Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Regulatory Decision Document PRDD2001-05

Trinexapac-ethyl

The active ingredient trinexapac-ethyl and associated end-use product Primo MAXX Turf Growth Regulator, for growth inhibition of turf grasses on commercial sod farms and golf courses, are proposed for full registration under Section 13 of the Pest Control Products (PCP) Regulations.

This proposed regulatory decision document (PRDD) provides a summary of data received and the rationale for the proposed full registration of these products. The Pest Management Regulatory Agency (PMRA) will accept written comment on this proposal up to 45 days from the date of publication of this document. Please forward all comments to the Publications Coordinator at the address listed below.

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Publications Coordinator
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6605C
Ottawa, Ontario
K1A 0K9

Internet: pmra_publications@hc-sc.gc.ca
www.hc-sc.gc.ca/pmra-arla/
Information Service:
1-800-267-6315 or (613) 736-3799
Facsimile: (613) 736-3798

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Foreword

The submissions for full registration of trinexapac-ethyl technical and the EUP Primo MAXX, a plant growth regulator developed by Syngenta Crop Protection Canada Inc. that retards growth of turf grasses on commercial sod farms and golf courses, has been reviewed by Health Canada's Pest Management Regulatory Agency (PMRA) under the User Requested Minor Use Registration Program (URMUR).

Reviews from the United States Environmental Protection Agency, the Australian National Registration Authority and the United Kingdom Pesticide Safety Directorate were provided with the submissions as required for URMURs. User support included commercial sod farms and golf course associations.

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 *trinexapac-ethyl technical and the end-use product Primo MAXX*. The Agency has concluded that the use of *trinexapac-ethyl technical and the end-use product Primo MAXX* in accordance with the label 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. Therefore, based on the considerations outlined above, the use of *trinexapac-ethyl technical and the end-use product Primo MAXX* is proposed for full registration for use on commercial sod farms and golf courses under Section 13 of the PCP Regulations.

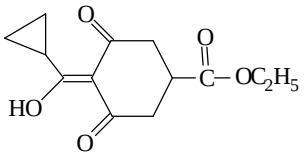
Methods for analyzing trinexapac residues in various environmental media can be provided to monitoring agencies and research institutions upon request to the PMRA.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed registration decision for this product.

Table of Contents

1.0 The active substance, its properties, uses, classification and labelling

1.1 Identity of the active substance and preparation containing it

Active substance	Trinexapac-ethyl
Function	Herbicide
Chemical name: International Union of Pure and Applied Chemistry Chemical Abstracts Service (CAS)	 4-cyclopropyl(hydroxy)methylene-3,5-dioxocyclohexanecarboxylic acid, ethyl ester 4-(cyclopropylhydroxymethylene)-3,5-dioxo-cyclohexanecarboxylate acid, ethyl ester
CAS number	95266-40-3
Molecular formula	$C_{13}H_{16}O_5$
Molecular weight	252.3
Structural formula	
Nominal purity of active	96% nominal (limits: 93.1– 98.9%)
Identity of relevant impurities of toxicological, environmental and (or) other significance	Based on the raw materials, the manufacturing process used and the chemical structures of the active and impurities, the technical substance is not expected to contain any toxic microcontaminants as identified in Section 2.13.4 of DIR98-04, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, or any Toxic Substances Management Policy (TSMP) Track-1 substances as identified in Appendix II of DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*.

1.2 Physical and chemical properties of active substance

Technical product: trinexapac-ethyl

Property	Result	Comment
Colour and physical state	Yellow to red-brown liquid or crystals	
Odour	Slightly sweet	
Melting point/range	36.1–36.6EC	
Boiling point/range	>270EC	
Specific gravity	1.215 g/cm^3	
Vapour pressure	Temperature Vapour pressure 20EC 1.03×10^{-3} Pa 25EC 2.16×10^{-3} Pa Obtained by extrapolation of curve from 38.0 to 170.2EC	Low volatility under field condition
Henry's Law Constant (*H*)	pH *H* 5.5 5.27×10^{-10} atm m^3/mole 8.2 2.54×10^{-10} atm m^3/mole	Non-volatile from a water or moist soil surface Lab study on volatilization not required
Ultraviolet (UV) – visible spectrum	Medium 8 (nm) , (L/mol cm) neutral 240.2 9 335 277.4 13 976 acidic 240.0 11 712 280.4 12 368 basic 270.8 21 320 No absorption at 8 340–750 nm	Low potential for phototransformation
Solubility in water	pH Solubility (g/L) 3.5 (distilled water) 1.1 4.9 (buffer) 2.8 5.5 (buffer) 10.2 8.2 (buffer) 21.2	Very soluble under all pH conditions

Property	Result	Comment
Solubility (g/L) in organic solvents	Solvent — Solubility (g/L) acetone — >500 methanol — >500 *n*-octanol — 420 toluene — >500 dichloromethane — >500 ethyl acetate — >500 *n*-hexane — 45	
n-Octanol–water partition coefficient (log K_{ow})	1.60 ± 0.22 at pH 5.3 and 25EC	Bioconcentration or bioaccumulation is unlikely
Dissociation constant (pK_a)	4.57	Likely mobile in soil at environmentally relevant pH
Stability (temperature, metals)	Active ingredient is not oxidized by molecular oxygen in air and is stable when in contact with reducing agents such as tin or steel Stable at 54EC for 2 weeks in glass	

End-use product: Primo MAXX Plant Growth Regulator

Property	Value
Colour	Amber
Odour	None
Physical state	Liquid
Formulation type	Emulsion
Guarantee	11.3% (nominal) (limits: 10.7–11.9%)
Formulants	The product contains U.S. Environmental Protection Agency (EPA) Inert List 3 and List 4B formulants only
Container material and description	37.8 L plastic refillable container 3.78 and 10 L plastic jugs with heat-sealed cap
Specific gravity	1.0698 g/cm^3 at 20EC (from product specification form dated September 15, 2000)

Property	Value
pH	3.63
Oxidizing or reducing action	Product does not contain any oxidizing and reducing agents
Storage stability	Stable after one year's storage in high-density polyethylene (HDPE) bottles with HDPE caps
Explodability	Product is not explosive

1.3 Details of uses

Trinexapac-ethyl is a cyclohexadione plant growth regulator that inhibits the biosynthesis of gibberellin (GA_1). Gibberellin is a phytohormone that promotes growth of various plant organs. The free acid of trinexapac-ethyl inhibits the hydroxylation of GA_{20} to GA_1 by competitively inhibiting the regulatory enzyme 3-$-hydroxylase, leading to a reduction in the size of leaves and stems.

Primo MAXX is proposed for application to turf grown on commercial sod farms and golf courses, including greens, fairways and rough areas, using backpack sprayers, hand sprayers, boom sprayers, and with spray gun application devices to creeping bentgrass, annual bluegrass, Kentucky bluegrass, tall fescue, and perennial ryegrass at rates ranging from 49 to 388 g a.i./ha, with specific rates being dependent on species and use site, at up to 7 times per year at full rates or 14 times per year at one-half rates.

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

Product	Analyte	Method ID	Method Type	Linearity range	Recovery (%)	Relative SD (%)	Method
Technical	Trinexapac-ethyl	AW-151/2	HPLC–UV at 280 nm	55–173 mg/mL	N/A	0.25	Acceptable
Technical	Major impurities	AK-151/3	HPLC–UV at 235 nm	0.1–2.5%	89–115	0.12–3.29	Acceptable

2.2 Method for formulation analysis

Product	Analyte	Method ID	Method	Linearity range	Recovery range	SD	Method
Primo MAXX	Trinexapac-ethyl	AF-1324/1	GC – flame ionization detection	251.3–752.5 mg	98–99% (n = 3)	0.4% (n = 5)	Acceptable

2.3 Methods for environmental residue analysis

Matrix	Method	CGA 163935				CGA 179500				Method (A or N)[a]
		Spike level	Mean % recovery (n)	SD (%)	LOQ	Spike level	Mean % recovery (n)	SD (%)	LOQ	
Soil	HPLC–UV	0.01–0.5 ppm	79 (14)	10	10 ppb	0.01–0.5 ppm	81 (12)	30	10 ppb	A
Sediment	The applicant referenced the soil method which was accepted for the following reasons: • No new final transformation products found in anaerobic sediments • Water solubility high for parent compound (21.2 g/L at pH 8.2) and expected to be higher for the transformation product at pH 8 • Only 4.6% of the material found bound to sediment • Extraction efficiency, using methanol/phosphate buffer at pH 8, expected to be comparable to soil matrix									A
Water	HPLC–UV	0.01–0.5 ppb	77 (25)	13.2	0.1 ppb	0.01–0.5 ppb	93 (37)	9.6	0.05 ppb	A
Turf, thatch	HPLC–UV	0.01–0.1 ppm	80.5 (12)	4.9	0.01 ppm	0.01–10 ppm	73 (8)	8	0.05, 0.01 ppm	A
Cattle liver	HPLC–UV	Not provided • 2 studies show bioaccumulation in fish unlikely • Low log K_{ow} value (1.6 at pH 5.3)				0.01–0.2 ppm	80.4 (8)	3.1	0.02 ppm	A

[a] A, acceptable for post-registration monitoring method; N, not acceptable.

3.0 Impact on human and animal health

3.1 Integrated toxicological summary

A detailed review of the toxicological database available for the technical grade active ingredient (TGAI), trinexapac-ethyl, and the end-use product (EUP), Primo MAXX Plant Growth Regulator for Turf, has been completed. Data submitted (including EPA Data Evaluation Reports) were complete and comprehensive, and included the full battery of studies currently required for registration of a new TGAI and EUP based on Use Site Category 30 (Turf). The scientific and regulatory quality of the toxicology database is

considered sufficient to adequately define the toxicity of this chemical for its intended purpose.

