ↑glucose and BUN (F), ↑ relative liver weight (M&F), hypertrophy of the hepatocytes, atrophy of pancreatic parenchyma (M&F), atrophy of salivary gland, uterus, thymus (F). Atrophy of pancreas in M after 4-week recovery. No effect on FOB and motor activity.
90-day/capsule	Beagle dog 4/sex/dose 0, 5, 30, 150, 500 mg/kg bw/day	NOAEL = 30 mg/kg bw/day (M&F) LOAEL = 150 mg/kg bw/day	**150 mg/kg bw/d:** clinical signs (vomiting, diarrhea), ↓ body weight, ↓ creatine levels, ↑liver weights (M&F), ↑ incidence liver hepatocytes hypetrophy (M). **500 mg/kg/d**: clinical signs (vomiting, diarrhea), ↓body-weight gain and food intake, ↑ incidence of hypochromatic anaemia, eosinopenia, ↓ plasma creatine, albumin, globulin, bilirubin, alanine amino-transferase, cholesterol and ↑ triglycerides, ↑ incidence of emaciation, ↑liver, kidneys, adrenal glands, brain, thyroid, ↓ weights of heart thymus, testis, ↑ incidence hypertrophy of hepatocytes (M&F).

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
12-month/capsule	Beagle dog 4/sex/dose 0, 2, 5, 50, 200 mg/kg bw/day	NOAEL = 5 mg/kg bw/day (M&F) LOAEL = 50 mg/kg bw/day	**50 mg/kg/d:** diarrhea, vomiting (M&F), ↓body-weight gains and food consumption (F), ↓ plasma albumin and ↑ alkaline phosphatase M), ↑ liver weights (M&F), ↑ incidence of liver hepatocytes hypertrophy (F). **200 mg/kg/d:** diarrhea, vomiting, (M&F) ↓ body-weight gains and food consumption (F), ↓ plasma albumin (M), ↑ alkaline phosphatase (M&F), ↑ liver weights (M&F), ↑ incidence liver hepatocyte hypertrophy (M&F).
CHRONIC TOXICITY/ONCOGENICITY			
80-week dietary	Tif:MAGf(SPF)—mice 70/sex/dose 0, 30, 300, 1000, 2000 ppm (equal to 3.9, 39.4,131.1, 274 mg/kg bw/day (M) 0, 3.5, 35.7, 124.1, 246 mg/kg bw/day (F)	NOAEL = 300 ppm (39.4/35.7 mg/kg bw/day (M/F) LOAEL = 1000 ppm (131.1/124.1 mg/kg bw/day, M/F) **No carcinogenic potential**	**131.1/124.1 mg/kg/d:** ↑ relative liver weights (F), single cell necrosis and/or necrosis in the liver (M&F), ↑ incidence hepatocellular hypertrophy (F). **274/246 mg/kg/d:** ↓body-weight gain (M&F), ↓food intake (F), ↑relative liver weights (M&F), enlarged liver (M), single cell necrosis and/or necrosis in the liver, ↑ incidence hepatocellular hypertrophhy (M&F), ↑incidence hepatocellular fatty changes (M)
2-year dietary	Tif:MAGf(SPF)—rats 70/sex/dose 0, 50, 250, 750 or 1500 ppm (equal to 0, 1.95, 9.81, 29.7 or 62.2 mg/kg bw/day (M) 0, 2.22, 11.4, 34.5 or 72.8 mg/kg bw/day (F)	NOAEL = 750/250 ppm (M/F) (29.7/11.4 mg/kg bw/day, M/F) LOAEL = 1500/750 ppm (M/F) (62.2/34.5 mg/kg bw/day, M/F) **No carcinogenic potential**	**62.2/34.5 mg/kg/d:** ↓body-weight gain (M&F), ↓ food intake, ↑ incidence of diarrhea towards the end of the study, ↑ water consumption and slightly ↑ incidence of cyst in pituitary gland and angiomatous hyperplasia of the mesenteric lymph node (M). **72.8 mg/kg/d (F):** ↓ body-weight gain, food and water consumption, ↑ relative liver weight (F)

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
REPRODUCTION/DEVELOPMENTAL TOXICITY			
Multi-generation 2 litters in F_0 1 litter in F_1	Tif:RAIf (SPF)—rat 30/sex/dose 0, 50, 750 or 1500 ppm—F_0&F_1 (equal to 0, 3.8/4.1, 55.3/58 or 110.6/123.1 mg/kg bw/day M/F—F_0 4.2/4.4, 65.5/67 or 143/146 mg/kg bw/day M/F—F_1	**Parental Toxicty** NOAEL = 50 ppm (3.8/4.1 mg/kg bw/day, M/F) LOAEL = 750 ppm (55.3/58 mg/kg bw/day, M/F) **Offspring Toxicity** NOAEL = 50 ppm (3.8/4.1 mg/kg bw/day, M/F) LOAEL = 750 ppm (55.3/58 mg/kg bw/day, M/F) **Reproductive** NOAEL = 1500 ppm (110/6/123.1 mg/kg bw/day, (M/F) LOAEL > 1500 ppm	**55.3/58-65.5/67 mg/kg/d (M/F):** ↓body-weight gains, food consumption (F_0&F_1), histopathological changes in liver hepatocellular hypertrophy —M&F—F_1), kidney (pigmentation of renal tubules, F_0—M) **110/123–143/146 mg/kg/d (M/F):** ↓body-weight gains, food consumption (F_0, F_1—M&F), histopathological changes in liver, hepatocellular hypertrophy—(F_0, F_1—M&F), kidney (pigmentation of renal tubules—F_0—M&F) **Offspring** ≥ **55.3/58 mg/kg/d**—F_{1a}, F_{1b} and F_2 pups:↓ body weight at lactation days 7, 14 and 21 **110.6/123–143/146 mg/kg/d**—F_{1a}, F_{1b} and F_2 pups: slight↑ in time of eye opening
Teratogenicity	Tif:RAIf (SPF), albino rats 24 females/dose 0, 10, 100, 1000 mg/kg bw/day in a 9.5% w/w aqueous solution of sodium carboxymethylcellulose	**Maternal** NOAEL = 10 mg/kg bw/day LOAEL = 100 mg/kg bw/day **Developmental** NOAEL = 100 mg/kg bw/day LOAEL = 1000 mg/kg bw/day	**Maternal** **100 mg/kg/d:** ↓ food consumption **1000 mg/kg/d:** ↓ body weight during the treatment and food consumption **Developmental:** **1000 mg/kg/d:** ↑ incidence of enlarged thymus **No evidence of teratogenicity**
Teratogenicity	Thomae Russian, Chbb:HM Rabbits 19 pregnant females/dose 0, 10, 50, 250, 500 mg/kg bw/day in a 0.5% w/w aqueous solution of sodium carboxymethylcellulose	**Maternal** NOAEL = 10 mg/kg bw LOAEL = 50 mg/kg bw/day **Developmental** NOAEL = 250 mg/kg bw/day LOAEL = 500 mg/kg bw/day	**Maternal** ≥ **50 mg/kg/d:** ↓body-weight gain, food consumption and food efficiencies **Developmental** **500 mg/kg/d:** ↑ incidence of skeletal variations (fused sternebrae 3 and 4) **No evidence of teratogenicity**

STUDY	SPECIES/STRAIN or CELL TYPE	DOSES EMPLOYED	EFFECTS
GENOTOXICITY			
Salmonella Typhimurium/ *E. coli* (Ames test) **CGA-373466—metabolite of CGA-279202**	TA 98, TA100, TA 102, TA 1535 TA1537, E.. *coli* WP2uvrA (Gene mutation)	0, 312.5, 625, 1250, 2500, 5000 µg/plate in the presence and absence S9	NEGATIVE
Salmonella Typhimurium/ *E. coli* (Ames test) **CGA-357261, Z, E-isomer of CGA-279202**	TA 98, TA100, TA 102, TA 1535 TA1537, E.. *coli* WP2uvrA (Gene mutation)	0, 312.5, 625, 1250, 2500, 5000 µg/plate in the presence and absence S9	NEGATIVE
Salmonella Typhimurium/ *E. coli* (Ames test) **NOA 414412 metabolite of CGA-279202**	TA 98, TA100, TA 102, TA 1535 TA1537, E.. *coli* WP2uvrA (Gene mutation)	0, 312.5, 625, 1250, 2500, 5000 µg/plate in the presence and absence S9	NEGATIVE
Mammalian chromosomal aberration (in vitro)	Chinese hamster lung fibroblasts (V79)	**Trial 1**—30, 87, 92.61, 277.83, 833.50 µg/mL (+S9) 1.14, 10.29, 92.61, 833.50 µg/mL (-S9) **Trial 2**—11.11, 33.33, 100, 300 µg/mL (+S9) 0.14, 1.23, 11.11 100 µg/mL (-S9) **Trial 3**—100, 150, 200, 250 µg/mL (+S9) 50, 75, 100 150 µg/mL (-S9)	POSITIVE (both activated and non-activated systems, at cytotoxic and precipitating conditions)
Mammalian chromosomal aberration (in vitro)	Chinese hamster ovary cells (CHO)	**At 18 hours**—0.049, 0.098, 0.78, 1.56, 1.75, 3.12 µg/mL (-S9) **At 42 hours**—0.049, 0.098, 0.175, 1.195 µg/mL (-S9) **At 3 hours**—12.5, 25, 50 µg/mL (+S9) **At 3 hours + 15 hours recovery**—25, 50, 100 µg/mL (+S9) **At 3 hours + 39 hours recovery**—12.5, 25, 50, 100 µg/mL (+S9)	NEGATIVE

STUDY	SPECIES/STRAIN or CELL TYPE	DOSES EMPLOYED	EFFECTS
Micronucleus Assay (in vivo) (Chromosomal aberrations)	Mouse bone marrow	0, 1250, 2500, 5000 mg/kg bw	NEGATIVE
UDS in vivo (DNA damage/repair)	Primary rat hepatocyte	0.39, 1.56, 6.25, 25, 50 µg/mL	NEGATIVE
Mammalian cytogenetics (in vitro) CGA-279202 CGA-321113	Primary rat hepatocyte and effects on mitochondrial function	5, 10, 30, 100, 300, 600 µM	CGA-279202—toxic at 30 and 100 µM CGA-321113—toxic at 600 µM
SPECIAL STUDIES			
Acute Range-finding Neurotoxicity	Tif:RAIf Sprague-Dawley rats 3/sex/dose 0, 1000, 2000, 3500 mg/kg bw—single dose suspended in 0.5% carboxymethylcellulose in 0.1% (w/v) aqueous polysorbate 80 Observation period—4 days	2000 mg/kg bw is a limit dose which should be used for acute neurotoxicity study	≥ **2000 mg/kg:** reduced activity appeared 2–4 hours after administration and reached a maximum at 6–8 hours post-dose **3500 mg/kg bw:** reduced activity lasted for 3 days in males while other animal had recovered on study day 2, piloerection at study day 1, ended on study day 2.
Acute Neurotoxicity	Tif:RAIf Sprague-Dawley rats, 10/sex/dose 0, 2000 mg/kg bw—single dose suspended in 0.5% carboxymethylcellulose in 0.1% (w/v) aqueous polysorbate 80. Observation period—15 days.	**Systemic toxicity** NOAEL = Not determined LOAEL = 2000 mg/kg bw **Neurotoxicity** NOAEL ≥ 2000 mg/kg bw/day	**2000 mg/kg bw:** ↓ in motor activity in F at study day 1 Considered systemic in origin

STUDY	SPECIES/STRAIN or CELL TYPE	DOSES EMPLOYED	EFFECTS
Subchronic Neurotoxicity [See 90-day dietary—rat (4-week recovery)]	Tif:MAGf (SPF)—rat 15/sex/dose 0, 100, 500, 2000 or 8000 (F only) ppm (equal to 0, 6.4, 30.6 or 127.3 mg/kg bw/day (M) 0, 6.8, 32.8, 132.5 or 618.3 mg/kg bw/day (F) 10/sex/dose dosed at 0, 2000 (M) and 8000 ppm (F)—treated for 90 days and 4-week recovery period (FOB and motor activity)	**Systemic toxicity** NOAEL = 100/500 ppm (M/F) (6.4/32.8 mg/kg bw/day, (M/F)) LOAEL = 500/2000 ppm (M/F) (30.6/132.5 mg/kg bw/day, M/F) **Neurotoxicity** NOAEL > 2000/8000 ppm (M/F) (127.3/613.8 mg/kg bw/day, M/F)	**30.6/132.5 mg/kg/d (M/F):** ↓ food consumption, ↓ body-weight gains, ↓relative liver and kidney weights (M&F),↓ food and water intake, ↓body-weight gains, ↓ total protein and globulin levels in plasma, atrophy of pancreatic parenchyma (F) **127.3/618.3 mg/kg/d (M/F):** ↓body-weight gain (M&F), ↓ water consumption (M&F),↓ total protein and globulin levels in plasma (F), ↑ cholesterol (M), ↑glucose and BUN (F), ↑ relative liver weight (M&F), hypertrophy of the hepatocytes, atrophy of pancreatic parenchyma (M&F), atrophy of salivary gland, uterus, thymus (F). Atrophy of pancreas in M after a 4-week recovery. **No effect on FOB and motor activity**
Compound-induced mortality: No treatment-related mortality in short or chronic toxicity studies.			
Recommended ARfD: Not recommended			
Recommended ADI: 0.038 mg/kg bw/day			

Appendix II Residues

Table 1 Integrated food residue chemistry summary

SUMMARY OF THE DIRECTIONS FOR USE IN EUROPE AND SOUTH AFRICA							
Crop	Country	Formulation	Application				
			Method	Rate (kg a.i./ha)	Number	Maximum rate (kg a.i./ha)	PHI (days)
Wheat	EU (N, S)	125 EC	Foliar	0.25	2	0.5	35
Barley	EU (N, S)	125 EC	Foliar	0.25	2	0.5	35
Grapes	EU (N, S)	50 WG	Foliar	0.188	6	1.128	35
	South Africa	50 WG	Foliar	0.09	6	0.54	14
Pomefruits	EU (N, S)	50 WG	Foliar	0.075	10	0.75	14
Apples	South Africa	50 WG	Foliar	0.005 kg a.i./hL	6	0.030 kg a.i./hL	7
Cucumber	EU (S)	50 WG	Foliar	0.188	5	0.94	3
Melons	EU (S)	50 WG	Foliar	0.125	5	0.625	3

DIRECTIONS FOR USE OF FLINT 50 WG ON GRAPES, POME FRUITS (apple, crabapple, loquat, mayhaw, pear, pear oriental and quince) AND WHEAT (winter, spring (including hard red, durum, Canada prairie, soft white)							
Crop		Formulation/type	Interval (day)	Rate g a.i./ha	No./ season	Maximum rate	PHI (days)
Grapes	Table and wine	water dispersible granule	7–14 or 21 depending on pest	70	4	280	14
	Other	water dispersible granule		70	3	210	14
Pome fruits		water dispersible granule	7–10 or 10–14 depending on pest	70–105	4	385	14
Wheat		water dispersible granule	14	123.5	2	245	35

Label Restrictions:

- Do not apply by air
- Do not apply Flint 50 WG to Concord grapes
- Bayer does not recommend the application of Flint 50 WG in combination with organosilicate surfactants at any time or crop injury may occur. Bayer does not recommend the application of Flint 50 WG in combination with tank mix adjuvants (such as nonionic surfactant, crop oil concentrates, penetrants, spreaders, stickers, etc.) at bloom or crop injury may occur.
- Grazing Restrictions:
  a) If two applications or a total of 490 g Flint 50 WG per hectare per season are applied, do not allow livestock to graze within the treated area and do not harvest the treated crop for forage or hay.
  b) If one application or a total of 245 g Flint 50 WG per hectare per season are applied, do not allow livestock to graze within the treated area within 30 days after application, and do not harvest the treated crop for forage within 30 days after application, 35 days for grain and straw and for hay within 45 days after application.

- Rotational Crops:
  Treated areas may be replanted immediately following harvest with any crop listed on this label. For crops not listed on this label, do not plant back within 30 days of last application.

DIRECTIONS FOR USE OF STRATEGO 250 EC ON WHEAT (winter, spring (including hard red, durum, Canada prairie, soft white), BARLEY (Spring) AND OATS

Crop	Formulation/type	Interval (day)	Rate g a.i./ha	No./ season	Maximum rate	PHI (days)
Wheat, barley, oats	emulsifiable concentrate	14	62.5	2	125	45

Label Restrictions:

- Do not apply Stratego 250 EC after the head is half emerged.
- Timing of Application(s)
  Single Application: 4-leaf stage before head is half emerged (GS 14-55)
  Two Applications: First application: 4-leaf stage to flag leaf stage
  Second application: before head is half emerged (GS 14-55), but not within 14 days of the first application.
- Grazing Restrictions:
  a) If 2 applications Stratego 250 EC per season are applied, do not allow livestock to graze within the treated area and do not harvest the treated crop for forage or hay.
  b) If 1 application of Stratego 250 EC per season is applied, do not allow livestock to graze within the treated area within 30 days after application, and do not harvest the treated crop for forage within 30 days after application and 45 days for grain, straw and for hay.
- Rotational Crops:
  Treated areas may be replanted immediately following harvest with any crop listed on this label. For crops not listed on this label, do not plant back within 30 days of last application.

PHYSICOCHEMICAL PROPERTIES

Water solubility at 25°C (mg/L)	0.61
Solvent solubility at 25°C (g/L)	<u>Solvent</u> — <u>Solubility</u> Methanol — 76 Acetone — > 500 Ethyl acetate — > 500 Dichloromethane — > 500 Toluene — 500 Hexane — 11 n-octanol — 18
Octanol–water partition coefficient (Log K_{ow}) at 25°C	<u>log K_{ow}</u> — <u>K_{ow}</u> 4.5 — 32 000
Dissociation constant (pK_a)	No dissociation constant in pH range 2–12
Vapour pressure at 25°C	3.4×10^{-6} Pa

Relative density at 21°C (g/mL)	1.36
Melting point (°C)	72.9
UV/Visible absorption spectrum	λmax / ϵ Methanol: 250 / 17 500 90% MeOH +10% HCl: 250 / 17 300 90% MeOH +10% NaOH: 252 / 15 800 No absorption between 340 and 750 nm.

ANALYTICAL METHODOLOGY

Parameters	Plant and animal matrices
Method ID	**AG-659A** (supersedes method AG-659 as it includes the extractability and accountability results from the ^{14}C-CGA-279202 animal sample validations, minor changes and suggestions from the ILV that has been made to improve the ruggedness of the method).
Type	Data gathering and enforcement
Analytes	Trifloxystrobin (CGA-279202) and the free form of the acetic acid metabolite (CGA-321113)
Instrumentation	GC/NPD
LOQ	All matrices 0.02 ppm/analyte Milk 0.01 ppm/analyte Peanut hay 0.05 ppm/analyte
Standard	An external standard method was used as marker for retention time, response and calibration.
ILV	An independent laboratory validation (ILV) was conducted to verify the reliability and reproducibility of Method AG-659, for the determination of trifloxystrobin and the acid metabolite (CGA-321113) in various plant and animal matrices. When incorporating the conditioning of the GC column with two injections of sample control matrix prior to the analytical run, the method trials for the determination of the two analytes were successful.
Extraction/clean-up	The analytical method involves extracting twice with acetonitrile (ACN):water (80:20, v:v). Liquid samples such as milk or juices are extracted by shaking for 15 min. in ACN:water and peanut oil is dissolved directly in ACN:water. After filtration, the extract volume is measured (and adjusted if necessary) and an aliquot is taken. A three-layer liquid–liquid partition is performed by adding water saturated with sodium chloride, toluene and hexane (peanut oil samples are extracted by adding four grams directly to a separatory funnel and forming the same three-layer partition). The middle layer is collected, partitioned a second time with hexane and evaporated. The sample is reconstituted in 0.085% aqueous phosphoric acid:acetone (95:5, v:v) and subjected to a C18 solid-phase extraction clean-up. After elution with 0.085% aqueous phosphoric acid:acetone (30:70, v:v), the sample is evaporated and partitioned into methyl-tert butyl ether (MTBE):hexane (1:1, v:v). The MTBE:hexane is evaporated to dryness and the sample is reconstituted in 0.1% polyethylene glycol in acetone (v:v) prior to analysis.

Radiovalidation	Plant matrices	Animal matrices
	Accountability results from the analysis of ^{14}C-CGA-279202 incurred plant samples during radiovalidation of this method appeared consistent with the results obtained in the apple and cucumber metabolism studies.	The analytical method AG-659A was not successfully radiovalidated for goat tissue as it was not capable of extracting all the radioactivity (66% extraction). As indicated in the lactating goat metabolism study, the extraction of liver with ACN and ACN:water released an average of 68%, however microwave assisted extraction released an additional 29% of the TRRs. Based on the results of the radiovalidation study and the ruminant metabolism study, a microwave extraction step should be included in the enforcement analytical method AG-659A for animal matrices to ensure that the majority of the residues are extracted.
Multiresidue method	The existing USFDA multiresidue methods of analysis, which are currently in common usage, were found to be suitable for the determination of CGA-279202 and CGA-321113 residues in plant and animal matrices.	

NATURE OF THE RESIDUE IN PLANTS—APPLES		
Radiolabel position	[Trifluoromethyl-Phenyl-(U)-^{14}C]	[Glyoxyl-Phenyl-(U)-^{14}C]
Test site	Greenhouse	Greenhouse
Treatment	Foliar spray	Foliar spray
Rate	100 g a.i./ha/application	100 g a.i./ha/application
Seasonal rate	400 g a.i./ha	400 g a.i./ha
PHI	14	14
The distribution of ^{14}C-residues between surface, peel and flesh of apples indicated that the majority of the applied radioactivity was surface-related, demonstrating minimal translocation from the peel to the flesh as a function of time post treatment. Accordingly, there was minimal evidence of translocation from the foliage to the apples. Hence, translocation appeared unlikely.		
Metabolites identified	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**
Radiolabel position	**[Trifluoromethyl-Phenyl-(U)-^{14}C]**	
Peel	Trifloxystrobin CGA-357261	CGA-331409 CGA-357262 CGA-321113 CGA-373466 NOA 417076 Sugar conjugate of NOA 417076 and its associated isomers
Flesh	Trifloxystrobin	CGA-357261 CGA-321113 CGA-373466 NOA 417076 Sugar conjugate of NOA 417076 and its associated isomers

Whole apple	Trifloxystrobin	CGA-331409 CGA-357261 CGA-357262 CGA-321113 CGA-373466 NOA 417076 Sugar conjugate of NOA 417076 and its associated isomers
Radiolabel position	**[Glyoxyl-Phenyl-(U)-^{14}C]**	
Peel	Trifloxystrobin	CGA-331409 CGA-357261 CGA-357262 CGA-321113 CGA-373466 NOA 417076 and its associated isomers Sugar conjugate of NOA 417076 and its associated isomers observed as single peak (8.7% TRR)
Flesh	Trifloxystrobin Sugar conjugate of NOA 417076 and the associated isomers observed as single peak (24.3% TRR)	CGA-357261 CGA-321113 CGA-373466 CGA-320299 NOA 417076 and its associated isomers
Whole apple	Trifloxystrobin	CGA-331409 CGA-357261 CGA-357262 CGA-321113 CGA-373466 CGA-320299 NOA 417076 and its associated isomers Sugar conjugate of NOA 417076 and its associated isomers observed as single peak (1.5% TRR)
NATURE OF THE RESIDUE IN PLANTS—CUCUMBERS		
Radiolabel position	[Trifluoromethyl-Phenyl-(U)-^{14}C]	[Glyoxyl-Phenyl-(U)-^{14}C]
Test site	Greenhouse	Greenhouse
Treatment	Foliar spray	Foliar spray
Rate	312.5 g a.i./ha/application	312.5 g a.i./ha/application
Seasonal rate	940 g a.i./ha	940 g a.i./ha
PHI	7	7
The distribution of ^{14}C-residues indicated that the majority of the applied radioactivity remained on the foliage, demonstrating that there no noticeable evidence of translocation from the foliage to the cucumbers as a function of time post treatment. Hence, translocation appeared unlikely.		

Metabolites identified	Major metabolites (> 10% TRRs)	Minor metabolites (< 10% TRRs)
Radiolabel position	**[Trifluoromethyl-Phenyl-(U)-^{14}C]**	
Mature large cucumber (7-day PHI) and small cucumber (7-day PHI)	Trifloxystrobin	CGA-331409 CGA-357262 CGA-321113 Metabolite I_{12} and its sugar conjugate NOA 414412 Sugar conjugate of NOA 417076 and its associated isomers
Radiolabel position	**[Glyoxyl-Phenyl-(U)-^{14}C]**	
Mature large cucumber (7-day PHI) and small cucumber (7-day PHI)	Trifloxystrobin	CGA-331409 CGA-357262 CGA-321113 Metabolite I_{12} and its sugar conjugate NOA 414412 Sugar conjugate of NOA 417076 and its associated isomers
NATURE OF THE RESIDUE IN PLANTS—SPRING WHEAT		
Radiolabel position	**[Trifluoromethyl-Phenyl-(U)-^{14}C]**	**[Glyoxyl-Phenyl-(U)-^{14}C]**
Test site	Outdoor test plot	Outdoor test plot
Treatment	Foliar spray	Foliar spray
Rate	2 applications at 250 g a.i./ha/application or 1 application at 500 g a.i./ha/application	2 applications at 250 g a.i./ha/application or 1 application at 500 g a.i./ha/application
Seasonal rate	500 g a.i./ha	500 g a.i./ha
PHI	49–52	49–52
The distribution of ^{14}C-residues indicated that the radioactivity applied to the shoots remained predominantly on the surface, demonstrating minimal translocation within the wheat shoots as a function of time post treatment. Accordingly, there was minimal evidence of translocation from the site of application (wheat shoots) to the grain. Hence, translocation appeared unlikely.		
Metabolites identified	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**
Radiolabel position	**[Trifluoromethyl-Phenyl-(U)-^{14}C]**	
Wheat ears	Trifloxystrobin, its isomers and related minor fraction NOA 413161 and NOA 413163 as a single peak (12.2%TRR)	—

Wheat stalk	Sugar conjugate of I_{10} Sugar conjugate of NOA 414412	Trifloxystrobin CGA-331409 CGA-357261 CGA-357262 NOA 413161 NOA 413163 Metabolite I_{10} Metabolite I_{12} and its associated sugar conjugate NOA 414412 Metabolite II_8
Grain	—	CGA-321113 NOA 413161 NOA 413163 Metabolite I_{10} and its associated sugar conjugate Metabolite I_{12} NOA 414412 Pectin
Husks	—	Trifloxystrobin CGA-331409 CGA-357261 CGA-357262 NOA 413161 NOA 413163 Metabolite I_{10} Metabolite I_{12} NOA 414412
Straw	—	Trifloxystrobin CGA-331409 CGA-357261 CGA-357262 NOA 413161 NOA 413163 Metabolite I_{10} and its associated sugar conjugate Metabolite I_{12} and its associated sugar conjugate NOA 414412 and its associated sugar conjugate Metabolite II_8
Radiolabel position	**[Glyoxyl-Phenyl-(U)-^{14}C]**	
Wheat ears	—	Trifloxystrobin CGA-331409 CGA-357261 CGA-357262 NOA 413161 NOA 413163 Metabolite I_{12} and its associated sugar conjugate NOA 414412 and its associated sugar conjugate Metabolite II_8
Wheat stalk	—	Trifloxystrobin CGA-331409 CGA-357261 CGA-357262 CGA-321113 NOA 413161 NOA 413163 Metabolite I_{10} and its associated sugar conjugate Metabolite I_{12} and its associated sugar conjugate NOA 414412 and its associated sugar conjugate