Trinexapac-ethyl (CGA 163935) was rapidly and extensively absorbed in both sexes with greater than 95% of the administered dose being absorbed following single or repeat oral low-dose (0.97 mg/kg bw) administration and single oral high-dose (166 mg/kg bw) administration. The highest residue levels were observed in the fat, lungs, kidneys and liver; however, mean recovery of radioactivity in tissues and carcass at sacrifice (at 168 h post-dosing) was less than 0.3% of administered dose for all dose groups indicating little potential for accumulation. Trinexapac-ethyl was rapidly excreted with greater than 85% of the administered dose being eliminated within 12 h via the urine and up to 2.0% of the administered dose being eliminated within 24 h via the feces. The major route of excretion was via urine, accounting for approximately 95% of administered dose at both dose levels. Fecal excretion accounted for approximately 1.0–2.4% of administered dose at both dose levels. By 72 h less than 0.01% of the administered dose was recovered in expired air. Data suggests that there was very little or no biliary excretion. The major component in urine and fecal extracts was identified as CGA-179500 [4-cyclopropyl-"-hydroxy-methylene)-3,5-dioxo-cyclohexanecarboxylic acid], the free acid derivative of trinexapac-ethyl resulting from hydrolysis of the ester bond of the parent compound, accounting for approximately 82.0–91.6% of the administered dose. The only other residue found (found in fecal extract only) was identified as the unchanged parent compound, trinexapac-ethyl; however, this accounted for less than 0.1% of the administered dose. There was no significant qualitative difference in absorption, distribution, metabolism or excretion of trinexapac-ethyl between the sexes, between single and repeat low-dose administration or between single low- and high-dose administration.

Technical trinexapac-ethyl has low acute toxicity by the oral, dermal and inhalation routes of exposure, is minimally irritating to the eyes and mildly irritating to the skin and is not considered to be a dermal sensitizer. The EUP, Primo MAXX Plant Growth Regulator, has low acute toxicity by the oral, dermal and inhalation routes of exposure, is moderately irritating to the eyes and minimally irritating to the skin and is not considered to be a dermal sensitizer.

Trinexapac-ethyl was tested in a battery of in vitro (bacterial and mammalian cell gene mutation assays, mammalian cell chromosomal aberration assay and unscheduled deoxyribonucleic acid synthesis [UDS] assay) and in vivo (mouse micronucleus assay) mutagenicity assays. There was no evidence of genotoxicity potential in any of these assays; therefore, the weight of evidence suggests that trinexapac-ethyl was not genotoxic under the conditions of the tests performed.

The subchronic and chronic toxicity of trinexapac-ethyl was investigated in the mouse, rat and dog. A repeat dose (22 consecutive days) dermal toxicity study was also carried out in rabbits.

In the mouse, there was no treatment-related finding in either sex at dose levels up to and including 10 000 ppm (equal to 1552 and 1970 mg/kg bw/d in males and females, respectively), the highest dose tested in the 90-day dietary study, and up to and including 7000 ppm (equal to 912 and 1073 mg/kg bw/d in males and females, respectively), the highest dose tested in the 78-week dietary study. In the 78-week dietary study, there was no evidence to indicate that trinexapac-ethyl was oncogenic in the mouse.

In the rat, increased cytoplasmic accumulation of hyaline droplets in the kidney was observed in males at 5000 ppm and above in the 90-day dietary study and at 20 000 ppm at the 52-week interim sacrifice in the 2-year dietary study. This appeared to be reversible and was not observed at the 104-week terminal sacrifice in the 2-year dietary study. Other treatment-related histopathological findings noted in the kidneys included increased incidences of tubular basophilia and tubular casts in males at 20 000 ppm in the 90-day dietary study and brown pigmentation in renal tubular epithelium in males at 20 000 ppm and in females at 10 000 ppm and above at the 52-week interim sacrifice in the 2-year dietary study. The histopathological findings in the kidney were considered to be minimal in severity. Histopathological findings noted at the 104-week terminal sacrifice in the 2-year dietary study included bile duct hyperplasia (males), mammary gland galactoceles (females) and acanthosis glandular stomach (females) at 20 000 ppm. Urinalysis examination revealed lower urinary pH in both sexes at 20 000 ppm and increased urinary specific gravity and urine volume in males at 20 000 ppm in the 90-day dietary study and lower urinary pH in both sexes at 10 000 ppm and above in the 2-year dietary study. Body weight, body-weight gain and food consumption were lower in both sexes at 20 000 ppm in the 90-day and 2-year dietary studies. In the 90-day dietary study, the no observable adverse effect level (NOAEL) was 500 ppm for males (equal to 34 mg/kg). In the 2-year dietary study the NOAEL for chronic toxicity was 3000 ppm (equal to 116 and 147 mg/kg bw/d in males and females, respectively).

In the rat 2-year dietary study, a low but statistically significant, increased incidence of squamous cell carcinoma of the non-glandular stomach (fore-stomach) was noted in males at 20 000 ppm, the highest dose tested. This was not observed in males at any other dose level, including controls and was not observed in females at any dose level, including controls. Extrapolation of the effects of trinexapac-ethyl on the non-glandular portion (fore-stomach) of the rat stomach to possible deleterious effects on the non-glandular areas of the pharynx and (or) esophagus in humans is not reasonable since it is doubtful that trinexapac-ethyl would be in contact with human pharyngeal or esophageal tissues for a significant length of time compared to the resident time in the non-glandular stomach in the rat. In addition, published literature indicates that for induction of carcinogenic activity, non-genotoxic carcinogens must be in contact with the epithelium of the forestomach for extended periods of time. Although this lesion may possibly be treatment-related it was not considered toxicologically relevant to humans.

In a repeat-dose (22 consecutive days) dermal toxicity study in the rabbit, there was no adverse treatment-related systemic finding at dose levels up to and including 1000 mg/kg bw/d, the highest dose tested.

In the dog 1-year dietary study, minimal focal bilateral vacuolation of the dorsal medial hippocampus and (or) lateral midbrain was observed in both sexes at 10 000 ppm and above. Additional analysis indicates that the vacuolation was associated with the astrocytes and oligodendrocytes. The lesions remained confined to the supporting cells in the central nervous system (CNS) and did not progress to more advanced or more extensive damage of the nervous tissue. The lesions were not associated with other neuropathological findings or overt neurological signs. There was no myelinopathy, astrocytosis or astrogliosis present. Nerve cells were not vacuolated and there was neither degradation of the nervous tissue, nor cellular reactions such as inflammatory cell infiltration, phagocytosis or gliosis present that is consistent with lack of overt neurological signs. The effects observed in the glial cells were considered to possibly reflect an interference with energy metabolism (energy deprivation syndrome) following prolonged exposure to extremely high doses of trinexapac-ethyl in the dog only. The glial cells, especially astrocytes, serve as glucose reservoirs in the brain and may react to energy deprivation by swelling. It has been noted in the literature that compounds disturbing the metabolism of glucose induce similar swelling of astrocytes and oligodendrocytes. Similar lesions were not observed in the rat (including neonates) or mouse following subchronic or chronic dietary exposure and there was no other evidence in any species tested to indicate a neurotoxicity potential. However, in the absence of human data, these lesions cannot be disregarded and must be considered relevant to humans.

In the dog, treatment-related findings in the 90-day dietary study were limited to lower body-weight gain in both sexes at 30 000 ppm. Other treatment-related findings in the 1-year dietary study included mucoid and (or) bloody feces and elevated serum cholesterol at 10 000 ppm and above and sporadic emesis, lower red blood cell (RBC) parameters (RBC counts, hematocrit [HCT] and hemoglobin [HB]) and body-weight gain in one or both sexes at 20 000 ppm. In the 90-day dietary study, the NOAEL was 15 000 ppm (equal to 516 and 582 mg/kg bw/d in males and females, respectively). In the 1-year dietary study the NOAEL was 1000 ppm (equal to 31.6 and 39.5 mg/kg bw/d in males and females, respectively).

The weight of evidence suggests that trinexapac-ethyl is not likely to be oncogenic in humans. There was no evidence to suggest a significant increase in toxicity with increased duration of exposure in mouse, rat or dog. No significant gender sensitivity was evident in any species.

In the rat, reproduction function, reproductive parameters and litter parameters were not influenced by treatment in the F_0/F_1 parental animals at any dose levels up to and including 20 000 ppm (equal to 1212 and 1484 mg/kg bw/d in males and females,

respectively), the highest dose tested. Parental findings were limited to lower body weight, body-weight gain and food consumption in F_0/F_1 males and females at 10 000 and 20 000 ppm. The NOAEL for parental toxicity was 1000 ppm (equal to 60 and 76 mg/kg bw/d in males and females, respectively). Lower pup body weights (F_1/F_2 pups) and a slight decreased pup survival (F_1 pups) were observed at 20 000 ppm. The lower pup body weight and survival may be associated with the lower body weight parameters in the parental females but they were considered to be treatment-related and toxicologically relevant. The NOAEL for offspring toxicity was 10 000 ppm (equal to 594 and 751 mg/kg bw/d in males and females, respectively). On the basis of the parental and offspring NOAELs in the rat 2-generation reproductive toxicity study (1 litter/generation) there was no indication that neonates were quantitatively more sensitive than adults to the toxic effects of trinexapac-ethyl. However, the increased severity of the findings in the offspring compared to the severity of the findings in the dams at the respective NOAEL suggests that neonates may be qualitatively more sensitive to the toxic effects of trinexapac-ethyl.

In the rat and rabbit developmental toxicity studies, there was no maternal finding at any dose level up to and including the highest dose tested (1000 and 360 mg/kg bw/d in rat and rabbit, respectively). In the rat developmental toxicity study, the NOAEL for developmental toxicity was 200 mg/kg bw/d based on an increased incidence of asymmetrically shaped vertebrae at the lowest observed adverse effect level (LOAEL), 1000 mg/kg bw/d, which was the highest dose tested (HDT). In the rabbit developmental toxicity study, the NOAEL for developmental toxicity was 60 mg/kg bw/d based on decreased number of live fetuses/litter and increased post-implantation loss at the LOAEL, 360 mg/kg bw/d (HDT). On the basis of the maternal and developmental NOAELs in the rat and rabbit developmental toxicity studies, there appears to an increased susceptibility of the fetus to in utero exposure to trinexapac-ethyl in both species. There was no evidence of teratogenicity in either species; therefore, trinexapac-ethyl was not considered to be teratogenic in rats or rabbits.

There was no rat acute or subchronic neurotoxicity screening study and no rat developmental neurotoxicity study available. In the dog 1-year dietary study, minimal focal bilateral vacuolation of the dorsal medial hippocampus and (or) lateral midbrain was noted in both sexes at 10 000 ppm and above. The vacuolation was associated with the astrocytes and oligodendrocytes. The lesions remained confined to the supporting cells in the CNS and did not progress to more advanced or more extensive damage of the nervous tissue. The lesions were not associated with other neuropathological findings or overt neurological signs. The effects observed in the glial cells were considered to possibly reflect an interference with energy metabolism (energy deprivation syndrome) following prolonged exposure to extremely high doses of trinexapac-ethyl in the dog only. Similar lesions were not observed in the rat (including neonates) or mouse following subchronic or chronic dietary exposure and there was no other evidence in any species tested to indicate a neurotoxicity potential. However, in the absence of human data, these lesions cannot be disregarded and must be considered relevant to humans. The registrant is not

submitting for food uses at this time; therefore a dietary risk assessment for trinexapac-ethyl is not required at this time. In addition, based on the intended uses for trinexapac-ethyl (turf use only) and possible exposure, and assuming that humans are as susceptible to cerebral vacuolation as dogs, it is highly unlikely that exposure to doses sufficient to cause such effects would occur in humans or dogs. The data also suggest that prolonged exposure is necessary, which would be highly unlikely given the intended uses.

3.2 Determination of acceptable daily intake

An acceptable daily intake (ADI) was not established, since trinexapac-ethyl is intended for turf use only (non-food use).

3.3 Acute reference dose

An acute reference dose (ARfD) was not established, since trinexapac-ethyl is intended for turf use only (non-food use).

3.4 Toxicology end-point selection for occupational and bystander risk assessment

Technical trinexapac-ethyl has low acute toxicity by the oral, dermal and inhalation routes of exposure, is minimally irritating to the eyes and mildly irritating to the skin and is not considered to be a dermal sensitizer. The EUP, Primo MAXX Plant Growth Regulator, has low acute toxicity by the oral, dermal and inhalation routes of exposure, is moderately irritating to the eyes and minimally irritating to the skin and is not considered to be a dermal sensitizer.

Trinexapac-ethyl is rapidly and extensively absorbed (greater than 95% of the administered dose) and rapidly eliminated (greater than 85% of the administered dose eliminated within 12 h). No significant tissue accumulation was evident (less than 0.3% of the administered dose remained in the carcass at 168 h post-dosing). Trinexapac-ethyl was extensively metabolised; however the only metabolite identified in the urine and fecal extracts was identified as CGA-179500, the free acid derivative of trinexapac-ethyl accounting for approximately 82.0–91.6% of the administered dose. The only other residue found (in fecal extracts only) was identified as the unchanged parent compound, trinexapac-ethyl, however, this accounted for less than 0.1% of the administered dose.

In the mouse there was no treatment-related finding in the subchronic and chronic dietary studies and there was no evidence to indicate that trinexapac-ethyl was oncogenic in the mouse. In the rat the subchronic and chronic dietary studies, treatment-related findings were observed in the kidney, liver, mammary glands and stomach (glandular and non-glandular). In the rat, increased cytoplasmic accumulation of hyaline droplets in the kidney was observed in males at 346 mg/kg bw/d and above in the 90-day study and at 806 mg/kg bw/d at the 52-week interim sacrifice in the 2-year dietary study. This appeared to be reversible and was not observed at the 104-week terminal sacrifice in the 2-year

dietary study. In the rat, there was also a low, but statistically significant, increased incidence of squamous cell carcinoma in the non-glandular stomach (fore-stomach) in males at 806 mg/kg bw/d, the highest dose tested in the 2-year dietary study. Although this lesion may be treatment-related it was not considered toxicologically relevant to humans. In addition, trinexapac-ethyl was not genotoxic.

In the dog 1-year dietary study, minimal focal bilateral vacuolation of the dorsal medial hippocampus and (or) lateral midbrain was noted in both sexes at 10 000 ppm and above. The vacuolation was associated with the astrocytes and oligodendrocytes. The lesions remained confined to the supporting cells in the CNS and did not progress to more advanced or more extensive damage of the nervous tissue. The lesions were not associated with other neuropathological findings or overt neurological signs. The effects observed in the glial cells were considered to possibly reflect an interference with energy metabolism (energy deprivation syndrome) following prolonged exposure to extremely high doses of trinexapac-ethyl in the dog only. Similar lesions were not observed in the rat (including neonates) or mouse following subchronic or chronic dietary exposure and there was no other evidence in any species tested to indicate a neurotoxicity potential. However, in the absence of human data, these lesions cannot be disregarded and must be considered relevant to humans. Based on the intended uses for trinexapac-ethyl (turf use only) and possible exposure, and assuming that humans are as susceptible to cerebral vacuolation as dogs, it is highly unlikely that exposure to doses sufficient to cause such effects would occur in humans or dogs. The data also suggests that prolonged exposure is necessary, which would be highly unlikely given the intended uses.

There was no evidence in the database to suggest a significant increase in toxicity with increased duration of exposure in mouse, rat or dog. No significant gender sensitivity was evident in any species tested.

In the 2-generation reproduction study (1 1itter/generation), the NOAEL for parental toxicity was 60 mg/kg bw/d based on lower body weight and body-weight gain at the LOAEL, 594 mg/kg bw/d. The NOAEL for offspring toxicity was 594 mg/kg bw/d based on lower pup body weights (F_1/F_2 pups) and a slight decreased pup survival (F_1 pups) at the LOAEL, 1212 mg/kg bw/d. On the basis of the parental and offspring NOAELs in the rat 2-generation reproductive toxicity study (1 litter/generation) there was no indication that neonates were quantitatively more sensitive than adults to the toxic effects of trinexapac-ethyl. However, the increased severity of the findings in the offspring compared to the severity of the findings in the dams at the respective NOAEL suggests that neonates may be qualitatively more sensitive to the toxic effects of trinexapac-ethyl.

On the basis of the maternal and developmental NOAELs in the rat and rabbit developmental toxicity studies, there appears to an increased susceptibility of the fetus to in utero exposure to trinexapac-ethyl in both species. In rats, the increased sensitivity was indicated by an increased incidence of asymmetrically shaped vertebrae at the LOAEL, 1000 mg/kg bw/d, the highest dose tested (maternal NOAEL greater than 1000 mg/kg

bw/d; developmental NOAEL was 200 mg/kg bw/d). In rabbits, the increased sensitivity was indicated by decreased live fetuses/litter and increased post-implantation loss at the LOAEL, 360 mg/kg bw/d, the highest dose tested (maternal NOAEL greater than 360 mg/kg bw/d; developmental NOAEL was 60 mg/kg bw/d). There was no evidence of teratogenicity in either species; therefore, trinexapac-ethyl was not considered to be teratogenic in rats or rabbits. Trinexapac-ethyl is not a reproductive or developmental toxicant.

There is a potential for occupational exposure of mixer/loader/applicators over an intermediate-term duration and post-application for re-entry workers on sod farms and golf courses, intermittently over an intermediate-term duration. Post-application, there is also a potential for exposure to the general population who re-enter golf courses for recreational purposes, intermittently, over an intermediate-term duration.

For mixer/loader/applicators, the most appropriate NOAEL for intermediate-term exposure is 31.6 mg/kg bw/d in the 1-year dietary study in dogs. At the LOAEL, 366 mg/kg bw/d, treatment-related findings included minimal focal bilateral vacuolation of the dorsal medial hippocampus and (or) lateral midbrain, mucoid or bloody feces and elevated serum cholesterol levels in both sexes.

For re-entry workers and the general population, including adults and children, the most appropriate NOAEL for intermittent intermediate-term exposure is 34 mg/kg bw/d in the rat 90-day dietary study. At the LOAEL, 346 mg/kg bw/d, increased accumulation of hyaline droplets in the kidney was observed in males.

For females 13+, the NOAEL for developmental effects (60 mg/kg bw/d) is also identified as an appropriate end point of concern for acute exposures.

For the identified toxicity end points, a safety factor of 1000 based on a safety factor of 100 to account for intra- and inter-species variations and an additional safety factor of 10 to account for the increased sensitivity of rat and rabbit fetuses for developmental end points, for the increased severity of the developmental end points in the rabbit and for the increased sensitivity of rat neonates is considered to be adequate.

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

3.5.1 Operators

Primo MAXX is a turf growth regulator to control excessive top growth of turfgrass species and is to be applied post-emergence on sod farms and golf courses.

It is formulated as a microemulsion concentrate in 3.78, 10, and 37.8 L plastic containers for dilution in water and application by ground equipment only including ground boom

sprayers, hand gun sprayers and backpack sprayers. The label specifies a range of application rates from 49 to 388 g a.i./ha depending on the turf species and site to be applied once every 4 weeks at recommended rates for a maximum of 7 applications per year, or every 2 weeks at half the recommended rates for a maximum of 14 applications per year. Personal protective equipment specified on the proposed label include long-sleeved shirt, long pants, coveralls, gloves, goggles or face-shield and apron for mixing/loading and clean-up and repair activities. No personal protective equipment statement is on the proposed label for application.

There is a potential for occupational exposure over an intermediate-term duration for mixer/loader/applicators for a period of up to 7 months.

Dermal absorption

Male Charles River CD® rats were treated with ^{14}C-CGA-163935 at nominal doses of 0.01 mg/cm^2, 0.1 mg/cm^2 and 1 mg/cm^2 (16 animals/dose group). Rats were sacrificed at the end of the exposure periods of 2, 4, 10, and 24 h (4 animals/exposure period/dose group). Skin washes took place after sacrifice of the animals. Urine, feces, protective appliance washes, skin washes, blood, cage washes and carcass were analysed for radioactivity. Recovery of the applied dose was acceptable and ranged from 97 to 117%.

The majority of the administered dose was recovered from skin washes and the urine. There was a trend of decreasing radioactivity in the skin washes with increased length of the exposure period corresponding with increasing radioactivity in the urine. For example, in the low dose group, at 2 hr, 41.7% of the applied dose was recovered in the skin washes and 25.6% of the applied dose was present in the urine. However, at the 24-hr exposure period, 15.4% of the applied dose was recovered in the skin washes and 61.7% of the applied dose was present in the urine. Less than 1% of the dose was recovered in the blood and feces and less than 4% was recovered in the carcass for all dose groups. The percentage of dose found in the skin test site ranged from 21 to 26%, 8 to 11% and 21 to 40% in the low, middle and high dose groups, respectively, depending on the duration of exposure. In the high dose group, % dermal absorption was less than the low dose group, suggesting saturation of dermal uptake at higher dose levels. The percent dermal absorption ranged from 61 to 91% for the low dose group, 27 to 74% for the middle dose group and 46 to 52% for the high dose group depending on the duration of exposure.

A dermal absorption value of 77.5% is recommended. This value is based on the results obtained from the low dose group at an exposure period of 10 h. This estimate is considered conservative since 21.9% of the applied dose is retained in the skin and is not considered likely to become systemically available in total. One of the limitations found in this study was that the skin washes took place after sacrifice of the animal, which may have increased the percentage of the applied dose retained on the skin at the application site.