Grain	NOA 413161 and NOA 413163 as a single peak (10.1%TRR)		Trifloxystrobin CGA-357261 Metabolite II_8 Metabolite II_{10} Sugar conjugate of NOA 414412	
Husks	—		Trifloxystrobin CGA-357261 CGA-321113 NOA 413161 and NOA 413163 as a single peak (5.1% TRR) Metabolite I_{12} NOA 414412	
Straw	—		Trifloxystrobin CGA-331409 CGA-357261 CGA-357262 CGA-321113 NOA 413161 and NOA 413163 as a single peak (6.0% TRR) Metabolite I_{12} and its associated sugar conjugate NOA 414412 and its associated sugar conjugate Metabolite II_8	
CONFINED ROTATIONAL CROP STUDY—SPINACH, TURNIPS AND WHEAT				
Radiolabel position	[Trifluoromethyl-Phenyl-(U)-^{14}C]		[Glyoxyl-Phenyl-(U)-^{14}C]	
Test site	Outdoor test plot		Outdoor test plot	
Formulation used for trial	250 EC		250 EC	
Application rate and timing	2.24 kg a.i./ha		2.24 kg a.i./ha	
Radiolabel position	**[Trifluoromethyl-Phenyl-(U)-^{14}C]**			
Plantback intervals	**PBI 30**		**PBI 120**	
Metabolites identified	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**
Spinach leaves	Trifluoroacetic acid	CGA-321113 CGA-373466 CGA-331409	Trifluoroacetic acid	Trifloxystrobin CGA-321113 CGA-373466 CGA-331409 CGA-357262
Turnip roots	Trifluoroacetic acid	—	Trifluoroacetic acid	Trifloxystrobin CGA-321113 CGA-373466 CGA-331409 CGA-373465 CGA-357262

Turnip leaves	Trifluoroacetic acid	—	Trifluoroacetic acid	Trifloxystrobin CGA-321113 CGA-373466 CGA-331409 CGA-373465 CGA-357262
Wheat 25% maturity	Trifluoroacetic acid	—	Trifluoroacetic acid	Trifloxystrobin CGA-321113
Wheat 50% maturity	Trifluoroacetic acid	—	Trifluoroacetic acid	—
Wheat straw	Trifluoroacetic acid	—	Trifluoroacetic acid	CGA-321113 CGA-373466
Wheat grain	Trifluoroacetic acid	—	Trifluoroacetic acid	—
Radiolabel position	**[Glyoxyl-Phenyl-(U)-^{14}C]**			
Plantback intervals	**PBI 30**		**PBI 120**	
Metabolites identified	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**
Spinach leaves	—	Trifloxystrobin CGA-321113 CGA-331409 CGA-357262	—	Trifloxystrobin Phthalic acid CGA-321113 CGA-373466 CGA-331409 CGA-357262
Turnip roots	Not further analysed due to low levels of radioactivity.		CGA-321113	Trifloxystrobin Phthalic acid CGA-373466 CGA-331409 CGA-373465 CGA-357262 CGA-320299
Turnip leaves	—	Trifloxystrobin CGA-321113 CGA-357261 CGA-331409 CGA-357262 CGA-320299	—	Trifloxystrobin Phthalic acid CGA-321113 CGA-373466 CGA-331409 CGA-357262 CGA-320299
Wheat 25% maturity	—	Trifloxystrobin CGA-331409 CGA-357262 CGA-320299	—	Phthalic acid CGA-321113 CGA-373465 CGA-320299
Wheat 50% maturity	The majority of the extractable radioactivity was either unidentified or unresolved.		—	Trifloxystrobin CGA-321113 CGA-373465 CGA-357262

Wheat straw	The majority of the extractable radioactivity was either not analysed due to low levels of ^{14}C-residues or unidentified	—	Trifloxystrobin CGA-321113 CGA-320299
Wheat grain	The extractable radioactivity was not analysed due to low levels of ^{14}C-residues	The majority of the extractable radioactivity was either not analysed due to low levels of ^{14}C-residues or unidentified	

NATURE OF THE RESIDUE IN LAYING HEN

Species	Dose level	Length of dosing (d)	Sacrifice
Hen	100 mg/kg feed/day	4	Six hours after final dose

During the dosing period, averages of 0.13% and 79% of the administered dose were eliminated via eggs and excreta, respectively. Tissue residues accounted for an average of ca. 1.2% (16.0 ppm) of the administered dose. The disposition of radioactivity in tissues was similar for both labels: kidney (0.17–0.19%, 7.75–9.49 ppm), liver (0.45–0.50%, 5.81–6.32 ppm), total fat and skin (0.35–0.38%, 0.83–1.48 ppm) and muscle (0.14–0.16%; 0.17–0.21 ppm). On average, approximately 87% of the administered dose was recovered.

Metabolites identified	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**
Radiolabel position	**[Trifluoromethyl-Phenyl-(U)-^{14}C]**	
Egg whites	CGA-321113 CGA-357276 Metabolite L_{13b}	Metabolite EW_{1b} Metabolite 6U Metabolite 2U Metabolite 1U
Egg yolk	—	Trifloxystrobin CGA-357276 Metabolite EW_{1b} Metabolite 2U Metabolite L_{13b}
Liver	Metabolite L_{13b} Metabolite L_{14}	Trifloxystrobin CGA-321113 CGA-357276 Metabolite EW_{1b} Metabolite 6U Metabolite L_{13a} (Metabolite 1G; glucuronic acid conjugate of 2F) Metabolite 3U Metabolite 2U Metabolite 2F Metabolite EW_{11} Metabolite L_{24}
Lean meat	Trifloxystrobin Metabolite 12U	Metabolite EW_{1b} Metabolite 5U Metabolite 2U Metabolite L_{13b} Metabolite L_{14} Metabolite EW_{11}

Fat and skin	Trifloxystrobin Metabolite L_{13b} Metabolite 2F	CGA-321113 CGA-357276 Metabolite 12U Metabolite EW_{1b} Metabolite L_{13a} Metabolite 3U Metabolite 2U Metabolite 3F	
Metabolites identified	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**	
Radiolabel position	**[Glyoxyl-Phenyl-(U)-^{14}C]**		
Egg whites	CGA-321113 Metabolite 6U Metabolite 1U	CGA-357276 Metabolite 3U Metabolite 2U Metabolite L_{13b}	
Egg yolk	—	Trifloxystrobin CGA-321113 CGA-357276 NOA 417076 Metabolite L_{13a} Metabolite 2U Metabolite L_{13b} Metabolite 2F	
Liver	—	Trifloxystrobin CGA-321113 CGA-357276 Metabolite 4U Metabolite 5U Metabolite L_{13a} Metabolite 2U Metabolite L_{13b} Metabolite 3F Metabolite 2F Metabolite EW_{11}	
Lean meat	—	Trifloxystrobin CGA-321113 CGA-357276 CGA-166988 Metabolite 5U Metabolite L_{13a} Metabolite L_{13b} Metabolite 3F Metabolite 2F	
Fat and skin	Trifloxystrobin	Metabolite L_{13a} Metabolite 3U Metabolite 2U Metabolite L_{13b} Metabolite 3F Metabolite 2F	
NATURE OF THE RESIDUE IN RUMINANT			
Species	Dose level	Length of dosing (d)	Sacrifice
Lactating goat	100 mg/kg feed/day	4	Six hours after final dose

Urinary and fecal excretion were the predominant routes of elimination accounting for 55–61% of the total administered dose. In the last interval (6 hours after the last administration), total radioactive residues in milk accounted for an average of 0.07% of the administered dose. Tissue residues accounted for an average of 0.7% (6.8 ppm) of the administered dose for both labels. The disposition of radioactivity in tissues was similar for both labels: liver (0.41–0.54%; 3.91–4.82 ppm), total muscle (0.04–0.10%; 0.06–0.08 ppm), total fat (0.08%; 0.19–0.36 ppm) and kidneys (0.03–0.04%; 1.83–2.33 ppm). On average, 84% of the administered dose was recovered.		
Metabolites identified	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**
Radiolabel position	**[Trifluoromethyl-Phenyl-(U)-^{14}C]**	
Muscle	Trifloxystrobin CGA-321113	Metabolite 12U Metabolite 2U Metabolite 1U Metabolite L_{7a} (taurine conjugate of CGA-321113) Metabolite L_{7b} (glycine conjugate of CGA-321113)
Fat	Trifloxystrobin CGA-321113	Metabolite 12U Metabolite 2U Metabolite 1U
Liver (after microwave assisted extraction)	CGA-321113 Metabolite L_{7a} Metabolite L_{7b}	Trifloxystrobin CGA-357276 Metabolite 6U
Kidneys	CGA-321113 Metabolite L_{7a}	Trifloxystrobin Metabolite 11U Metabolite 2U Metabolite 1U Metabolite L_{7b}
Milk	Trifloxystrobin Metabolite L_{7a}	CGA-321113 Metabolite 12U Metabolite 6U Metabolite 2U Metabolite 1U
Metabolites identified	**Major metabolites (> 10% TRRs)**	**Minor metabolites (< 10% TRRs)**
Radiolabel position	**[Glyoxyl-Phenyl-(U)-^{14}C]**	
Muscle	Trifloxystrobin CGA-321113	Metabolite 12U Metabolite 2U Metabolite 1U Metabolite L_{7a} Metabolite L_{7b}
Fat	Trifloxystrobin CGA-321113	Metabolite 12U Metabolite 2U Metabolite 1U
Liver (after microwave assisted extraction)	CGA-321113 CGA-166988 Metabolite L_{7b}	Trifloxystrobin Metabolite 6U Metabolite 1G (glucuronic acid conjugate of 2F) Metabolite 2U Metabolite L_{7a} Metabolite 3F Metabolite 2F

Kidneys	CGA-321113	Trifloxystrobin Metabolite 1G Metabolite 2U Metabolite 1U Metabolite L_{7a} Metabolite L_{7b}
Milk	Trifloxystrobin	CGA-321113 Metabolite 6U Metabolite 2U Metabolite L_{7a} Metabolite L_{7b} Metabolite 3F Metabolite 2F

CROP FIELD TRIALS TO SUPPORT DOMESTIC REGISTRATION

BARLEY

A total of 12 trials were conducted in Zones 5(1), 5B(1), 7(2) and 14(8). A 25% reduction in the total number of trials required was granted on the basis that residues were all < LOQ (0.04 ppm).

Commodity	Total rate g a.i./ha	PHI (days)	Analyte	Residue levels (ppm)					
				n	Min.	Max.	HAFT	Median	SDEV
Grain	121–136	39–62	Combined residues of trifloxystrobin and CGA-321113	24	0	0	0.04	0.04	0

OATS

A total of 12 trials were conducted in Zones 1(1), 5(2), 5B(1), 7(2) and 14(6). A 25% reduction in the total number of trials required was granted on the basis that residues were all < LOQ (0.04 ppm).

Commodity	Total rate g a.i./ha	PHI (days)	Analyte	Residue levels (ppm)					
				n	Min.	Max.	HAFT	Median	SDEV
Grain	120–133	38–83	Combined residues of trifloxystrobin and CGA-321113	24	0	0	0.04	0.04	0

TOTAL CROP FIELD TRIALS TO SUPPORT DOMESTIC REGISTRATION AND PROMULGATION OF MRLs IN/ON IMPORTED CROPS

WHEAT

Under submission 1999-1220, a total of 21 trials were conducted in Zones 2(1), 4(1), 5(6), 6(1), 7(4), 8(6), 10(1), 11(1).
Under submissions 2000-3149 (Stratego 250 EC) and 200-3150 (Flint 50 WG), 14 additional trials were conducted in Zones 2 (1), 5(1), 6(1), 7(3), 7A(1), 8(1) and 14(6).

Commodity	Total rate g a.i./ha	PHI (days)	Analyte	Residue levels (ppm)					
				n	Min.	Max.	HAFT	Median	SDEV
Grain	122–137	34–75	Combined residues of trifloxystrobin and CGA-321113	18	0	0	0.04	0.04	0
	125	27–43		34	0	0.1	0.05	0.04	0.002
	250	27–43		34	0	0.1	0.055	0.04	0.004
	251–263	52–62		12	0	0	0.04	0.04	0
	750	36		2	0	0	0.04	0.04 (mean)	—
	1250	36		2	0.1	0.1	0.05	0.05 (mean)	—

APPLES

Under submission 1999-1220, a total of 13 trials were conducted in Zones 1 (3), 2 (1), 5(2), 9(1), 10(2) and 11(4). In addition, 22 trials conducted throughout Europe (EU) and in South Africa (SA) were submitted.
Under submission 2000-3150, a total of 3 trials were conducted in Zone 5.

Commodity	Total rate g a.i./ha	PHI (days)	Analyte	Residue levels (ppm)					
				n	Min.	Max.	HAFT	Median	SDEV
U.S. and Canada									
Apple, fruit	400–424.5	13–15	Combined residues of trifloxystrobin and CGA-321113	39	0	0.39	0.32	0.15	0.068
	400	57–60		26	0	0.1	0.06	0.045	0.014
	1200	14		4	0.43	0.6	0.6	0.58	0.079
	2000	14		4	1.12	1.52	1.47	1.37	0.171
EU and SA									
Apple, fruit	450	14	Combined residues of trifloxystrobin and CGA-321113	7	0.1	0.29	0.29	0.1	0.079
	750	10–14		28	0.1	0.46	0.46	0.12	0.122

PEARS

Under submission 1999-1220, a total of 6 trials were conducted in Zones 1(1), 10(2) and 11(3).
Under submission 2000-3150, a total of 3 trials were conducted in Zones 1A(1) and 5(2).