Exposure assessment

(*i*) Groundboom and backpack sprayer equipment

Total daily exposure was estimated for applicators who mix, load and apply 0.388 kg a.i./ha to 20 ha of turf per day using groundboom equipment and for applicators who mix, load and apply 0.338 kg a.i./ha to 2 ha of turf per day using backpack sprayer equipment.

A PHED (v1.1) exposure assessment provided an adequate basis for estimating occupational exposure for the proposed use and generally conformed with NAFTA Guidelines for using and reporting PHED data with the exception that backpack spray equipment exposure estimates were based on PHED runs with low replicates (<15) and grade C hand data. PHED data does not provide exposure estimates for clean-up and repair activities nor quantify the variability of exposure estimates.

Daily systemic exposures were based on total absorbed unit exposure (total dermal absorbed plus inhalation deposition), application rate, area treated per day and adult body weight. A dermal absorption factor of 77.5% was applied to dermal deposition values for all scenarios. For the groundboom mixer/loader, exposure was estimated from PHED subsets for single layer clothing with gloves and incorporated a 75% correction factor for use of coveralls. For the groundboom applicator, exposure was estimated from PHED subsets for single layer clothing without gloves. For backpack sprayers (M/L/A), exposure was estimated from PHED subsets for single layer clothing with gloves and incorporated a 75% correction factor for use of coveralls.

The primary route of exposure was dermal, where #8% of the total absorbed unit exposure was by inhalation. Exposure estimates are provided in Table 3.5.1-1.

Table 3.5.1-1 Scenario specific exposure estimates

Turf scenario	PHED exposure estimate (Fg a.i./kg handled)[a]		Exposure pattern (kg a.i. handled/d)	Daily exposure (Fg a.i./kg bw/d)[b]	
	Total deposition	Total absorbed		Total deposition	Total absorbed
Groundboom M/L/A[c]	68.31	53.52	20 ha at 0.388 kg a.i./ha = 7.8 kg a.i.	7.61	5.96
Backpack sprayer M/L/A[d]	2659.2	2074.85	2 ha at 0.388 kg a.i./ha = 0.78 kg a.i.	29.63	23.12

[a] sum of mixer + loader + applicator totals for dermal (absorbed) and inhalation
[b] calculated as Fg a.i./kg a.i. handled × application rate/area × area treated/body weight (70 kg)
[c] single layer clothing with gloves and coveralls for M/L
[d] single layer clothing with gloves and coveralls for M/L/A

(*ii*) Low pressure spray gun

Acceptable surrogate data were used to estimate exposure to workers treating turf with a liquid flowable formulation using low pressure spray gun equipment. For mixer/loader/applicators wearing a single layer of clothing with coveralls and gloves, the daily systemic exposure was estimated to be 2.6 Fg/kg bw/d (Table 3.5.1-2).

Table 3.5.1-2 Scenario specific exposure estimates

Turf scenario	Exposure estimate (Fg a.i./kg handled)[a]		Exposure pattern (kg a.i. handled/d)	Daily exposure (Fg a.i./kg bw/d)[b]	
	Total deposition	Total absorbed		Total deposition	Total absorbed
Low pressure spray gun M/L/A[c]	309	237	2 ha at 0.388 kg a.i./ha = 0.78 kg a.i.	3.4	2.6

[a] sum of mixer + loader + applicator totals for dermal (absorbed) and inhalation deposition

[b] calculated as Fg a.i./kg a.i. handled × application rate/area × area treated/body weight (70 kg)

[c] single layer clothing and coveralls with gloves

For mixer/loader/applicators using groundboom equipment, backpack spray equipment or low pressure spray gun equipment, margins of exposure (MOE) exceeded the target MOE of 1000 for the identified toxicity end point in the 1-year dog study (NOAEL 31.6 mg/kg bw/d) as presented in Table 3.5.1-3.

Table 3.5.1-3 Exposure estimates and MOEs

Turf scenario (M/L/A)	Systemic exposure (Fg a.i./kg bw/d)[a]	MOE
Groundboom[b]	5.96	5 300
Backpack sprayer[c]	23.12	1 400
Low pressure gun sprayer[c]	2.6	12 000

[a] sum of mixer + loader + applicator dermal (absorbed) and inhalation exposures

[b] single layer clothing and coveralls with gloves for mixer/loader

[c] single layer clothing and coveralls with gloves for mixer/loader/applicator

3.5.2 Bystanders

For the proposed application scenarios, bystander exposure was considered to be less than re-entry scenarios for which adequate MOEs were obtained.

3.5.3 Post-application exposure

Post-application, there is a potential for occupational exposure intermittently over an intermediate-term duration for workers on sod farms and golf courses re-entering treated areas for activities such as mowing, scouting, irrigation, weeding and sod harvesting and transplanting. Post-application, there is also a potential for intermittent, intermediate exposure to the general population who re-enter golf courses for recreational purposes.

Post-application exposures were based on dislodgeable turf residue upon re-entry for specific occupational or recreational activities. Two dislodgeable foliar residue (DFR) studies were submitted for trinexapac-ethyl on turf in North Carolina and Illinois using a similar emulsifiable concentrate formulation containing a higher amount of active (23.4%), applied once at an application rate (1.5 kg a.i./ha) approximately 4 times the proposed Canadian maximum application rate (0.388 kg a.i./ha). In the North Carolina study, application was by backpack sprayer and in the Illinois study, application was by groundboom. Turf clippings were collected prior to application, immediately after application (hour 0, 4, 8) and on days 7 or 8, 14, 21, and 30 or 31 post-application and dislodged in a detergent solution to determine Fg a.i./cm^2 of grass surface. Dislodgeable residues of both parent (trinexapac-ethyl) and acid metabolite were determined to estimate total DFR. In both studies, DFR peaked on the day of application and declined rapidly thereafter. Peak total DFR (parent equivalents) were 0.42 Fg/cm^2 and 1.38 Fg/cm^2 in North Carolina and Illinois, respectively, and represented 2–9% of the application rate. DFR declined rapidly after application and are not anticipated to accumulate when applied according to the proposed use pattern (at 2- or 4-week intervals). Total DFR was near the limit of detection (LOD) by day 7.

The DFR studies were limited in several areas that reduced their applicability to the Canadian scenario. The DFR results were considered overly conservative due to the higher application rate and type of dislodge methodology used. Therefore, dislodgeable turf residues were estimated using a default assumption of 5% of the Canadian application rate.

Post-application exposure estimates and MOEs were determined for re-entry workers on sod farms and golf courses and for recreational users of golf courses (Table 3.5.3-1). Daily systemic exposure estimates were derived from DFR coupled with transfer coefficients for various activities and durations according to the dissipation rates defined in the DFR studies, based on the following equation:

exposure (µg/kg bw/d) = DFR × TC × T × DA / bw

where DFR = dislodgeable foliar residue (µg/cm^2)
TC = transfer coefficient (cm^2/h)
T = time for activity (h)
DA = percent dermal absorption
bw = body weight (kg)

Re-entry workers

For re-entry workers, systemic exposure was estimated using activity-specific transfer coefficients for re-entry activities involving low foliar contact (e.g., mowing) and involving high foliar contact (sod harvesting and transplanting) over an 8-h duration. Both peak and time-weighted average exposures were determined.

For the developmental toxicity end point identified for female 13+, acceptable MOEs were obtained for low foliar contact activities at peak exposure times (day of application) but not for high foliar contact activities. However, an acceptable MOE for high foliar contact activities was obtained on day 3 post-application following dissipation of dislodgeable turf residues and thus a re-entry interval of 3 days is recommended for workers re-entering treated areas for sod harvesting and transplanting activities.

For the 90-day oral toxicity end point identified for re-entry workers exposed intermittently over an intermediate-term duration, an acceptable MOE was obtained for low and high foliar contact activities and time-weighted average exposure.

Golfers

For recreational users of golf courses, systemic exposures for adult and adolescents were estimated using activity-specific transfer coefficients for low foliar contact activities similar to re-entry workers (mowing) over a 4-h duration. Both peak and time-weighted average exposures were determined.

For the developmental toxicity end point identified for female 13+, an acceptable MOE was obtained for low foliar contact activity at peak exposure times (day of application).

For the 90-day oral toxicity end point identified for adult and adolescent golfers exposed intermittently over an intermediate-term duration, acceptable MOEs were obtained for low foliar contact activities and time-weighted average exposure.

Table 3.5.3-1 Exposure estimates and MOEs

Re-entry scenario				Systemic[a] exposure (Fg/kg bw/d)	MOE
Worker	Low foliar contact	Peak exposure	day 0	8.59[c]	7 000
		TWA[b]		0.73[d]	46 000
	High foliar contact	Peak exposure	day 0 day 3[e]	283.5[c] 53.24[c]	200 1 100
		TWA[b]		24.20[d]	1 400
Golfer	Adult	Peak exposure	day 0	4.30[c]	14 000
		TWA[b]		0.37[d]	93 000
	Adolescent	TWA[b]		0.58[d]	58 000

[a] Dislodgeable foliar residue × transfer coefficient × activity duration × dermal absorption factor / bw

[b] TWA, time-weighted average

[c] Based on developmental toxicity no observable effect level (NOEL) of 60 mg/kg bw/d in the rabbit

[d] Based on 90-day oral toxicity NOEL of 34 mg/kg bw/d in the rat

[e] Dissipation of DFR based on regression curve from Illinois DFR study (40–50% dissipated per day)

4.0 Residues

Primo MAXX is proposed for use on turf only and the draft label contraindicates the grazing of livestock on treated turf and the feeding of clippings from treated areas to livestock. Therefore, residue data were not required for this non-food or feed use.

5.0 Fate and behaviour in the environment

5.1 Physical and chemical properties relevant to the environment

The solubility of trinexapac-ethyl in reagent water at pH 4.9, pH 5.5, and pH 8.2 is 2.8, 10.2, and 21.2 g/L, respectively. Trinexapac-ethyl is very soluble at all pH conditions. The vapour pressure is 1.03×10^{-3} Pa at 20EC and 2.16×10^{-3} Pa at 25EC, which indicates that trinexapac-ethyl will have a low potential for volatility under field conditions. Based on the values for solubility, vapour pressure, and the molecular weight, the Henry's Law Constant (H) is 5.27×10^{-10} atm m^3 mol^{-1} at pH 5.5 and 2.54×10^{-10} atm m^3 mol^{-1} at pH 8.2. These values indicate that trinexapac-ethyl is non-volatile from water or moist soil

surfaces. The log K_{ow} values are 2.10, 1.60, and –0.38 for pH 3, pH 5.3, and pH 7, respectively, indicating that bioconcentration or bioaccumulation is unlikely. The pK_a is 4.57, indicating the active substance is negatively charged at pH greater than 4.57 and therefore, will likely be mobile in soil at environmentally relevant pHs. The UV–visible absorption maxima are at 240.2 and 277.4 nm in the neutral form, at 240.0 and 280.4 nm in acidic form, and at 270.8 nm in basic form. No absorption maxima are observed at wavelengths above 290 nm, indicating that trinexapac-ethyl has a low potential for phototransformation under normal environmental conditions. The physical and chemical properties of trinexapac-ethyl relevant to the environment are summarized in Appendix 3, Table 1.

For the primary transformation product from most transformation processes, CGA-179500 [free acid derivative of trinexapac-ethyl, 4-(cyclopropyl-a-hydroxy-methylene)-3,5-dioxocyclohexane carboxylic acid], the solubility in reagent water at pH 5, pH 6.8, and pH 8.4 is 13, 200, and 260 g/L, respectively. CGA-179500 is, therefore, very soluble at these pH values. The vapour pressure is 1.0×10^{-6} Pa at 20EC and 2.3×10^{-6} Pa at 25EC, indicating that it is relatively non-volatile under field conditions. The Henry's Law Constants, as calculated by the reviewer, are 3.916×10^{-13}, 2.546×10^{-14} and 1.958×10^{-14} atm m^3 mol^{-1} for pH 5, pH 6.8, and pH 8.4, respectively, indicating that CGA-179500 is relatively non-volatile from water or moist soil surface. The log K_{ow} value is 1.8 at pH 2. As water solubility increases with pH, the log K_{ow} values will decrease with pH, indicating that bioconcentration or bioaccumulation of CGA-179500 is unlikely at environmentally relevant pHs. The pK_as are 5.32 and 3.93. The UV–visible absorption maxima are at 239.3 and 280.0 nm. No absorption maxima are observed at wavelengths above 290 nm, indicating that it has a low potential for phototransformation. The physical and chemical properties of CGA-179500 relevant to the environment are summarized in Appendix 3, Table 2.

5.2 Abiotic transformation

Trinexapac-ethyl hydrolyzes very slowly at pH 5 and pH 7 with first order half-lives of 228 and 455 days, respectively. The hydrolysis at pH 9 is rapid with the first order half-life of 8.1 days. The major hydrolysis product at pH 9 is CGA-179500. Hydrolysis may be an important route of transformation in basic media. The phototransformation first order half-life in soil is 43.7 days. Two major transformation products were detected, CGA-179500 and open-chain CGA-163935. The first-order half-life of phototransformation in water is 5.3 days and the major transformation product is ethyl ester of tricarballylic acid. Phototransformation is not an important route of transformation in soil; but may, however, be an important route of transformation in water.

5.3 Biotic transformation

In aerobic soil, trinexapac-ethyl transformed rapidly with half-lives of 3–6 h. Two major transformation products were formed, CGA-179500 and another unidentified polar

compound, which resulted from the cleavage of the CGA-179500 ring at the carbonyl group. The half life of CGA-179500 was 16–18 days. Further transformation of the other major transformation product was rapid. Trinexapac-ethyl is non-persistent and CGA-179500 is slightly persistent. There are no concerns regarding the persistence of the parent compound and the transformation products under aerobic conditions.

In anaerobic soil, the half-life of trinexapac-ethyl was 10–25 days. The major transformation products were CGA-179500 and an unidentified compound. These major transformation products did not mineralize significantly and, therefore, have the potential to persist and accumulate under anaerobic conditions.

In aerobic water and sediment systems, the first order half-lives were 3.9–5.5 days. The major transformation product was CGA-179500, which was transient. Two minor unidentified transformation products were also detected, but never reached 5% of applied radioactivity. CO_2 is the final transformation product. Trinexapac-ethyl is non-persistent in aerobic aquatic systems.

5.4 Mobility

The laboratory adsorption and desorption study showed that trinexapac-ethyl will be highly mobile in loam and sandy loam, and moderately mobile in sand. CGA-179500 will be highly mobile in sandy loam, moderately mobile in loam, and the mobility will be low in sand. Both the parent and the transformation product will have low mobility in clay.

The laboratory leaching study indicated that trinexapac-ethyl and CGA-179500 were leachable in sand, sandy loam, and loam soils, but little leaching occurred in clay soils. These results are in very good agreement with conclusions drawn from adsorption and desorption data.

The laboratory volatility studies indicated that trinexapac-ethyl did not volatilize from dry or moist soil, and it volatilized only slightly (1% of applied) from turf, during the 15 days of incubation at 15–25EC under continuous air flow. The mean daily air concentration of trinexapac-ethyl ranged from 8.9 to 21.9 Fg/m^3, and volatility rates ranged from 1.6×10^{-3} to 3.2×10^{-3} Fg/cm^2/h. Volatilization is not expected to be an important route of movement of trinexapac-ethyl. Based on the values for vapour pressure and Henry's Law Constant, volatilization of CGA-179500 is not expected to be an important route of dissipation. These are confirmed by the results of the soil and aquatic transformation studies that show that, under laboratory conditions, no volatile transformation products other than CO_2 are produced.

The high solubility of trinexapac-ethyl and CGA-179500 in water indicate that they will primarily remain in the water phase. This is confirmed by the results of the aerobic transformation study in aquatic systems, in which the quantities of extractable residues in sediment were low. In addition, the relatively rapid transformations in soil and water and

sediment systems would decrease the potential for accumulation of the residues of both parent and transformation product in sediment.

5.5 Dissipation and accumulation under field conditions

Results of a terrestrial field study of dissipation and accumulation in sandy loam soil conducted in Illinois, U.S.A. (Mixed-Wood Plains ecozone of the Great Lakes region) indicated that, under field conditions, the time required for 50% dissipation (DT_{50}) of trinexapac-ethyl in the 0–15 cm layer was 1.1 days. The major transformation product was CGA-179500 and it had a DT_{50} of 5.1 days. In treated turf plots, residues of trinexapac-ethyl were not detected below the 15 cm depth. CGA-179500 was never detected at depths below 30 cm. For the bare ground plot, the concentrations of both compounds were below the LOD at depths lower than 15 cm.

Trinexapac-ethyl and the transformation product, CGA-179500, are non-persistent in the field. Supplementary data from the U.S.A. indicated that CGA-179500 could be slightly persistent. Carryover of these compounds is not expected. Neither the parent nor the transformation product leached significantly under field conditions.

5.6 Bioaccumulation

Trinexapac-ethyl and the transformation product, CGA-179500, have low bioconcentration factor (BCF) in bluegill sunfish. Measured BCFs for the parent compound were 2.5, 11, and 6 for edible, non-edible, and whole body tissues, respectively. The parent compound depurated rapidly from all tissues, with a half-life of between 1 and 3 days. Trinexapac-ethyl and CGA-179500 are not expected to bioaccumulate or bioconcentrate.

5.7 Summary of fate and behaviour in the terrestrial environment

The hydrolysis half-life of trinexapac-ethyl is 455, 228, and 8.1 days at pH 5, pH 7, and pH 9, respectively, with formation of one major transformation product, CGA-179500. The first-order half-life of the phototransformation in soil is 43.7 days, with formation of two major transformation products, CGA-179500 and open-chain CGA-163935. Hydrolysis may be an important route of transformation in basic media. Phototransformation is not an important route of transformation in soil.

The half-life of trinexapac-ethyl in aerobic soil was 3–6 h with production of two major transformation products, CGA-179500 and another unidentified polar compound, which resulted from the cleavage of the CGA-179500 ring at the carbonyl group. The half-life of CGA-179500 was 16–18 days. Trinexapac-ethyl is non-persistent and CGA-179500 is slightly persistent in aerobic soil. There are no concerns regarding the persistence of the parent compound and the transformation products in aerobic soil.

In anaerobic soil, the half-life of trinexapac-ethyl was 10–25 days. The major transformation products were CGA-179500 and an unidentified compound. These major transformation products did not mineralize significantly and, therefore, have the potential to persist and accumulate under anaerobic conditions.

Trinexapac-ethyl will be highly mobile in loam and sandy loam, and moderately mobile in sand. CGA-179500 will be highly mobile in sandy loam, moderately mobile in loam, and the mobility will be low in sand. Both the parent and the transformation product will have low mobility in clay.

The laboratory leaching study indicated that trinexapac-ethyl and CGA-179500 will leach in sand, sandy loam, and loam soils, but that little leaching will occur in clay.

The laboratory volatility studies indicated that trinexapac-ethyl was non-volatile from dry or moist soil, and trinexapac-ethyl volatilized only slightly (1% of applied) from turf. Volatilization is not expected to be an important route of movement of trinexapac-ethyl. Based on the values for vapour pressure and Henry's Law Constant, volatilization of CGA-179500 is not expected to be an important route of dissipation.

The high solubilities of trinexapac-ethyl and CGA-179500 in water indicate that they will primarily partition to the water phase. The results of the aerobic aquatic transformation study indicated that the quantities of extractable residues in sediment are low. In addition, the relatively rapid transformations in soil and water and sediment systems indicate a low potential for accumulation of extractable residues in sediment.

Under field conditions, the DT_{50} of trinexapac-ethyl was 1.1–1.4 days. The major transformation product was CGA-179500 and it had a DT_{50} of 5.1–31.5 days. Trinexapac-ethyl is non-persistent and the transformation product, CGA-179500, is non-persistent to slightly persistent in the field. Carryover of these compound is not expected. Neither the parent nor the transformation product leached significantly under field conditions.

The low log K_{ow} value and high water solubility of trinexapac-ethyl and CGA-179500 indicate that these compounds are not expected to bioaccumulate in organisms. This was confirmed by the bioconcentration studies with bluegill sunfish.

The fate and behaviour data are summarized in Appendix 3, Table 3 and the transformation products are summarized in Appendix 3, Table 4.

5.8 Summary of fate and behaviour in the aquatic environment

The hydrolysis half-life of trinexapac-ethyl was 455, 228, and 8.1 days at pH 5, pH 7, and pH 9, respectively, with formation of one major transformation product, CGA-179500. The first-order phototransformation half-life in water is 5.3 days and the major transformation product is ethyl ester of tricarballylic acid. Hydrolysis may be an

important route of transformation in basic aquatic media. Phototransformation is an important route of transformation in water.