Commodity	Total rate g a.i./ha	PHI (days)	Analyte	Residue levels (ppm)					
				n	Min.	Max.	HAFT	Median	SDEV
Pear, fruit	400–423	13–15	Combined residues of trifloxystrobin and CGA-321113	18	0.1	0.25	0.22	0.15	0.052
	400	59–60		12	0	0.1	0.05	0.04	0.003

GRAPES									
Under submission 1999-1220, a total of 12 trials were conducted in Zones 1(2), 10(8) and 11(2). In addition, 20 trials conducted throughout Europe (EU) and in South Africa (SA) were submitted. Under submission 2000-3150, one trial in each of Zones 5 and 11 were conducted.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Canada and U.S.									
Grape, fruit	350	14	Combined residues of trifloxystrobin and CGA-321113	1	—	2.22	—	—	—
	420	14		2	0.1	0.1	0.07	0.070 (mean)	0.011
	855	13–14		28	0	1.15	1.099	0.255	0.27
EU									
Grape, fruit	1128–1135	35–41	Combined residues of trifloxystrobin and CGA-321113	12	0.73	2.27	1.13	1.5	0.55
	1316	14		1	—	1.1	—	—	—
	1504–1536	35		16	0	2.11	1.82	0.82	0.586
SA									
Grape, fruit	688	14	Combined residues of trifloxystrobin and CGA-321113	2	0.15	0.38	—	0.27 (mean)	—
	1374	14		1	—	1.52	—	—	—
CROP FIELD TRIALS TO SUPPORT THE PROMULGATION OF MRLS IN/ON IMPORTED CROPS									
ALMONDS									
Four trials were conducted in Zone 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Almond, nutmeat	570	62–63	Combined residues of trifloxystrobin and CGA-321113	10	0	0	0.04	0.04	0
CROP GROUP 9—CUCURBIT VEGETABLES (CUCUMBERS, CANTALOUPE AND SQUASH)									
Cucumbers: A total of 8 trials were conducted in Zones 2(2), 3(1), 5(2), 6(1) and 10(2). In addition, 9 trials conducted throughout Europe (EU) were submitted. Cantaloupe: A total of 5 trials were conducted in Zones 2(1), 6(1) and 10(3). Summer squash: One trial was conducted in each of the Zones 1, 2, 3, 5 and 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
U.S.									
Cucumber	1130–1140	0	Combined residues of trifloxystrobin and CGA-321113	36	0	0.3	0.26	0.075	0.07
	1140–1312	0		2	0.15	0.24	0.2	0.20 (mean)	—
Cantaloupe	1130–1140	0		20	0.1	0.6	0.49	0.16	0.158
	1260	0		1	—	0.12	—	—	—

Summer squash	1130–1140	0		24	0	0.35	0.32	0.125	0.085
EU									
Cucumber	921–940	3	Combined residues of trifloxystrobin and CGA-321113	9	0	0.17	—	0.06	0.053
HOPS									
A total of 3 trials were conducted in Zones 11(2) and 12(1).									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Hops, dried cones	855	14	Combined residues of trifloxystrobin and CGA-321113	6	4.8	10.5	8.25	7.5	2.581
	1710	14		6	7.9	26.8	26.4	12.75	8.356
CROP GROUP 8—FRUITING VEGETABLES (TOMATOES, BELL PEPPERS, NON-BELL PEPPERS)									
Tomatoes: A total of 12 trials were conducted in Zones 1(1), 2(1), 3(2), 5(1) and 10(7). Bell pepper: A total of 6 trials were conducted in Zones 2 (1), 3(1), 5A(1), 6(1) and 10(2). Non-bell pepper: One trial was conducted in each of the Zones 6, 8 and 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
U.S.									
Tomato	1140	3	Combined residues of trifloxystrobin and CGA-321113	24	0	0.51	0.44	0.09	0.117
	3420			3	0.71	1.34	1.12	1.3	0.353
	5700			6	0.61	3.51	2.25	1.06	1.119
Bell pepper	1140	3		12	0.1	0.16	0.15	0.1	0.044
Non-bell pepper	1140	3		6	0	0.29	0.29	0.07	0.117
POTATOES									
A total of 16 trials were conducted in Zones 1(2), 2(1), 3(1), 5(4), 9(1), 10(1) and 11(6).									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Potato, tuber	855	7	Combined residues of trifloxystrobin and CGA-321113	30	0	0	0.04	0.04	0
	1130			4	0	0	0.04	0.04	0
	3390			4	0	0	0.042	0.041	0.001
	5650			4	0	0.12	0.097	0.05	0.04

SUGAR BEETS									
A total of 11 trials were conducted in Zones 5(5), 7(1), 8(1), 9(1), 10(1) and 11(2).									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Sugar beet, root	375	21–23	Combined residues of trifloxystrobin and CGA-321113	22	0	0.1	0.06	0.04	0.008
	1125	23		1	—	0	—	—	—
	1875	23		1	—	0.11	—	—	—
RESIDUE DECLINE									
CROP GROUP 9—CUCURBIT VEGETABLES (CUCUMBER, CANTALOUPE, SUMMER SQUASH)									
Two residue decline trials were conducted in Zone 3.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Cucumber, fruit	1130–1140	0	Combined residues of trifloxystrobin and CGA-321113	4	0.1	0.13	0.12	0.09	0.026
		1		4	0.1	0.1	0.07	0.06	0.012
		3		4	0	0.1	0.06	0.05	0.01
		5		4	0	0.1	0.05	0.04	0.005
Two residue decline trials were conducted in Zone 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Cantaloupe	1130–1140	0	Combined residues of trifloxystrobin and CGA-321113	4	0.24	0.6	0.49	0.32	0.165
		1		4	0.19	0.23	0.23	0.22	0.021
		3		4	0.1	0.25	0.2	0.18	0.068
		5		4	0.1	0.29	0.24	0.2	0.078
Two residue decline trials were conducted in Zone 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Summer squash	1130–1140	0	Combined residues of trifloxystrobin and CGA-321113	4	0.2	0.35	0.33	0.28	0.065
		1		4	0.16	0.32	0.31	0.23	0.085
		3		4	0.1	0.21	0.2	0.15	0.055
		5		4	0.1	0.22	0.2	0.17	0.05

WHEAT									
One residue decline trial was conducted in each of Zones 6 and 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Mean**	**SDEV**
Wheat, grain	125	21	Combined residues of trifloxystrobin and CGA-321113	2	0	0.1	—	0.05	—
		28		2	0	0.1	—	0.05	—
		63		2	0	0	—	0.04	—
		70		2	0	0	—	0.04	—
	125	34		2	0	0	—	0.04	—
		38		2	0	0	—	0.04	—
		44		2	0	0	—	0.04	—
		51		2	0	0	—	0.04	—
	250	21		2	0.1	0.1	—	0.07	—
		28		2	0.1	0.1	—	0.06	—
		63		2	0	0	—	0.04	—
		70		2	0	0	—	0.04	—
	250	34		2	0	0	—	0.04	—
		38		2	0	0	—	0.04	—
		44		2	0	0	—	0.04	—
		51		2	0	0	—	0.04	—

POTATOES									
One residue decline trial was conducted in each of Zones 5 and 11.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Potato, tuber	1130	0	Combined residues of trifloxystrobin and CGA-321113	4	0	0	0.04	0.04	0
		1		4	0	0	0.04	0.04	0
		3		4	0	0	0.04	0.04	0
		7		4	0	0	0.04	0.04	0
		14		4	0	0	0.04	0.04	0

ALMONDS									
One residue decline trial were conducted in Zone 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Mean**	**SDEV**
Almond, nutmeat	570	40	Combined residues of trifloxystrobin and CGA-321113	2	0	0	—	0.04	—
		49		2	0	0	—	0.04	—
		55		2	0	0	—	0.04	—
		63		2	0	0	—	0.04	—
		68		2	0	0	—	0.04	—

HOPS									
One residue decline trial was conducted in Zone 11.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Mean**	**SDEV**
Hops, dried cones	855	0	Combined residues of trifloxystrobin and CGA-321113	2	20.5	20.7	—	20.6	—
		3		2	10.7	17.6	—	14.2	—
		6		2	12.7	18.2	—	15.4	—
		10		2	15.4	19.9	—	17.7	—
		13		2	9.03	9.87	—	9.45	—
		18		2	6.08	9.58	—	7.83	—
SUGAR BEETS									
One residue decline trial was conducted in each of Zones 5 and 11.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Sugar beet, root	375	0	Combined residues of trifloxystrobin and CGA-321113	4	0.1	0.1	0.1	0.08	0.01
		7		4	0	0	0.04	0.04	0
		14		4	0.1	0.1	0.07	0.06	0.01
		21		4	0	0.1	0.05	0.04	0.01
		28		4	0	0	0.04	0.04	0
APPLES									
Two residue decline trials were conducted in each of Zones 1 and 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Apple, fruit	400	0	Combined residues of trifloxystrobin and CGA-321113	6	0.14	0.34	0.29	0.14	0.082
		1		5	0.13	0.35	0.32	0.17	0.091
		3		4	0.12	0.26	0.19	0.13	0.067
		7		4	0.1	0.16	0.15	0.14	0.025
		14		4	0.11	0.2	0.16	0.12	0.044
		21		6	0.1	0.1	0.1	0.1	0.02
PEARS									
One residue decline trial was conducted in Zone 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Mean**	**SDEV**
Pear, fruit	400	0	Combined residues of trifloxystrobin and CGA-321113	2	0.45	0.56	—	0.51	—
		1		2	0.41	0.47	—	0.44	—
		3		2	0.46	0.78	—	0.62	—
		7		2	0.23	0.46	—	0.35	—
		14		2	0.16	0.2	—	0.18	—
		21		2	0.16	0.18	—	0.17	—

GRAPES									
Two residue decline trials were conducted in Zone 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Grape, fruit	855	0	Combined residues of trifloxystrobin and CGA-321113	4	0.22	1	0.93	0.67	0.361
		1		4	0.47	0.93	0.77	0.68	0.2
		3		4	0.47	1	0.81	0.56	0.246
		7		4	0.33	0.7	0.65	0.48	0.181
		14		4	0.27	1.15	1.1	0.7	0.459
		21		4	0.11	0.58	0.5	0.29	0.218

TOMATOES									
Two residue decline trials were conducted in Zones 3 and 10.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Median**	**SDEV**
Tomato	1140	0	Combined residues of trifloxystrobin and CGA-321113	6	0.1	0.27	0.18	0.15	0.068
		1		4	0	0.38	0.35	0.18	0.178
		3		4	0	0.31	0.26	0.13	0.133
		5		4	0	0.18	0.16	0.09	0.069

BELL PEPPERS									
One residue decline trial was conducted in Zone 3.									
Commodity	**Total rate g a.i./ha**	**PHI (days)**	**Analyte**	**Residue levels (ppm)**					
				n	**Min.**	**Max.**	**HAFT**	**Mean**	**SDEV**
Pepper	1140	0	Combined residues of trifloxystrobin and CGA-321113	2	0.14	0.14	—	0.14	—
		1		2	0.1	0.1	—	0.09	—
		3		2	0.1	0.1	—	0.06	—
		5		2	0	0	—	0.04	—

MAXIMUM RESIDUE LIMITS	
Commodity	**Limit (ppm)**
Grapes	2
Raisins	5
Pome fruits (Crop Group 11, which includes apple, crabapple, loquat, mayhaw, pear, pear (oriental) and quince)	0.5
Wheat, barley, oats	0.05
Meat, meat by-products and fat of cattle, goat, hog, horse and sheep	0.04
Milk	0.02
Meat, meat by-products and fat of poultry, eggs	0.04
Almonds, potatoes	0.04

Cucurbit vegetables [Crop Group 9 which includes balsam apple, balsam pear, cantaloupe, chayote, cucumber, cucumber (Chinese), gherkin (West Indian), gourd (edible), melon, melon (citron), muskmelon, pumpkin, squash, squash (summer, winter), watermelon and waxgourd (Chinese)], Fruiting Vegetables [Crop Group 8 which includes chili, eggplant, groundcherry, pepino, pepper, pepper (bell, non-bell, non-bell (sweet)), tomatillo and tomato]	0.5
Sugar beets	0.1

FIELD ACCUMULATION IN ROTATIONAL CROPS—LEAF LETTUCE, TURNIPS AND WHEAT

Seven field accumulation studies were conducted in Zones 1(2), 4(2) and 10(3). CGA-279202 50 WG was applied either to a primary crop (cucumber or squash) in six of the studies or to bare soil with plantback intervals of 30 and 120 days, respectively.