In aerobic water and sediment systems, the first-order half-lives were 3.9–5.5 days. The major transformation product was CGA-179500, which further mineralized to CO_2. Trinexapac-ethyl is non-persistent in aerobic aquatic systems.

Results of the bioconcentration studies indicated that trinexapac-ethyl has a low bioconcentration factors (BCF) in bluegill sunfish. This compound depurated rapidly from all tissues, with a half-life between 1 and 3 days. The bioconcentration of trinexapac-ethyl and CGA-179500 in aquatic organisms is negligible.

The fate and behaviour data are summarized in Appendix 3, Table 5 and the transformation products are summarized in Appendix 3, Table 6.

5.9 Expected environmental concentrations

The concentrations of trinexapac-ethyl in various environmental compartments were estimated based on calculations using maximum exposure scenarios. It was assumed that, in accordance with the Canadian label for Primo MAXX, a maximum of 7 applications per year were made at intervals of 28 days, at the label rate of 388 g a.i./ha. Half-life values of 25 days on soil and 5.5 days in water were used in these calculations. The anaerobic soil half-life was used because the laboratory mobility studies indicated that the compound is mobile and leachable in certain types of soils, and the U.S. field dissipation study showed that the compound leached up to 45 cm depth, thus, anaerobic transformation could dominate under certain circumstances. The resulting value is referred to as the “maximum environmental rate.”

5.9.1 Soil

Assuming a soil bulk density of 1.5 g/cm^3 and a soil depth of 15 cm, the concentration of trinexapac-ethyl at the maximum environmental rate of 715.6 g a.i./ha, which is calculated as described above, will be 0.318 mg a.i./kg.

5.9.2 Aquatic systems

Assuming a water density of 1 g/mL and a water depth of 30 cm, the concentration of trinexapac-ethyl at the maximum environmental rate of 399.7 g a.i./ha, which is calculated as described above, will be 0.133 mg a.i./L.

5.9.3 Vegetation and other food sources

Data that could be used to estimate the decrease in the concentration of trinexapac-ethyl on contaminated food sources for wildlife were not provided. Therefore, the estimated

expected environmental concentrations (EEC) in vegetation were calculated using a nomogram from the U.S. EPA (Appendix 3, Table 7). Based on these values, the estimated EEC in the diet of non-target species after application of trinexapac-ethyl at the maximum environmental rate of 715.6 g a.i./ha, expressed as mg trinexapac-ethyl/kg dw diet, are 85.87, 24.2, 361.02, 358.85, and 474.13 for bobwhite quail, mallard duck, rat, mouse, and rabbit, respectively (Appendix 3, Table 8).

6.0 Effects on non-target species

Most of the studies with non-target organisms were conducted with trinexapac-ethyl technical. The toxicity of CGA-179500 was examined in acute toxicity studies with daphnids, rainbow trout, carp, and three freshwater algae (diatom, blue algae and green algae). The end-use formulation Primo MAXX was not tested in any of the ecotoxicity studies. A different formulation (CGD 40010 W, containing trinexapac-ethyl at 250 g/L) was the test material in several studies, but these studies were not included in the review, because this test formulation is not relevant to the proposed EUP. The toxicity to non-target organisms is summarized in Appendix 3, Tables 9 and 10.

6.1 Effects on terrestrial organisms

All studies on terrestrial organisms were conducted with trinexapac-ethyl technical. Trinexapac-ethyl is practically non-toxic to bees based on the acute contact basis. It is practically non-toxic to bobwhite quail and mallard duck on the oral acute and dietary basis. Trinexapac-ethyl at rates up to 93.1 mg/kg soil, which is equivalent to 209.5 kg a.i./ha or 292 times higher than the maximum label rate, is not toxic to earthworm on an acute basis. Acute oral toxicity data indicated that trinexapac-ethyl has low toxicity to rats. For terrestrial vascular plants, trinexapac-ethyl at application rates up to 841 g a.i./ha did not have any effect on seedling emergence in any of the test species. However, plant vigour study indicated that it affected plant growth with a most sensitive concentration effective against 25% of test organisms (EC_{25}) of 299 g a.i./ha on carrot plant dry weight. The effects on terrestrial organisms are summarized in Appendix 3, Table 9.

6.2 Effects on aquatic organisms

Trinexapac-ethyl is practically non-toxic to daphnids and bluegill sunfish. It is slightly toxic to rainbow trout, carp and channel fish. The acute values for mysid shrimp, eastern oyster and sheepshead minnow indicated that trinexapac-ethyl is slightly to moderately toxic to crustacean and practically non-toxic to marine fish. However, it had phytotoxic effects on freshwater and marine algae, and a freshwater vascular plant. The transformation product CGA-179500 is practically non-toxic to daphnids, rainbow trout, carp, freshwater diatom and green algae, but this transformation product had toxic effects on blue algae and marine diatom. The effects on aquatic organisms are summarized in Appendix 3, Table 10.

6.3 Risk assessment

6.3.1 Terrestrial organisms

Margins of safety (MOS) were calculated using the EEC values and the no observable effect concentration (NOEC) or an estimated NOEC equivalent to 1/10 of the median effective concentration (EC_{50}) or median lethal concentration (LC_{50}) for the most sensitive species per group.

Terrestrial invertebrates
The major route of exposure for earthworms is through ingested soil in treated fields. The MOS, based on a 14-day acute NOEC of 93.1 mg a.i./kg soil, was calculated as 292.8 and thus earthworms are not expected to be at risk from the proposed use of trinexapac-ethyl.

The major route of exposure to honey bee is through contact with contaminated plants. Using assumptions of Atkins et al. (1981), an median lethal dose (LD_{50}) of 47 Fg a.i./bee is equivalent to an LD_{50} of 52.6 kg a.i./ha. Assuming a worst case of overspray, the EEC is the maximum application rate, i.e., 715.6 g a.i./ha, and the MOS is, therefore, 735, indicating that bees are not at risk from the proposed application of trinexapac-ethyl.

Avian species
The major route of exposure to birds is through ingestion of food contaminated by trinexapac-ethyl. The MOS for bobwhite quail, based on the reproduction NOEC of 200 mg a.i./kg dw and EEC of 85.87 mg a.i./kg dw diet, is 2.3. Based on the acute oral LD_{50} of >2000 mg a.i./kg bw and EEC of 24.2 mg a.i./kg dw diet for mallard duck, the number of days of intake of trinexapac-ethyl required to reach NOEL is 73.4 days. Therefore, the proposed use of trinexapac-ethyl will pose a low risk to birds.

Small wild mammals
The major risk to small mammals is through ingestion of food sources contaminated by exposure to trinexapac-ethyl during and shortly after application. For acute oral toxicity in rat, the MOS is expressed as 19.6 days of intake required to produce the equivalent of the dose administered to reach NOAEL in laboratory population. The MOS for dietary toxicity in the rat and mouse are 1.38 and 27.87, respectively, based on the NOAEL of 500 mg a.i./kg dw diet for rat and 10 000 mg a.i./kg dw diet for mouse. Based on a NOAEL of 1000 mg a.i./kg dw diet (parental) for rat, the MOS for reproductive toxicity is 2.77. Therefore, the proposed use of trinexapac-ethyl will pose low risk to rat and no risk to mouse.

Terrestrial plants
The most sensitive plant species tested was carrot. Based on the EC_{25} value of 299 g a.i./ha (plant dry weight of carrots), the MOS is 0.42. Therefore, trinexapac-ethyl poses a moderate risk to non-target terrestrial plants.

In conclusion, the proposed use of trinexapac-ethyl would expect to pose no risk to terrestrial invertebrates, low risk to wild birds and mammals, and moderate risk to certain non-target plants (Appendix 3, Table 11).

6.3.2 Aquatic organisms

Freshwater invertebrates and fish
Based on a chronic NOEC of 2.4 mg a.i./L for daphnids, a 96-h NOEC of 30 mg a.i./L for rainbow trout, a 96-h acute NOEC of 48.3 mg a.i./L for bluegill sunfish, and an early life NOEC of 0.41 mg a.i./L for fathead minnow, the MOS values are 18.05, 225.56, 363.16, and 3.08, respectively. Therefore, the proposed use of trinexapac-ethyl will pose no risk to freshwater invertebrates, but it will pose a low risk to certain species of fish.

Freshwater plants
Based on the 5-day growth inhibition NOEC of 0.11 mg a.i./L for the blue-green alga and a 14-day NOEC of 0.018 mg a.i./L for the duckweed, the MOS values for algae and duckweed are 0.83 and 0.14, respectively. Therefore, use of trinexapac-ethyl poses a moderate risk to freshwater algae and aquatic vascular plants.

Marine species
Among crustacean, marine fish and marine algae, the crustacean is the most sensitive group. Based on a 96-h LC_{50} of 6.5 mg a.i./L for mysid shrimp, the MOS is 4.89. Therefore, marine species are at low risk from the proposed use of trinexapac-ethyl.

In conclusion, the proposed use of trinexapac-ethyl poses no risk to the freshwater invertebrates, low risk to freshwater fish and moderate risk to freshwater algae and vascular plants. For various marine species, it poses no risk to marine fish and marine algae, and low risk to crustaceans (Appendix 3, Table 12).

6.4 Risk mitigation

Exposure to trinexapac-ethyl through direct overspray will pose a moderate risk to non-target terrestrial and aquatic vascular plants and freshwater algae; however, spray drift will not pose a significant risk and, therefore, buffer zones are not necessary for both terrestrial and aquatic habitats. The applicators, however, should be warned that a direct overspray will pose a risk to terrestrial and aquatic environments. Therefore, the addition on the product label of the following statement is recommended:

> Do not overspray non-target plants or any body of water. Do not contaminate aquatic systems through the disposal of waste or the cleaning/rinsing of spray equipment.

7.0 Efficacy

7.1 Effectiveness

7.1.1 Intended uses

Syngenta Crop Protection Canada Inc. has applied for the registration of Primo MAXX, a commercial class end-product, under the User Requested Minor Use Registration (URMUR) Program. The product is proposed for use on commercial sod farms and golf courses (including greens, fairways, roughs and other turf within golf course properties) to inhibit growth of turf and reduce the number of mowing operations. The rates proposed are specific to use site and species, and are shown in Table 7.1.1-1. The proposed rates are claimed to provide 50% growth inhibition when applied to actively growing turf every 4 weeks. It is also proposed that during summer when temperatures are higher, the product may be applied at one-half rates every 2 weeks.

Additionally, it is proposed that Primo MAXX has a number of other benefits, including that use of the product may increase turf colour, quality and density. It is proposed to partially suppress annual bluegrass and Kentucky bluegrass seedheads and can be used to precondition turf to environmental stresses, in part by increasing turf density and thereby reducing evaporation of moisture from soil, and by increasing root mass and root depth. It was also proposed that Primo MAXX could be used in mixture with turf marking paint. However, as such a mixture is not typically used on sod farms and golf courses, this proposal was not considered.

It is proposed that Primo MAXX can be used as a component of a program aimed at renovating turf infested with annual bluegrass. Specifically, it is proposed that use of the product would permit better seedling growth of more desirable turfgrass species that are overseeded into the stand. Application is proposed for application 1–5 days prior to seeding, and before verticutting, scalping, and (or) spiking operations. It is cautioned on the submitted draft label that use of “aggressive” application rates, implying use of rates higher than those listed in Table 7.1.1-1, could cause temporary yellowing of turf. The label rate would then be applied the following spring.

Table 7.1.1-1 Proposed Primo MAXX rates

Turf type	Sod farms and golf courses, including roughs	Golf course fairways (1.3 cm high or less)	Golf course greens
	mL/100 m^2 (equivalent rates in g a.i./ha)		
Bentgrass	24.0 (291)	8.0 (97)	4.0 (49)
Tall fescue	24.0 (291)		
Kentucky bluegrass	19.0 (230)	8.0 (97)	
Bentgrass / annual bluegrass mixture		8.0 (97)	4.0 (49)
Kentucky bluegrass / tall fescue / perennial ryegrass	24.0 (291)		
Kentucky bluegrass / perennial ryegrass / annual bluegrass mixture		16.0 (194)	
Perennial ryegrass	32.0 (388)	16.0 (194)	

7.1.2 Mode of action

Trinexapac-ethyl is a cyclohexadione plant growth regulator that inhibits the biosynthesis of gibberellin (GA), specifically GA_1. Gibberellin is a phytohormone that promotes growth of various plant organs. The free acid of trinexapac-ethyl inhibits the hydroxylation of GA_{20} to the final biologically active form GA_1 by competitively inhibiting the regulatory enzyme 3-$-hydroxylase. Trinexapac-ethyl is foliarly absorbed and results in inhibition of cell elongation, leading to a reduction in the size of leaves and stems.

7.1.3 Crops

Primo MAXX is proposed for use on creeping bentgrass, annual bluegrass, Kentucky bluegrass, tall fescue and perennial ryegrass situated on sod farms and golf courses.

7.1.4 Effectiveness as a growth suppressor

Data were submitted from field and greenhouse trials that were conducted in the U.S. from 1993 until 1999 and in Canada in 2000. Trials were conducted on turf that was maintained at canopy heights typical for fairways, usually 1–2 cm, or at heights typical for golf course roughs, usually 5–7.5 cm. The efficacy of the older formulation, Primo 1EC, first registered in the U.S. in 1993, was included in the U.S. trials. The field performance of

Primo MAXX was bridged to that of Primo 1EC in seven U.S. trials conducted in 1998 and 1999. The efficacy of Primo MAXX only was assessed in the Canadian trials.

The efficacy of Primo EC and that of Primo MAXX were directly compared in trials conducted on annual bluegrass in 1998 (1 trial), Kentucky bluegrass in 1998 (2 trials), perennial ryegrass in 1998 (1 trial) and 1999 (2 trials), and tall fescue in 1999 (1 trial). The performance of each formulation was compared with the other on annual bluegrass maintained at 1.6 cm height, Kentucky bluegrass maintained at approximately 3.8 cm, perennial ryegrass maintained at 1.3–1.9 cm (2 trials) or 3.8 cm (1 trial) and tall fescue maintained at 12.5 cm. In six trials, the two formulations performed similarly in suppressing turf growth, as assessed by canopy height (4 trials) and clippings biomass (6 trials). In 1 trial, the clippings biomass of fairway-height perennial ryegrass was similar or greater than that of the untreated control at 42 days after application; and this may have been a result of the late evaluation date, at which time the effect of the growth regulator may have diminished completely. Data were not available for creeping bentgrass or any turfgrass species maintained at a canopy height typical for greens (0.4–0.5 cm); however, given the similarity in performance of the two formulations in these bridging trials, no difference in performance between these two formulations on greens or creeping bentgrass would be expected. Therefore, data generated with the Primo EC formulation were used in consideration of the application to register Primo MAXX.

Creeping bentgrass at fairway height

In each of the five Canadian trials that were conducted on golf course fairways, and that were replicated once or twice, three applications of 96 g a.i./ha Primo MAXX were made 4 weeks apart. One trial was conducted on a solid stand of creeping bentgrass and four were conducted on mixtures of creeping bentgrass and annual bluegrass, in which the turf was comprised of 30–80% creeping bentgrass. When assessed about 2 weeks after treatment in these trials, clippings were reduced by 56–80% after the first application, 49–74% after the second application, and 46–65% after the third application. Responses after each application were similar.

In five U.S. field trials, clippings were reduced by a maximum of 33–63% after application of 76–98 g a.i./ha Primo 1EC. In two of these trials conducted over 2 years, a total of six applications were made about 1 month apart. Clippings were reduced by a maximum of 33–50% in one trial and 42–63% in the other. The response of creeping bentgrass to the growth regulator did not change with successive applications. In a sixth trial, growth suppression, rated on a scale of 0 (no growth suppression) to 10 (complete growth suppression), of 16 cultivars following application of 97 g a.i./ha Primo 1EC was similar, ranging from 3 to 4 when evaluated 10 days after the first application and from 2 to 3 when assessed 17 days after the second application. In a trial conducted in lysimeters, clippings were reduced by a maximum of 47 and 53% after the third and fourth applications, respectively.

In four of five greenhouse trials, clippings biomass was reduced by a maximum of 25–65% following application of 95–100 g a.i./ha, while in the fifth trial, clippings yield was greater for Primo 1EC-treated turf than that which was untreated.

A treatment of 48 g a.i./ha Primo 1EC was included in three of the above trials, including the two in which six sequential applications were made. Clippings were reduced by a maximum of 18–50% over the three trials following application at this rate.

The data submitted support the proposed use of Primo MAXX applied at 97 g a.i./ha once every 4 weeks (or later as required) on creeping bentgrass fairways. The data also support use of the 49 g a.i./ha rate on creeping bentgrass fairways once every 2 weeks (or later as required). The data can also be considered in support of the proposed use of 49 g a.i./ha Primo MAXX on golf course greens, which are typically maintained at lower canopy heights than fairways; however, the claim that application of 49 g a.i./ha will result in 50% turf growth reduction on greens cannot be supported. The growth suppression claim for greens should be revised to one-third. No data were submitted to support use of Primo MAXX applied at the one-half rate for greens (24 g a.i./ha).

Creeping bentgrass at golf course rough height

Primo MAXX is proposed for use at 291 g a.i./ha for creeping bentgrass at heights typical for golf course roughs. Data were submitted from only one field trial conducted in Michigan in 1993 in which Primo 1EC was applied at 293 g a.i./ha to creeping bentgrass maintained at fairway height. This trial also included rates of 98 and 196 g a.i./ha. At most evaluation dates, reduction in clippings biomass was similar among rates, with maximum reductions of 60, 61, and 82% observed for the 98, 196, and 293 g a.i./ha, respectively. Given that no data were submitted for creeping bentgrass maintained at heights greater than that typical of fairways, and that limited crop tolerance data suggest that creeping bentgrass may not be fully tolerant of the proposed rate of 291 g a.i./ha (see Section 7.4), creeping bentgrass maintained at heights over that typical of fairways is not acceptable.

Kentucky bluegrass at golf course rough height

Data were submitted from four field trials conducted in 1993, 1998 (2 trials), and 1999 in which trinexapac-ethyl, applied as Primo MAXX (2 trials) or Primo 1EC (4 trials) was applied to Kentucky bluegrass at 224–230 g a.i./ha, near or at the proposed rate of 230 g a.i./ha. A one-half rate of 115 g a.i./ha was included in the two trials to include treatments of Primo 1EC and Primo MAXX.

Height and clippings biomass of Kentucky bluegrass were consistently reduced by Primo MAXX and Primo 1EC applied at or near 230 g a.i./ha. Height, assessed in three of four trials, was reduced by a maximum of 5–31%. In these trials, clippings biomass was consistently reduced by a maximum of 57–75% when assessed from 1 to 5 weeks after application. In the fourth trial, the growth suppressing effect of 224 g a.i./ha Primo 1EC was more pronounced under higher nitrogen fertility levels. Clippings biomass, evaluated 31 days after treatment, was reduced by 59, 70, and 75% for turf on which 98, 196, and

294 kg nitrogen had been applied, respectively. Clippings biomass was reduced by only 25% for turf that received no nitrogen fertilizer. In one trial where five applications were made 3–5 weeks apart, the growth-inhibiting effect following the last application had diminished by 36 days after treatment. In this trial, the degree of growth suppression was similar after each application. In the two trials that included a one-half rate treatment, reduction in height and clippings biomass of turf treated with 115 g a.i./ha were approximately one-half that observed of turf treated with the 230 g a.i./ha rate at 3 weeks after treatment.

The data submitted support the proposed use of Primo MAXX applied at 230 g a.i./ha once every 4 weeks, or later as required on Kentucky bluegrass maintained at typical canopy heights for golf course roughs. The data also support use of a one-half rate once every 2 weeks, or later as required.

Kentucky bluegrass at fairway height

No field trial was conducted in which Kentucky bluegrass maintained at canopy heights typical of fairways was treated with the proposed rate of 97 g a.i./ha. In a field trial in which turf was maintained at 5.1 cm, Primo 1EC applied at 67 g a.i./ha reduced height by a maximum of 18%. Clippings biomass was not assessed in this trial, but height reductions of 18% have equated to clippings biomass reductions of about 50% in other trials. In two trials that were discussed above, clippings dry weight was reduced by a maximum of 23 and 35% following application of 115 g a.i./ha Primo MAXX to Kentucky bluegrass mowed to a canopy height of 3.8 cm. Two greenhouse studies were conducted in which Primo 1EC was applied to Kentucky bluegrass at 95–96 g a.i./ha. Turf was maintained at 2 cm in one study and at 4 cm in the other. Each study consisted of two experiments. In one study, Primo 1EC applied at 97 g a.i./ha increased growth of newly sown Kentucky bluegrass in one trial, but reduced clippings biomass of established Kentucky bluegrass by up to 18% in the second trial. In the second greenhouse study, clippings biomass was reduced by up to 24% after application of 95 g a.i./ha, when averaged over the two experiments.