Commodity	Total rate kg a.i./ha	PHI (days)	Analyte	Residue levels (ppm)					
				n	Min.	Max.	HAFT	Median	SDEV
30–35 DAT plantback interval									
Leaf lettuce	1140	96–181	Combined residues of trifloxystrobin and CGA-321113	6	< 0.04	< 0.04	< 0.04	< 0.04	0
Turnip Roots		96–181		6	< 0.04	< 0.04	< 0.04	< 0.04	0
Tops		96–181		6	< 0.04	< 0.04	< 0.04	< 0.04	0
Wheat Forage		91–273		9	< 0.04	< 0.04	< 0.04	< 0.04	0
Hay		184–329		6	< 0.04	< 0.04	< 0.04	< 0.04	0
Straw		270–282		9	< 0.04	< 0.04	< 0.04	< 0.04	0
Grain		270–282		21	< 0.04	< 0.04	< 0.04	< 0.04	0
119–120 DAT plantback interval									
Leaf lettuce	1140	181–198	Combined residues of trifloxystrobin and CGA-321113	Samples were not analysed since there were no measurable residues in the RACs of crops planted 30–35 DAT to the primary crop.					
Turnip Roots		181–208							
Tops		181–208							
Wheat Forage		180–343							
Hay		265–399							
Straw		355–428							
Grain		355–428							

PROCESSED FOOD AND FEED

Fraction	Mean combined residue of Trifloxystrobin and CGA-321113	Mean concentration factors
Tomato		
Tomato, whole fruit (RAC)	0.16 (1128 g a.i./ha/season) 0.71 (3384 g a.i./ha/season) 0.71 (5640 g a.i./ha/season)	— — —
Puree	0.06 (1128 g a.i./ha/season) 0.51 (3384 g a.i./ha/season) 0.66 (5640 g a.i./ha/season)	0.97 0.72 0.87
Paste	0.19 (1128 g a.i./ha/season) 0.85 (3384 g a.i./ha/season) 1.60 (5640 g a.i./ha/season)	1.15 1.20 2.13

Grapes		
Grape, fruit (RAC)	0.46 (855 g a.i./ha/season) 1.39 (2565 g a.i./ha/season) 1.70 (4275 g a.i./ha/season) 1.58 (1135 g a.i./ha/season) 0.73 (1500 g a.i./ha/season)	— — — — —
Pasteurized juice	0.066 (855 g a.i./ha/season) 0.166 (2565 g a.i./ha/season) 0.274 (4275 g a.i./ha/season)	0.14 0.12 0.16
Raisins	0.852 (855 g a.i./ha/season)	1.84
Wine	0.095 (1135 g a.i./ha/season) 0.05 (1500 g a.i./ha/season)	0.06 0.07
Apple		
Apple, unwashed whole fruit (RAC)	0.117 (400 g a.i./ha/season) 0.270 (1200 g a.i./ha/season) 0.535 (2000 g a.i./ha/season)	— — —
Juice	0.040 (400 g a.i./ha/season) 0.045 (1200 g a.i./ha/season) 0.055 (2000 g a.i./ha/season)	0.34 0.17 0.10
Pomace	1.225 (400 g a.i./ha/season) 3.590 (1200 g a.i./ha/season) 6.170 (2000 g a.i./ha/season)	10.47 13.30 11.53
Potato		
Potato, tuber (RAC)	0.040 (1130 g a.i./ha/season) 0.042(3390 g a.i./ha/season) 0.050 (5650 g a.i./ha/season)	— — —
Culls	0.040 (1130 g a.i./ha/season) 0.041(3390 g a.i./ha/season) 0.047 (5650 g a.i./ha/season)	1.0 0.98 0.94
Wet peel and trimmings	0.044 (1130 g a.i./ha/season) 0.060 (3390 g a.i./ha/season) 0.102 (5650 g a.i./ha/season)	1.1 1.43 2.04
Flakes	0.04 (1130 g a.i./ha/season) 0.04 (3390 g a.i./ha/season) 0.04 (5650 g a.i./ha/season)	1.0 1.0 1.0
Chips	0.04 (1130 g a.i./ha/season) 0.04 (3390 g a.i./ha/season) 0.04 (5650 g a.i./ha/season)	1.0 1.0 1.0
Sugar beets		
Sugar beet, root	0.04 (375 g a.i./ha/season) 0.13 (1125 g a.i./ha/season) 0.14 (1875 g a.i./ha/season)	— — —
Refined sugar	0.04 (375 g a.i./ha/season) 0.04 (1125 g a.i./ha/season) 0.04 (1875 g a.i./ha/season)	1.0 0.31 0.28

Dried pulp	0.08 (375 g a.i./ha/season) 0.23 (1125 g a.i./ha/season) 0.59 (1875 g a.i./ha/season)	2.0 1.77 4.21
Molasses	0.05 (375 g a.i./ha/season) 0.13 (1125 g a.i./ha/season) 0.22 (1875 g a.i./ha/season)	1.25 1.0 1.57
Wheat		
Wheat, grain (RAC)	0.04 (125 g a.i./ha/season) 0.04 (250 g a.i./ha/season) 0.04 (750 g a.i./ha/season) 0.04 (1250 g a.i./ha/season)	— — — —
Germ	0.04 (125 g a.i./ha/season) 0.04 (250 g a.i./ha/season) 0.04 (750 g a.i./ha/season) 0.04 (1250 g a.i./ha/season)	1.0 1.0 1.0 1.0
Bran	0.04 (125 g a.i./ha/season) 0.04 (250 g a.i./ha/season) 0.044 (750 g a.i./ha/season) 0.07 (1250 g a.i./ha/season)	1.0 1.0 1.1 1.75
Middlings, shorts, low-grade flour, patent flour	0.04 (125 g a.i./ha/season) 0.04 (250 g a.i./ha/season) 0.04 (750 g a.i./ha/season) 0.04 (1250 g a.i./ha/season)	1.0 1.0 1.0 1.0
Aspirated grain fractions	0.125 (125 g a.i./ha/season) 0.17 (250 g a.i./ha/season) 0.48 (750 g a.i./ha/season) 1.58 (1250 g a.i./ha/season)	3.12 4.25 12.00 39.41

LIVESTOCK FEEDING

Among all the proposed uses on the Flint 50 WG and Stratego 250 EC labels, apple wet pomace, wheat, barley and oat forage, hay, straw and grain constitute the only animal feed items, as per Table 1, Section 8, of the Residue Chemistry Guidelines, DIR98-02. The maximum anticipated dietary burdens to beef cattle, dairy cattle and poultry were calculated to be 5.01 ppm, 2.98 ppm and 0.16 ppm, respectively.

Dairy Cattle

Tissues/matrices	Maximum combined residues of trifloxystrobin and CGA-321113 (ppm)			Anticipated residues (ppm)
Feeding levels (ppm)	2	6	20	
Liver	< 0.04	< 0.04	< 0.11	< 0.1070[2]
Fat (omental and perirenal)	< 0.04	< 0.04	< 0.08	< 0.04
Muscle (round and tenderloin)	N/A	N/A	< 0.04	< 0.04[1]
Kidney	< 0.04	< 0.04	< 0.04	< 0.04
Milk	N/A	N/A	< 0.02	< 0.02[1]

Notes:

1 Since there were no measurable residues detected in the lower feeding levels of 2 and 6 ppm, and the maximum anticipated dietary burden (MADB) is 5.01 ppm and 2.98 ppm for beef cattle and dairy cattle, respectively, anticipated combined residues of trifloxystrobin and CGA-321113 are not expected to exceed the LOQ following exposure to treated feed.

2 In the lactating goat metabolism study, the metabolite L_{7a} was detected in liver at 1.3366 ppm (TFMP-^{14}C) based on a feeding level of 100 ppm (ca. 20× the maximum anticipated dietary burden to beef cattle). Therefore, assuming a linear relationship between residues and dosage level, at a feeding level equivalent to the MADB (5.01 ppm), residues of the metabolite would be ca. 0.0670 ppm. Combining this residue value with the 0.04 ppm proposed MRL/anticipated residue in liver, a residue level of 0.1070 ppm trifloxystrobin equivalents, respectively, will be used for the liver contribution for risk assessment purposes.

Poultry

Tissues/Matrices	Maximum Combined Residues of Trifloxystrobin and CGA-321113 (ppm)			Anticipated Residues (ppm)[1]
Feeding levels (ppm)	1.5	4.5	15	
Eggs	N/A	N/A	< 0.04	< 0.04
Skin with adhering fat	N/A	N/A	< 0.04	< 0.04
Breast and thigh muscle	N/A	N/A	< 0.04	< 0.04
Liver	N/A	N/A	< 0.04	< 0.04

Note:

1 Since there were no measurable residues detected in the lower feeding levels of 1.5 and 4.5 ppm, and the maximum anticipated dietary burden is 0.16 ppm, anticipated combined residues of trifloxystrobin and CGA-321113 are not expected to exceed the LOQ following exposure to treated feed.

Table 2 Food residue chemistry overview of metabolism studies and risk assessment

PLANT STUDIES		
ROC FOR ENFORCEMENT **Primary crops** **Rotational crops**	Trifloxystrobin and CGA-321113 Trifloxystrobin and CGA-321113	
ROC FOR RISK ASSESSMENT **Primary crops** **Rotational crops**	Trifloxystrobin and CGA-321113 Trifloxystrobin and CGA-321113	
METABOLIC PROFILE IN DIVERSE CROPS	Similar in apples, cucumbers and wheat	
ANIMAL STUDIES		
ANIMALS	**Poultry**	**Ruminant**
ROC FOR ENFORCEMENT	Trifloxystrobin and CGA-321113	
ROC FOR RISK ASSESSMENT	Trifloxystrobin and CGA-321113	Trifloxystrobin and CGA-321113 (for milk and all tissues, except liver) Trifloxystrobin, CGA-321113 and taurine conjugate of CGA-321113—metabolite L_{7a} (liver only)
METABOLIC PROFILE IN ANIMALS	Similar in both animals	

FAT SOLUBLE RESIDUE		Yes	
Level II DIETARY RISK from food and water (EEC)			
Chronic non-cancer dietary risk **ADI = 0.038 mg/kg bw Combined EECs (Trifloxystrobin and CGA-321113) = 300 µg/L**	**POPULATION**	**ESTIMATED RISK (% of ADI)**	
		Food (STMdRs)	**Food (STMdRs) + EEC**
	All infants < 1 yr old	18	73
	Children 1 to 2 yrs	29	54
	Children 3 to 5 yrs	20	44
	Children 6 to 12 yrs	11	27
	Youth 13 to 19 yrs	6	18
	Adults 20 to 49 yrs	5	21
	Adults 50 + yrs	5	22
	Total Population	8	24

Appendix III Environmental assessment

Table 1 Physical and chemical properties of trifloxystrobin relevant to the environment

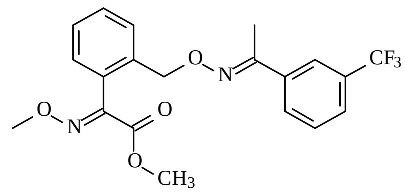
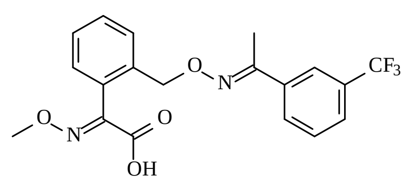
Property	Value	Comments
Chemical structure		
Water solubility	0.61 mg/L RSD 9.1% (25°C)	Low solubility.
Vapour pressure	3.4×10^{-6} Pa (25°C)	Relatively non-volatile.
Henry's Law constant K 1/H	 2.25×10^{-8} atm m^3/mol 1.09×10^{6}	 Non-volatile under field conditions from water and moist soil surfaces.
log K_{ow}	4.5 ± 0.009	Potential to bioaccumulate.
pK_a	No dissociation constant in pH range 2–12.	Is not expected to dissociated in water.
UV–visible absorption	No absorption between 340 and 750 nm. Maximum adsorption at 250 and 252 nm.	Minimal phototransformation is expected under natural environment.

Table 2 Physical and chemical properties of the major transformation product, CGA-321113, relevant to the environment

Property	Value	Comments
Chemical structure		
Water solubility	30.9 mg/L (deionized water) 62 mg/L at pH 4.1 (water) 470 mg/L at pH 5.0 (buffer solution) 21 000 mg/L at pH 6.6 (buffer solution)	Soluble to very soluble at environmentally relevant pH.
Vapour pressure	< 5.5×10^{-6} Pa (25°C)	Relatively non-volatile.

Property	Value	Comments
Henry's Law constant K 1/H	 4.27×10^{-10} atm m^3/mol 5.73×10^7	 Non-volatile under field conditions from water and moist soil surfaces.
log K_{ow}	2.2 at pH 5.5 0.60 at pH 6.9 0.34 at pH 9.0	Low potential to bioaccumulate.
pK_a	Not determined	Based on the chemical structure, CGA-321113 is expected to dissociate in acidic pH.
UV–visible absorption	Expected to be similar to trifloxystrobin	Minimal phototransformation is expected under natural environment.

Table 3 Fate and behaviour in the terrestrial environment (transformation studies)

Property	Test substance	Trifloxystrobin	CGA-321113	Comments
Abiotic transformation				
Hydrolysis	CGA-279202	pH 5: stable pH 7: $t_{1/2}$ = 56 days pH 9: $t_{1/2}$ = 20 hours	Concentrations continued to increase until study termination.	Important route for trifloxystrobin transformation in alkaline conditions. Major transformation product: CGA-321113 Minor transformation product: none
Phototransformation on soil	CGA-279202	Rate could not be determined	Rate could not be determined	Route of transformation (isomerization) for trifloxystrobin. Transformation products: CGA-373466, CGA-331409 and CGA-327262
Phototransformation in air	CGA-279202	Not required—not volatile		

Property	Test substance	Trifloxystrobin	CGA-321113	Comments
Biotransformation				
Biotransformation in aerobic soil	CGA-279202	DT_{50} = <1 day	DT_{50}: 315–350 days	Important route for transformation of trifloxystrobin. Major transformation product: CGA-321113 (persistent) Minor transformation products: CGA-357276, CGA-373466, CGA-357261, CGA-331409, CGA-357262 and NOA 413161
Biotransformation in anaerobic soil	CGA-279202	DT_{50}: < 1 day	DT_{50}: 1733 days	Important route of transformation for trifloxystrobin. Major tranformation product: CGA-321113 (persistent) Minor transformation product: none
Field studies				
Field dissipation (Canadian and equivalent U.S. site)	Flint 50 WG and Stratego 250 EC	DT_{50}: 3–23 days Detected in the top 25 cm	DT_{50}: 36–350 days Detected down to 45 cm depth	CGA-279202: Non-persistent and low potential of leaching. CGA-321113: Slightly persistent to persistent and a potential of leaching.

Table 4 Fate and behaviour in the terrestrial environment (mobility)

Property	Test substance	Results	Comments
Adsorption/desorption in soil	CGA-279202	adsorption K_{oc}:951–3064	Immobile–slight mobility
	CGA-321113	adsorption K_{oc}:48–235	Moderate–very high mobility
	CGA-357261	adsorption K_{oc}:389–567	Low–moderate mobility
	CGA-373466	adsorption K_{oc}:30.1–166	Moderate–very high mobility
	CGA-357276	adsorption K_{oc}:6587–9756	Immobile
Soil leaching	CGA-279202	remained in the top 30 cm	CGA-279202: Immobile–low mobility CGA-321113: Mobile–very mobile
Volatilization	CGA-279202	not volatile based on vapour pressure	

Table 5 Fate and behaviour in the aquatic environment

Property	Trifloxystrobin	CGA-321113	Comments
Abiotic transformation			
Hydrolysis	pH 5: stable pH 7: $t_{1/2}$ = 56 days pH 9: $t_{1/2}$ = 20 hours	Concentrations continued to increase until study termination.	Important route of transformation for trifloxystrobin in alkaline conditions. Major transformation product: CGA-321113 Minor transformation product: none
Phototransformation in water	Rate was not determined.	Rate was not determined.	Important route of isomerization for trifloxystrobin. Major transformation product: CGA-357261 Minor transformation products: CGA-357262, CGA-321113
Biotransformation			
Biotransformation in aerobic water systems	DT_{50} < 8 hours	DT_{50} = 289 days	Important route of transformation for trifloxystrobin. Major transformation product:CGA-321113 Minor transformation products: Unknown A and CGA-331409
Biotransformation in anaerobic water systems (based on anearobic flooded soil/water system)	DT_{50}: < 1 day	DT_{50}: 1733 days	Important route of transformation for trifloxystrobin. Major tranformation product: CGA-321113 (persistent) Minor transformation product: none
Bioaccumulation			
Bioaccumulation	BCF: Edible tissue: 130–166× Non-edible tissue: 1144–1172× Whole fish tissues: 542–547× (based on total residues: CGA-279202 and all transformation products)	N/A	Trifloxystrobin is not likely to bioaccumulate based on rapid aquatic biotransformation and rapid depuration in fish.
Partitioning			
Adsorption/ desorption in sediment	Not required		
Field studies			
Field dissipation	Not required		

Table 6 EECs of trifloxystrobin in soil and water (direct overspray)

End-use product	Guarantee of trifloxy-strobin	Crop	Rate of application		EEC of trifloxystrobin[1]		EEC of EP formulation		EEC of CGA-321113[2]	
			Product rate × number of applications (interval between applications)	Maximum seasonal rate	Soil (mg/kg soil)	Water (mg/L)	Soil (mg/kg soil)	Water (mg/L)	Soil (mg/kg soil)	Water (mg/L)
Compass 50 WG	50%	turf	6.1 g/100 m^2 × 4 (14 d)	2.4 kg/ha	**0.321**	**0.102**	**0.642**	**0.203**	**0.520**	**0.387**
		ornamental	150 g/ha × 4 (7 d)	4 applications	0.100	0.025	N/A	N/A	N/A	N/A
Stratego 250 EC[3]	125 g/L	wheat, barley and oats	500 mL/ha × 2 (14 d)	2 applications	**0.046**	**0.021**	**0.404**	**0.183**	N/A	N/A
Flint 50 WG	50%	grapes	140 g/ha × 4 (7d)	560 g/ha	0.093	0.023	N/A	N/A	N/A	N/A
		pome fruits	210 g/ha × 4 (10 d) or 175 g/ha × 4 (7 d)	770 g/ha	**0.119** 0.117	**0.035** 0.029	**0.238**	**0.070**	N/A	N/A
		wheat	245 g/ha × 2 (14 d)	490 g/ha	0.090	0.041	N/A	N/A	N/A	N/A

1 For trifloxystrobin, a DT_{50} of 23 days was used in the estimation of the soil EEC and the aerobic water biotransformation half-life of 8 hours was used in the estimation of the water EEC.

2 For CGA-321113, a DT_{50} of 350 days was used in the estimation of the soil EEC and the aerobic water biotransformation half-life of 289 days was used in the estimation of the water EEC.

3 The Stratego soil EEC was calculated using the following: Application rate of 0.500 L/ha × 1.0968 g/cm^3 × 1000 mL/L and using the trifloxystrobin transformation rates.

- The values in bold indicate the highest EEC estimated for each product.
- N/A: Not Applicable. EEC values were only calculated for the highest proposed application rate on the label.

Table 7 Water model inputs for drinking water assessment—trifloxystrobin residues

Crop(s) that use the maximum label rate	Maximum rate per year (kg a.i./ha)	Maximum rate each application (kg a.i./ha)	Maximum number of applications per year	Minimum interval between applications (d)	Timing of applications	Method of application
turf (reservoir and groundwater)	1.2	0.305	4	14	all season (April 1)	field sprayer
wheat (dugout)	0.25	0.123	2	14	mid-April	airblast and broadcast field sprayer

Table 8 Summary of concentrations of trifloxystrobin in potential drinking water sources from the water models PRZM/EXAMS and LEACHM (90th percentile values)

Compound	Groundwater		Reservoir		Dugout	
	Acute Concentration (µg a.i./L)[1]	Chronic Concentration (µg a.i./L)[2]	Acute Concentration (µg a.i./L)[3]	Chronic Concentration (µg a.i./L)[4]	Acute Concentration (µg a.i./L)[3]	Chronic Concentration (µg a.i./L)[4]
Trifloxystrobin	0	0	4.78	0.16	2.02	0.04
CGA-321113	301	300	19.86	7.44	8.26	4.18

1 90th percentile of daily flux-averaged concentrations
2 90th percentile of yearly flux-averaged concentrations
3 90th percentile of yearly peak concentrations
4 90th percentile of yearly averages

Table 9 Maximum EEC in vegetation and insects after a direct overspray

Compass 50 WG			
Matrix	**EEC (mg a.i./kg fw)[a]**	**Fresh/dry weight ratios**	**EEC (mg a.i./kg dw)**
Short range grass	256.81	3.3[b]	847.46
Leaves and leafy crops	134.40	11[b]	1478.40
Long grass	117.60	4.4[b]	517.44
Forage crops	144.00	5.4[b]	777.60
Small insects	62.40	3.8[c]	237.12
Pods with seeds	12.84	3.9[c]	50.08
Large insects	10.68	3.8[c]	40.58
Grain and seeds	10.68	3.8[c]	40.58
Fruit	16.08	7.6[c]	122.21

Stratego 250 EC			
Matrix	**EEC (mg a.i./kg fw)[a]**	**Fresh/dry weight ratios**	**EEC (mg a.i./kg dw)**
Short range grass	26.75	3.3[b]	88.28
Leaves and leafy crops	14.00	11[b]	154.00
Long grass	12.25	4.4[b]	53.90
Forage crops	15.00	5.4[b]	81.00
Small insects	6.50	3.8[c]	24.70
Pods with seeds	1.34	3.9[c]	5.22
Large insects	1.11	3.8[c]	4.23
Grain and seeds	1.11	3.8[c]	4.23
Fruit	1.68	7.6[c]	12.73
Flint 50 WG			
Matrix	**EEC (mg a.i./kg fw)[a]**	**Fresh/dry weight ratios**	**EEC (mg a.i./kg dw)**
Short range grass	82.39	3.3[b]	271.89
Leaves and leafy crops	43.12	11[b]	474.32
Long grass	37.73	4.4[b]	166.01
Forage crops	46.20	5.4[b]	249.48
Small insects	20.02	3.8[c]	76.08
Pods with seeds	4.12	3.9[c]	16.07
Large insects	3.43	3.8[c]	13.02
Grain and seeds	3.43	3.8[c]	13.02
Fruit	5.16	7.6[c]	39.21

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973), and modified according to Fletcher et al. (1994)

[b] Fresh to dry weight ratios from Harris (1975)

[c] Fresh to dry weight ratios from Spector (1956)

Table 10 Maximum EEC in diets of birds and mammals

Organism	Matrix	EEC (mg a.i./kg dw diet)		
		Compass 50 WG	Stratego 250 EC	Flint 50 WG
Bobwhite quail	30% small insects 15% forage crops 55% grain	210.1	21.89	67.41
Mallard duck	30% large insects 70% grain	40.58	4.23	13.02
Rat	70% short grass 20% grain/seeds 10% large insects	605.4	63.06	194.23
Mouse	25% short grass 50% grain/seeds 25% leaves and leafy crops	601.76	62.68	193.06
Rabbit	25% short grass 25% leaves and leafy crops 25% long grass 25% forage crops	905.22	94.29	290.43

Table 11 Effects on terrestrial organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]
Invertebrates				
Earthworm (*Eisenia foetida*)	Acute	Trifloxystrobin	LC_{50}: > 1000 mg a.i./kg soil dw NOEC (W): < 12.3 mg a.i./kg soil dw	Not acutely toxic
		Stratego 312 EC	LC_{50}: > 1000 mg EP/kg soil dw NOEC (M): 1000 mg EP/kg soil dw NOEC (W): 37 mg EP/kg soil dw	Not acutely toxic
		Flint 50 WG	LC_{50}: > 1000 mg EP/kg soil dw NOEC (M, W): 1000 mg EP/kg soil dw	Non-toxic
Honeybee (*Apis mellifera*)	Oral	Trifloxystrobin	LC_{50}: > 200 µg a.i./bee NOEC (M): 200 µg a.i./bee	Relatively non-toxic
		Stratego 250 EC	LC_{50}: 136.7 µg EP/bee NOEC (M): 10.7 µg EP/bee	Relatively non-toxic
		Flint 50 WG	LC_{50}: > 186.7 µg EP/bee NOEC (M): 186.7 µg EP/bee	Relatively non-toxic
	Contact	Trifloxystrobin	LD_{50}: > 200 µg a.i./bee NOEC (M): 200 µg a.i./bee	Relatively non-toxic

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]
		Stratego 250 EC	LD_{50}: > 100 µg EP/bee NOEL (M): 100 µg EP/bee	Relatively non-toxic
		Flint 50 WG	LD_{50}: > 200 µg EP/bee NOEL (M): 186.7 µg EP/bee	Relatively non-toxic
Predatory arthropods: Ground beetle (*Poecilus cupreus*)	Contact	Stratego 312 EC	Tested rate: 186 g a.i./ha CGA-279202 + 125 g a.i./ha CGA-64250 and 372 g a.i./ha CGA-279202 + 250 g a.i./ha CGA-64250 LC_{50}: > tested rate NOEC (M, S): = tested rate	Harmless
		Flint 50 WG	Tested rate: 250 g a.i./ha and 500 g a.i/ha CGA-279202 LC_{50}: > tested rate NOEC (M,S): = tested rate	Harmless
Rove beetle (*Aleochara bilineata*)	Contact	Stratego 312 EC	Tested rate: 186 g a.i./ha CGA-279202 + 125 g a.i./ha CGA-64250 and 372 g a.i./ha CGA-279202 + 250 g a.i./ha CGA-64250 LC_{50}: > tested rate NOEC (M): = tested rate NOEC (P): < tested rate	Harmless
Aphid predator (*Orius laevigatus*)	Contact	Flint 50 WG	Tested rate: 250 g a.i./ha and 500 g a.i./ha CGA-279202 LC_{50}: < tested rate NOEC (M): < tested rate NOEC (F): N/A	Harmful
Seven-spotted lady beetle (*Coccinella septem-punctata*)	Contact	Flint 50 WG	Tested rate: 250 g a.i./ha and 500 g a.i./ha CGA-279202 LC_{50}: > tested rate NOEC (M, S): < tested rate	Slightly harmful
		Stratego 312 EC	Tested rate: 186 g a.i./ha CGA-279202 + 125 g a.i./ha CGA-64250 and 372 g a.i./ha CGA-279202 + 250 g a.i./ha CGA-64250 LC_{50}: < tested rate NOEC (M, S): < tested rate	Slightly harmful
Predaceous mite (*Typhlo-dromus pyri*)	Contact	Stratego 312 EC	Tested rate: 187.5 g a.i./ha CGA-279202 + 125 g a.i./ha CGA-64250 LC_{50}: < tested rate NOEC (M, F): < tested rate	Moderately harmful
		Flint 50 WG	Tested rate: 250 g a.i./ha CGA-279202 LC_{50}: > tested rate NOEC (M): < tested rate NOEC (F): = tested rate	Harmless

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]
			Tested rate: 500 g a.i./ha CGA-279202 LC_{50}: > tested rate NOEC (M, F): = tested rate	
Parasitic arthropods: Parasitic wasp (*Aphidius colemani*)	Contact	Stratego 312 EC	Tested rate: 186 g a.i./ha CGA-279202 + 125 g a.i./ha CGA-64250 and 372 g a.i./ha CGA-279202 + 250 g a.i./ha CGA-64250 LC_{50}: < tested rate NOEC (M): < tested rate NOEC (P): N/A due to complete mortality	Harmful
		Flint 50 WG	Tested rate: 250 g a.i./ha CGA-279202 LC_{50}: > tested rate NOEC (M, P): = tested rate	Harmless
			Tested rate: 500 g a.i./ha CGA-279202 LC_{50}: > tested rate NOEC (M): < tested rate NOEC (P): = tested rate	
			Birds	
Bobwhite quail	Acute oral	Trifloxystrobin	LD_{50}: > 2000 mg a.i./kg bw NOEL: 2000 mg a.i./kg bw	Practically non-toxic
	Dietary	Trifloxystrobin	LC_{50}: > 5200 mga.i./kg diet NOEC: 5200 mg a.i./kg diet	Practically non-toxic
	Reproduction	Trifloxystrobin	EC_{50}: > 323 mg a.i./kg diet NOEC: 323 mg a.i./kg diet	—
Mallard duck	Acute oral	Trifloxystrobin	LD_{50}: > 2250 mg a.i./kg bw NOEL: 2250 mg a.i./kg bw	Practically non-toxic
	Dietary	Trifloxystrobin	LC_{50}: > 5200 m ga.i./kg diet NOEC: 5200 mg a.i./kg diet	Practically non-toxic
	Reproduction	Trifloxystrobin	EC_{50}: > 474 mg a.i./kg diet NOEC: 474 mg a.i./kg diet	—
Japanese quail	Reproduction	MNP	EC_{50} > 403 mg a.i./kg diet NOEC: 403 mg a.i./kg diet	—

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]
Mammals				
Rat	Acute	Trifloxystrobin	Oral LD_{50}: > 5000 mg a.i./kg bw	Low toxicity
		CGA-373466	Oral LD_{50}: > 2000 mg a.i./kg bw	Low toxicity
		NOA-414412	Oral LD_{50}: > 2000 mg a.i./kg bw	Low toxicity
		CGA-357261	Oral LD_{50}: > 2000 mg a.i./kg bw	Low toxicity
		Flint 50 WG	Oral LD_{50}: > 2000 mg a.i./kg bw	Low toxicity
		Stratego 250 EC	Oral LD_{50}: > 2000 mg a.i./kg bw	Low toxicity
	Short term	Trifloxystrobin	28-d Oral study NOAEL: 200/1000 ppm (♂/♀) LOAEL: 1000/4000 ppm (♂/♀)	—
	Reproduction	Trifloxystrobin	Multi-generation Reproductive: NOAEL: 1500 ppm (♂/♀)	—
Mouse	Acute	Trifloxystrobin	Oral LD_{50}: > 5000 mg/kg dw	Low toxicity
	Dietary	Trifloxystrobin	90-d Dietary study NOAEL: 500 ppm (♂/♀) LOAEL: 2000 ppm (♂/♀)	—
Vascular plants				
Vascular plants	Seedling emergence	Flint 50 WG	EC_{25} > 113 g a.i./ha	—
	Vegetative vigour	Flint 50 WG	EC_{25} > 113 g a.i./ha	—

[a] Atkins et al. (1981) for bees, Hassan (1992) for IOBC classification of beneficial arthropods, and USEPA classification for others, where applicable

M = mortality, S = sublethal effects, P = parasitization, W = weight loss, F = fecundity,
MNP = 1-methyl-2-pyrolidinone

Table 12 Effects on aquatic organisms

Organism and exposure	Test system	Test substance	Endpoint value	Degree of toxicity[a]
Freshwater species				
Freshwater invertebrates				
Daphnia magna Acute	Flow-through	Trifloxystrobin	EC_{50} range: 0.0180–0.0286 mg a.i./L NOEC (I): 0.0180 mg/L	Very highly toxic
	Static	Trifloxystrobin	EC_{50} range: 0.010–0.021 mg a.i./L NOEC (I): 0.0056 mg/L	Very highly toxic
	Static	Stratego 312 EC	EC_{50}: 0.071 mg EP/L NOEC (I): 0.041 mg EP/L	Very highly toxic
	Static	Flint 50 WG	EC_{50}: 0.010 mg EP/L NOEC (I): 0.006 mg EP/L	Very highly toxic
	Semi-static	Flint 50 WG	EC_{50}: 0.017 mg EP/L NOEC (I): 0.0059 mg EP/L	Very highly toxic
	Static	CGA-321113	EC_{50}: > 95.3 mg/L NOEC (I): 95.3 mg/L	Practically non-toxic
Daphnia pulex Acute	Static	Trifloxystrobin	EC_{50}: > 0.027 mg/L NOEC (I): 0.0089 mg/L	Very highly toxic
Daphnia longispina Acute	Static	Trifloxystrobin	EC_{50}: 0.015 mg/L NOEC (I): < 0.0043 mg /L	Very highly toxic
Chydorus sp. (cladoceran) Acute	Static	Trifloxystrobin	EC_{50}: 0.13 mg/L NOEC (I): 0.028 mg/L	Highly toxic
Cyclopidae (copepod) Acute	Static	Trifloxystrobin	EC_{50} range: 0.028–0.11 mg/L NOEC (I): 0.014 mg/L	Very highly toxic
Chaoborus sp. (dipteran) Acute	Static	Trifloxystrobin	EC_{50}: 0.20 mg/L NOEC (I): 0.053 mg/L	Highly toxic
Baetis sp. (ephemeropteran) Acute	Static	Trifloxystrobin	EC_{50}: 0.078 mg/L NOEC (I): 0.014 mg/L	Very highly toxic
Thamnocephalus platyurus (fairy shrimp) Acute	Static	Trifloxystrobin	EC_{50} range: 0.018–0.053 mg/L NOEC (I): 0.0091 mg/L	Very highly toxic

Organism and exposure	Test system	Test substance	Endpoint value	Degree of toxicity[a]
Brachionus calyciflorus (rotifer) Acute	Static	Trifloxystrobin	EC_{50}: > 0.053 mg/L NOEC (I): 0.029 mg/L	Very highly toxic
Procambarus acutus acutus (crayfish) Acute	Static	Trifloxystrobin	LC_{50}: > 0.310 mg/L NOEC (M): 0.120 mg/L	Highly toxic
Gammarus sp. (amphipod) Acute	Static	Trifloxystrobin	EC_{50}: 0.094 mg/L NOEC (M): 0.0087 mg/L	Very highly toxic
Daphnia magna Chronic	Flow-through	Trifloxystrobin	21-d EC_{50} range: 0.00598–0.025mg/L NOEC (F, L, W): 0.00276 mg/L LOEC (F, L, W): 0.00598 mg/L	—
	Static renewal	CGA-321113	NOEC (I): 3.2 mg/L LOEC (I): 10.0 mg/L	—
	Semi-static	Flint 50 WG	NOEC (I, F, T): 0.011 mg EP/L LOEC (I, F, T): 0.020 mg EP/L	—
Chironomus riparius Chronic	Static	Trifloxystrobin	EC_{50} > 0.40 mg/L NOEC = 0.20 mg/L	—
Freshwater fish				
Oncorhynchus mykiss Acute	Flow-through	Trifloxystrobin	LC_{50}: 0.012–0.041 mg/L NOEC (M): 0.0072 mg/L	Very highly toxic
	Static	Trifloxystrobin	LC_{50} range: 0.021–0.038 mg/L NOEC (S): 0.013 mg/L	Very highly toxic
	Flow-through	Flint 50 WG	LC_{50} range: 0.033–0.040 mg EP/L NOEC (S): 0.015 mg EP/L	Very highly toxic
	Flow-through	Stratego 312 EC	LC_{50} range: 0.074–0.12 mg EP/L NOEC (S): 0.074 mg EP/L	Very highly toxic
	Flow-through	CGA-321113	LC_{50}: > 106 mg/L NOEC: 106 mg/L	Practically non-toxic

Organism and exposure	Test system	Test substance	Endpoint value	Degree of toxicity[a]
Oncorhynchus mykiss Chronic (early life-stage)	Flow-through	Trifloxystrobin	95-d EC_{50} range: 0.0077–0.015 mg/L NOEC (M): 0.0043 mg/L LOEC (M): 0.0077 mg/L NOEC (HR): 0.0077 mg/L LOEC (HR): 0.015 mg/L	—
Bluegill sunfish (*Lepomis macrochirus*) Acute	Flow-through	Trifloxystrobin	LC_{50}: 0.046–0.076 mg/L NOEC (S): 0.028 mg/L	Very highly toxic
	Static	Trifloxystrobin	LC_{50} range: 0.091–0.135 mg/L NOEC (M): 0.053 mg/L	Very highly toxic
Carp (*Cyprinus carpio*) Acute	Static	Trifloxystrobin	LC_{50} range: 0.025–0.041 mg/L NOEC (M): 0.025 mg/L	Very highly toxic
Fathead minnow (*Pimephales promelas*) Acute	Static	Trifloxystrobin	LC_{50} range: 0.019–0.034 mg/L NOEC (M): 0.019 mg/L	Very highly toxic
Zebrafish (*Brachydanio rerio*) Acute	Static	Trifloxystrobin	LC_{50} range: 0.12–0.22 mg/L NOEC (M): 0.12 mg/L	Highly toxic
Golden orfe (*Leuciscus idus*) Acute	Static	Trifloxystrobin	LC_{50} range: 0.048–0.093 mg/L NOEC (M): 0.048 mg/L	Very highly toxic
Guppy (*Poecilia reticulata*) Acute	Static	Trifloxystrobin	LC_{50}: 0.52 mg/L NOEC (M): 0.28 mg/L	Highly toxic

Organism and exposure	Test system	Test substance	Endpoint value	Degree of toxicity[a]
Freshwater algae				
Selenastrum capricornutum (green alga) Acute	Static	Trifloxystrobin	EC_{50} (CD): 0.0385 mg/L NOEC (CD): 0.010 mg/L	—
		CGA-321113	EC_{50} (CD): > 0.100 mg/L NOEC (CD): 0.018 mg/L	—
		Stratego 312 EC	EC_{50} (B): 0.0438 mg EP/L EC_{50} (GR): 0.246 mg EP/L NOEC (B, GR): 0.0072 mg EP/L	—
		Flint 50 WG	EC_{50} (B): 0.0193 mg EP/L EC_{50} (GR): 0.197 mg EP/L NOEC (B, GR): 0.0056 mg EP/L	—
Scenedesmus subspicatus (green alga) Acute	Static	Trifloxystrobin	EC_{50} (B): 0.00682 mg/L EC_{50} (GR): 0.0168 mg/L NOEC (B, GR): 0.00192 mg/L	–
Navicula pelliculosa (diatom) Acute	Static	Trifloxystrobin	EC_{50} (CD, GR): > 0.135 mg/L EC_{50} (B): < 0.006 mg/L NOEC (CD, GR): 0.006 mg/L NOEC (B): < 0.006 mg/L	–
Anabaena flos-aquae (blue-green alga) Acute	Static	Trifloxystrobin	EC_{50} (CD, B, GR):> 0.120 mg/L NOEC (CD, B, GR): 0.120 mg/L	–
Aquatic vasular plant				
Vascular plant (*Lemna gibba)* Dissolved 14-d exposure	Static	Trifloxystrobin	EC_{50}: > 1.93 mg/L NOEC: 0.41 mg/L	—

Organism and exposure	Test system	Test substance	Endpoint value	Degree of toxicity[a]
Marine species				
Marine invertebrates				
Crustacean Mysid shrimp (*Mysidopsis bahia*) Acute	Flow-through	Trifloxystrobin	LC_{50}: 0.00862 mg/L NOEC (M): 0.00360 mg/L	Very highly toxic
Mollusk Eastern oyster (*Crassostrea virginica*) Acute	Flow-through	Trifloxystrobin	EC_{50}: 0.0293 mg/L NOEC (M): < 0.0098 mg/L	Very highly toxic
Marine fish				
Sheepshead minnow (*Cyprinodon variegatus*) Acute	Flow-through	Trifloxystrobin	LC_{50}: 0.078 mg/L NOEC (M): 0.0323 mg/L	Very highly toxic

[a] USEPA classification, where applicable
M = mortality, I = immobilization, F = fecundity, L = length, W = weight, CD = cell density, B = biomass, GR = growth rate, S = sublethal effects, HR = hatching rate, T = time to first brood

Table 13 Risk to terrestrial organisms

Organism	Exposure	Test substance	Endpoint value based on test substance	EEC	RQ	Risk
Invertebrates						
Earthworm	Acute	Trifloxystrobin technical	NOEC: < 12.3 mg/kg soil (weight loss)	0.321 mg a.i./kg (Compass 50 WG)	0.03	negligible
		Flint 50 WG	NOEC: 1000 mg EP/kg soil (weight loss)	0.642 mg EP/kg	< 0.01	
		Stratego 312.5EC	NOEC: 37 mg EP/kg soil (weight loss)	0.404 mg EP/kg	0.01	
		Flint 50 WG	NOEC: 1000 mg EP/kg soil (weight loss)	0.238 mg EP/kg	< 0.01	

Organism	Exposure	Test substance	Endpoint value based on test substance	EEC	RQ	Risk
Bee	Oral	Trifloxystrobin technical	LC_{50} > 200 µg/bee	N/A	N/A	relatively non-toxic
		Flint 50 WG	LC_{50} > 186.7 µg EP/bee	N/A	N/A	
		Stratego 250 EC	LC_{50} = 136.7 µg EP/bee	N/A	N/A	
	Contact	Trifloxystrobin technical	LD_{50} > 200 µg/bee	N/A	N/A	Negligible (relatively non-toxic)
		Flint 50 WG	LD_{50} > 200 µg EP/bee	N/A	N/A	
		Stratego 250 EC	LD_{50} > 100 µg EP/bee	N/A	N/A	
Predators and parasites	Oral/Contact	Compass/Flint 50 WG and Stratego	See Table 6.1.1	See Table 6.1.1	N/A	Harmless to harmful
Birds						
Bobwhite quail	Acute[1]	Trifloxystrobin technical	NOEL = 2000 mg/kg bw (highest dose tested)	210.1 mg a.i./kg (Compass 50 WG)	99 days	Negligible
	Dietary	Trifloxystrobin technical	NOEC = 5200 mg/kg diet (highest dose tested)	210.1 mg a.i./kg (Compass 50 WG)	0.04	Negligible
	Reproduction	Trifloxystrobin technical	NOEC = 323 mg/kg diet (highest dose tested)	210.1 mg a.i./kg (Compass 50 WG)	0.65	Low risk
				21.9 mg a.i./kg (Stratego 250 EC)	0.07	Negligible risk
				67.41 mg a.i./kg (Flint 50 WG)	0.21	Negligible risk
Mallard duck	Acute[2]	Trifloxystrobin technical	NOEL = 2250 mg/kg diet (highest dose tested)	40.58 mg a.i./kg (Compass 50 WG)	472 days	Negligible
	Dietary	Trifloxystrobin technical	NOEC = 5200 mg/kg diet (highest dose tested)	40.58 mg a.i./kg (Compass 50 WG)	< 0.01	Negligible
	Reproduction	Trifloxystrobin technical	NOEC = 474 mg/kg diet (highest dose tested)	40.58 mg a.i./kg (Compass 50 WG)	0.44	Low risk
				4.23 mg a.i./kg (Stratego 250 EC)	< 0.01	Negligible risk
				13.02 mg a.i./kg (Flint 50 WG)	0.02	Negligible risk

Organism	Exposure	Test substance	Endpoint value based on test substance	EEC	RQ	Risk
Mammals						
Rat	Acute	Trifloxystrobin technical	Oral LD_{50} > 5000 mg/kg bw 1/10 LD_{50} = 500 mg/kg bw	605.4 mg a.i./kg dw (Compass 50 WG)	4.82	Negligible risk
	Dietary	Trifloxystrobin technical	NOEL = 200 mg/kg dw (reduced bodyweights)	605.4 mg a.i./kg dw (Compass 50 WG)	3.03	Moderate risk
				63.06 mg a.i./kg dw (Stratego 250 EC)	0.32	Low risk
				194.23 mg a.i./kg dw (Flint 50 WG)	0.97	Low risk
	Reproduction	Trifloxystrobin technical	NOEL = 1500 mg/kg dw (no effects at the highest dose tested)	605.4 mg/kg dw (Compass 50 WG)	0.4	Low risk
				63.06 mg/kg dw (Stratego 250 EC)	0.04	Negligible risk
				194.23 mg/kg dw (Flint 50 WG)	0.13	Low risk
Mouse	Acute	Trifloxystrobin technical	Oral LD_{50} > 5000 mg/kg bw 1/10 LD_{50} = 500 mg/kg bw	601.76 mg/kg dw (Compass 50 WG)	4.57	Negligible risk
	Dietary	Trifloxystrobin technical	NOEL = 500 mg/kg (increased incidence of liver weights, necrosis of hepatocytes and spleen)	601.76 mg/kg dw (Compass 50 WG)	1.2	Moderate risk
				62.68 mg/kg dw (Stratego 250 EC)	0.12	Low risk
				193.06 mg/kg dw (Flint 50 WG)	0.39	Low risk
Vascular plants						
Vascular plant	Seedling emergence and vegetative vigour	Flint 50 WG	EC_{25} > 113 g a.i./ha (no effects shown at highest level tested)	305 g a.i./ha (Compass 50 WG)	2.7	Moderate risk
				105 g a.i./ha (Flint 50 WG)	0.93	Low risk

1 For the acute oral toxicity of trifloxystrobin to bobwhite quail, food consumption (FC) was 19.6 g/ind/day and the body weight per individual (BWI) was 0.204 kg bw/ind based on the study raw data.

2 For the acute oral toxicity of trifloxystrobin to mallard duck, food consumption (FC) was 134 g/ind/day, body weight per individual (BWI) was 1.14 kg bw/ind based on the study raw data.

Table 14 Risk to aquatic organisms

Organism	Exposure	Test substance	Endpoint value	EEC	RQ	Risk
Freshwater species						
Freshwater aquatic inverte-brates	Acute	Trifloxystrobin technical	1/10 EC_{50} = 0.0015 mg a.i./L (immobilisation) *Daphnia longispina*	0.102 mg a.i./L (Compass 50 WG)	68	High risk
				0.021 mg a.i./L (Stratego 250 EC)	14	High risk
				0.035 mg a.i./L (Flint 50 WG)	23.33	High risk
		Flint 50 WG	NOEC = 0.006 mg EP/L (immobilisation) *Daphnia magna*	0.203 mg EP/L (Compass 50 WG)	33.83	High risk
				0.070 mg EP/L (Flint 50 WG)	11.67	High risk
		Stratego 250 EC	NOEC = 0.041 mg EP/L (immobilisation) *Daphnia magna*	0.183 mg EP/L (Stratego 250 EC)	4.46	Moderate risk
		CGA-321113	NOEC: 95.3 mg a.i./L (immobilisation) *Daphnia magna*	0.387 mg/L (Compass 50 WG)	< 0.01	Negligible risk
	Chronic	Trifloxystrobin technical	NOEC: 0.00276 mg a.i./L (dry weight, mean length and mean young per surviving adult) *Daphnia magna*	0.102 mg a.i./L (Compass 50 WG)	36.96	High risk
				0.021 mg a.i./L (Stratego 250 EC)	7.61	Moderate risk
				0.035 mg a.i./L (Flint 50 WG)	12.68	High risk
		Flint 50 WG	NOEC = 0.011 mg EP/L (immobilisation, fecundity and time to first brood) *Daphnia magna*	0.203 mg EP/L (Compass 50 WG)	18.45	High risk
				0.070 mg EP/L (Flint 50 WG)	6.36	Moderate risk
		CGA-321113	NOEC: 3.2 mg a.i./L (immobilisation) *Daphnia magna*	0.387 mg/L (Compass 50 WG)	0.12	Low risk

Organism	Exposure	Test substance	Endpoint value	EEC	RQ	Risk
Freshwater fish (Rainbow trout)	Acute	Trifloxystrobin technical	NOEC: 0.0072 mg a.i./L (mortality, sublethal effects)	0.102 mg a.i./L (Compass 50 WG)	14.17	High risk
				0.021 mg a.i./L (Stratego 250 EC)	2.92	Moderate risk
				0.035 mg a.i./L (Flint 50 WG)	4.86	Moderate risk
		Flint 50 WG	NOEC = 0.015 mg EP/L (mortality, sublethal effects)	0.203 mg EP/L (Compass 50 WG)	13.53	High risk
				0.070 mg EP/L (Flint 50 WG)	4.67	Moderate risk
		Stratego 250 EC	NOEC = 0.074 mg EP/L (abnormal swimming and loss of equilibrium)	0.183 mg EP/L (Stratego 250 EC)	2.47	Moderate risk
		CGA-321113	NOEC = 106 mg a.i./L (no effects in highest test concentration)	0.387 mg/L (Compass 50 WG)	< 0.01	Negligible risk
	Chronic	Trifloxystrobin technical	NOEC: 0.0043 mg a.i./L (survival)	0.102 mg a.i./L (Compass 50 WG)	23.72	High risk
				0.021 mg a.i./L (Stratego 250 EC)	4.88	Moderate risk
				0.035 mg a.i./L (Flint 50 WG)	8.14	Moderate risk
Bluegill sunfish	Acute	Trifloxystrobin technical	NOEC: 0.028 mg a.i./L (mortality/sublethal effects)	0.102 mg a.i./L (Compass 50 WG)	3.64	Moderate risk
				0.021 mg a.i./L (Stratego 250 EC)	0.75	Low risk
				0.035 mg a.i./L (Flint 50 WG)	1.25	Moderate risk

Organism	Exposure	Test substance	Endpoint value	EEC	RQ	Risk
Freshwater alga	Acute	Trifloxystrobin technical	NOEC = 0.002 mg a.i./L (growth rate and biomass) *S. Subspicatus*	0.102 mg a.i./L (Compass 50 WG)	51	High risk
				0.021 mg a.i./L (Stratego 250 EC)	10.5	High risk
				0.035 mg a.i./L (Flint 50 WG)	17.5	High risk
		Flint 50 WG	NOEC = 0.0056 mg EP/L (biomass, growth rate) *S. Capricornutum*	0.203 mg EP/L (Compass 50 WG)	36.25	High risk
				0.070 mg EP/L (Flint 50 WG)	12.5	High risk
		Stratego	NOEC = 0.0072 mg EP/L (biomass, growth rate) *S. Capricornutum*	0.183 mg EP/L	25.42	High risk
		CGA-321113	NOEC = 0.018 mg a.i./L (cell density) *S. Capricornutum*	0.387 mg/L (Compass 50 WG)	21.5	High risk
Vascular plant	14-day	Dissolved trifloxystrobin technical	NOEC = 0.41 mg a.i./L *L. gibba*	0.102 mg/L (Compass 50 WG)	0.25	Low risk
				0.021 mg a.i./L (Stratego 250 EC)	0.05	Negligible risk
				0.035 mg a.i./L (Flint 50 WG)	0.08	Negligible risk
Marine species						
Crustacean	Acute	Trifloxystrobin technical	NOEC = 0.0036 mg a.i./L (mortality)	0.102 mg a.i./L (Compass 50 WG)	28.33	High risk
				0.021 mg a.i./L (Stratego 250 EC)	5.83	Moderate risk
				0.035 mg a.i./L (Flint 50 WG)	9.72	Moderate risk
Mollusk	Acute	Trifloxystrobin technical	1/10 EC_{50} = 0.00293 mg/L	0.102 mg a.i./L (Compass 50 WG)	34.81	High risk
				0.021 mg a.i./L (Stratego 250 EC)	7.17	Moderate risk
				0.035 mg a.i./L (Flint 50 WG)	11.94	High risk

Organism	Exposure	Test substance	Endpoint value	EEC	RQ	Risk
Sheepshead minnow	Acute	Trifloxystrobin technical	NOEC = 0.0323 mg a.i./L (mortality)	0.102 mg a.i./L (Compass 50 WG)	3.16	Moderate risk
				0.021 mg a.i./L (Stratego 250 EC)	0.65	Low risk
				0.035 mg a.i./L (Flint 50 WG)	1.08	Moderate risk

Appendix IV Summary of efficacy results

Table 1 Alternative fungicides for control of diseases of turf, ornamentals, grapes, pome fruit, wheat, barley and oats

Crop	Diseases	Available active ingredients
Turfgrass	Brown patch	azoxystrobin, chlorothalonil, iprodione, propiconazole, thiophanate methyl, thiram
	Leaf spot	chlorothalonil, iprodione, propiconazole
	Gray leaf spot	none registered
Ornamentals (container plants)	Myrothecium	none registered
	Powdery mildew	thiophanate methyl, *Pseudozyma*
	Rhizoctonia root rot	thiophanate methyl, *Trichoderma*
Ornamentals (non-bearing fruit trees and hawthorn)	Powdery mildew	none registered
	Scab	chlorothalonil—crabapple
Grape	Powdery mildew	azoxystrobin, myclobutanil, sulphur
	Black rot	azoxystrobin, captan, fenhexamid, metiram, myclobutanil
Apples, pears, crabapples	Scab	captan, cyprodinil, flusilazole, kresozim-methyl, mancozeb, metiram, myclobutanil, thiophanate methyl
	Sooty blotch	captan, thiram, zineb
	Fly speck	captan, thiram
	Powdery mildew	captan, cyprodinil, flusilazole, metiram, myclobutanil, thiophanate methyl
	Cedar apple rust	captan, cyprodinil, flusilazole, metiram, myclobutanil, thiophanate methyl
Wheat	Rust (leaf and stem) Powdery mildew Septoria leaf blotch Tan spot Stripe rust	chlorothalonil, mancozeb, propiconazole, pyraclostrobin carbathiin, triadimenol seed treatments
Barley	Net blotch Scald Septoria leaf blotch	propiconazole, pyraclostrobin carbathiin, triadimenol seed treatments
Oats	Septoria leaf blotch Crown rust	propiconazole

Table 2 Summary of accepted label recommendations

Crop/disease	Rate product	Application interval (days)	Comments
COMPASS 50 WG			
Turfgrass	**g/100 m^2**		
Brown patch	4.6–6.1	14–21	Preventative and curative applications.
Leaf spot	3.1	14–21	Preventative applications.
Gray leaf spot	3.1–6.1	14	Preventative applications.
Do not apply more than one application for gray leaf spot control. Do not apply more than two sequential applications for all other diseases. Alternate with a fungicide having a different mode of action. Apply up to 2.4 kg/ha per year.			
Ornamentals	**g/100 L**		
Myrothecium leaf spot	7.5–15	7–14	remove crabapple and hawthorn
Powdery mildew (container plants)	7.5–15	7–14	remove roses
Powdery mildew (non-bearing trees)	14–21	7–14	remove citrus
Scab (non-bearing apple and hawthorn)	14–17.5	7–14	
Rhizoctonia root rot	3.8	once at seeding	
Added notes: If the response of a variety is not known, test on a small lot of plants before using for commercial scale production. Do not make more than one application of Compass 50 WG before alternating with one or more applications of a registered fungicide with a different mode of action. Do not make more than four applications per crop cycle or season. Add standard resistance management statements.			

Crop/disease	Rate product	Application interval (days)	Comments
FLINT 50 WG			
Grapes	**g/ha**		
Powdery mildew	105–140	14–21	
Black rot	140	7–14	efficacy data required to confirm lowest effective rate
Do not apply to Concord grapes. Do not apply where spray drift may reach Concord grapes. Spray equipment should be rinsed before application of other products to Concord grapes. Do not apply more than 560 g per ha per season. Maximum no. of applications per year: table and wine grapes four; other grapes three. Do not apply more than two sequential applications of strobilurin fungicides before alternating to a non-strobilurin fungicide.			
Pome fruit	**g/ha**		**includes apple, crabapple, loquat, mayhaw, pear, oriental pear and quince**
Scab	140–175	7–10	revise to 96 hours postinfective activity
Sooty blotch	140–175	10–14	alternate with non-strobilurin fungicide
Fly speck	140–175	10–14	alternate with non-strobilurin fungicide
Powdery mildew	140–210	10–14	use higher rate during pink to bloom stage
Cedar apple rust	140–210	10–14	
Do not apply more than 770 g per ha per season. Do not exceed four applications of strobilurins per season. Do not apply more than two sequential applications of strobilurin fungicides before alternating to a non-strobilurin fungicide for at least two applications.			
Wheat	**g/ha**		**includes winter, spring, hard red, durum, Canada prairie and soft white**
Rust	245	> 14	begin applications preventatively when conditions are favourable for disease development, typically before boot stage
Powdery mildew			
Leaf blight			
Tan spot			
Do not apply more than two applications or a total of 490 g per hectare per season. Do not apply within 45 days of harvest. Add standard resistance-management statements.			

Crop/disease	Rate product	Application interval (days)	Comments
STRATEGO 250 EC			
Wheat	**mL/ha**		**includes winter, spring, hard red, durum, Canada prairie and soft white**
Septoria leaf blotch	500	> 14	Typically one application from tillering up to flag leaf emergence. Single application and second application: up to before head is half emerged (GS 55) May be applied by ground and air equipment
Tan spot			
Powdery mildew			
Leaf and stem rust			
Stripe rust			
Spring Barley	**mL/ha**		
Net blotch	500	> 14	
Scald			
Septoria leaf blotch			
Oats	**mL/ha**		
Septoria leaf blotch	500	> 14	
Crown rust			
Do not apply more than two applications per season. Do not apply within 45 days of harvest. Add standard resistance-management statements.			

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