Data generated in field trials indicated that application of 67–115 g a.i./ha could be expected to reduce Kentucky bluegrass growth, usually by less than 50%, but by at least 25%. Field trials were conducted on turf maintained at heights over that typical of fairways, and at any given rate, percentage growth reduction is expected to be greater on turf with lower canopy heights. Therefore, it could be expected that Kentucky bluegrass growth on fairways would be reduced by approximately one-third following application of 97 g a.i./ha Primo MAXX.

Tall fescue at golf course rough height

Seven field trials, including one conducted in lysimeters, were conducted over 4 years in which Primo 1EC was applied at 270–287 g a.i./ha (near the proposed 291 g a.i./ha) to tall fescue turf maintained at mowing heights of 5.1–12.5 cm. Canopy height, evaluated in three trials, was reduced by a maximum of 14–28%. Clippings biomass, assessed in five

trials, was reduced by a maximum of 40–92%. In one additional field trial, application of Primo MAXX or Primo 1EC at 192 g a.i./ha to tall fescue turf reduced clippings biomass by up to 71%. A rate of 190 g a.i./ha was also included in a trial that included a treatment of Primo 1EC at 286 g a.i./ha. In this trial, height and clippings biomass was reduced by a maximum of 16 and 26%, respectively, following treatment of 190 g a.i./ha. This was less than the maximum height and clippings reduction of 24 and 40%, respectively, observed for the 286 g a.i./ha rate.

Three trials included one-half rates of 136–144 g a.i./ha. Height was reduced by a maximum of 19% in one trial and clippings were reduced by up to 64 and 77% in two trials. In these trials, it was evident that to maintain growth inhibition, reapplication after 4–10 weeks would have been required.

In a greenhouse study, tall fescue clippings biomass was reduced by a maximum of 21 and 39% following application of 95 and 191 g a.i./ha Primo 1EC.

The data submitted support the proposed use of Primo MAXX applied at 291 g a.i./ha once every 4 weeks, or later as required on tall fescue mowed at canopy heights typical for golf course roughs. The data also support use of a one-half rate once every 2 weeks, or later as required.

Perennial ryegrass at golf course rough height

Primo 1EC was applied near the proposed rate of 388 g a.i./ha to turf in 1994 (1 trial) and 1999 (2 trials). Two of these trials included a one-half rate treatment. In one trial mowed to 1.3–1.9 cm, canopy height was reduced by a maximum of 15–28% and 16–35%, respectively, after each of three applications of 192 and 385 g a.i./ha. Clippings dry weight was evaluated only occasionally in this trial; however, after the second application, clippings were reduced by 30 and 55% when assessed 13 days after the second application. In a second trial conducted on turf maintained at 3.8 cm, clippings were reduced by a maximum of 25 and 56% after the application of 183 and 366 g a.i./ha, respectively. In the latter trial, it was evident that a second application was needed to maintain inhibition of growth 14 and 28 days after application of the lower and higher rate, respectively. In a third trial, clippings of perennial ryegrass turf maintained at 3.8 cm were reduced by a maximum of 53% after each of two applications made 6 weeks apart. Growth of turf was adequately inhibited throughout the 6 weeks following the first application, but it was apparent that retreatment would have been required 4 weeks after the second application to maintain growth inhibition.

The data submitted support the proposed use of Primo MAXX applied at 388 g a.i./ha once every 4 weeks, or later as required on perennial ryegrass maintained at canopy heights typical for golf course roughs. The data also support use of a one-half rate once every 2 weeks, or later as required.

Perennial ryegrass at fairway height
Five field trials were conducted over 3 years in which perennial ryegrass turf, maintained at a canopy height of 1.3–3.8 cm, was treated with Primo 1EC at 183–196 g a.i./ha, near the proposed rate of 194 g a.i./ha. Clippings biomass of fairway-height turf treated with 96 or 192 g a.i./ha Primo 1EC or Primo MAXX was similar or greater than that of the untreated check at 6 weeks after application, by which time, the growth suppressing effect would have diminished or disappeared. Height and clippings biomass were assessed in three and two of the remaining four trials, respectively. Height was reduced by a maximum of 28% in one trial that included four sequential applications made from 1 week to 1 month apart. Height, assessed as area under a growth curve, was reduced by 9–13% in one trial and 4–14% in another after each of three applications. Clippings biomass was reduced by a maximum of 25–30% in two trials. Clippings biomass was evaluated in an additional two trials: one maintained at 1.9 cm and the other at 5.1 cm, with Primo 1EC applied at 146 and 152 g a.i./ha, respectively. In these trials, clippings were reduced by a maximum of 45–54%. Application of 76 g a.i./ha in the latter trial maintained at fairway height resulted in a maximum clipping yield reduction of 43%.

Six greenhouse studies were conducted in which Primo 1EC was applied to perennial ryegrass at a rate of 191 g a.i./ha. The clippings biomass in the Primo 1EC treatment was greater than that of the untreated check in one trial. In the remaining five trials, the maximum reduction in clippings ranged from 31 to 88%. A rate of 95 g a.i./ha assessed in two of these five trials, in which clippings were reduced by a maximum of 24 and 49%.

Clippings biomass following application of 146–196 g a.i./ha ranged from 25–54% over six field trials. The proposed claim that application of Primo MAXX at 194 g a.i./ha will result in 50% growth reduction of perennial ryegrass on fairways was not supported. The data collectively indicate that the growth regulator applied at 194 g a.i./ha every 4 weeks (or later as required) can be expected to inhibit growth by approximately one-third. The proposal for use of a one-half rate every 2 weeks (or later as required) is also acceptable.

Mixtures of annual bluegrass and creeping bentgrass at fairway height
As previously mentioned for creeping bentgrass, the efficacy of 96 g a.i./ha Primo MAXX for growth inhibition of fairway managed turf comprised of annual bluegrass and creeping bentgrass, was assessed in four of five unreplicated or twice-replicated trials that were conducted in southern Ontario in 2000. The maximum reduction in clippings biomass was usually 50% or greater.

Data were submitted from three field trials conducted over 2 years in which Primo 1EC was applied at 76–98 g a.i./ha to fairway height annual bluegrass. One of these trials also included a treatment of 48 g a.i./ha. In the latter trial, application of 96 g a.i./ha reduced canopy height and clippings biomass by a maximum of 24% and 82%, respectively. Application of 48 g a.i./ha resulted in height and clippings biomass reductions of about one-half that observed for the higher rate. In the second trial, clippings biomass was reduced by a maximum of 61% following application of 98 g a.i./ha. In the third trial, a

maximum reduction of 43% following application of 76 g a.i./ha was observed. In one greenhouse study, application of 100 g a.i./ha reduced clippings by a maximum of 30%.

The data submitted indicate that application of Primo MAXX at 97 g a.i./ha can be expected to inhibit growth of annual bluegrass, alone or in mixtures with creeping bentgrass, on golf course fairways by 50% or greater. The data submitted support the proposed use of Primo MAXX applied at 97 g a.i./ha every 4 weeks (or later as required) to fairways consisting of mixtures of annual bluegrass and creeping bentgrass. A claim that a one-half rate of 48 g a.i./ha may be applied every 2 weeks (or later as needed) is also acceptable.

Mixtures of annual bluegrass, Kentucky bluegrass and perennial ryegrass at fairway height

No data were submitted from trials conducted on mixtures of annual bluegrass, Kentucky bluegrass and perennial ryegrass. Therefore, data generated in trials that were conducted on solid stands of these turf species were considered in support of the proposed use of Primo MAXX at 194 g a.i./ha on this turf mixture.

Data were submitted from three field trials conducted over 2 years in which Primo 1EC was applied at 152–196 g a.i./ha to fairway height annual bluegrass. These trials also included lower rates of 76–98 g a.i./ha. In the first trial, application of 96 and 192 g a.i./ha reduced canopy height by a maximum of 24 and 22%, respectively, and clippings biomass was reduced by a maximum of 82 and 88%, respectively. In the second trial, clippings biomass was reduced by a maximum of 61 and 67% following application of 98 and 196 g a.i./ha, respectively. In the third trial, maximum reductions of 43 and 54% following application of 76 and 152 g a.i./ha Primo 1EC were observed. In one greenhouse study, application of 100 and 190 g a.i./ha reduced clippings by a maximum of 30 and 35%, respectively.

No field data were submitted for Kentucky bluegrass maintained at canopy heights typical of fairways. However, data were submitted from seven field trials conducted on Kentucky bluegrass turf maintained at heights of 5.1–6.4 cm in which Primo 1EC was applied at 190–202 g a.i./ha. Clippings biomass, assessed in six trials, was reduced by a maximum of 45–91%. Canopy height, assessed in two trials, was reduced by up to 15–27%. It was evident that retreatment after 5–7 weeks was necessary to maintain growth inhibition. The degree of growth inhibition was similar, on average, after the first and second applications in the five trials in which two applications were made. In an additional field trial in which 143 g a.i./ha of Primo 1EC was applied to Kentucky bluegrass mowed to 6.3 cm, clipping yield was reduced by up to 47%. The level of growth reduction on fairway height turf would be expected to be at least that observed for turf at greater canopy heights. Therefore, 194 g a.i./ha would be expected to provide 50% or more growth suppression of Kentucky bluegrass turf on fairways.

Data generated in field trials indicated that the application of this rate could be expected to reduce Kentucky bluegrass and annual bluegrass growth by at least 50%. Submitted data indicated that there was little difference in efficacy of the 97 and 194 g a.i./ha rates for annual bluegrass growth suppression but the higher rate is required for growth suppression of perennial ryegrass. As previously indicated, application of this rate to perennial ryegrass can be expected to reduce growth by about one-third. Application of 194 g a.i./ha every 4 weeks (or later as required) to a fairway-grown turf consisting of a mixture of these three species could be anticipated to result in approximately 50% growth suppression. The data also support use of a one-half rate once every 2 weeks, or later as required.

Note that for mixtures of Kentucky bluegrass and annual bluegrass on fairways, the rate of Primo MAXX should be restricted to 97 g a.i./ha.

Mixture of annual bluegrass and creeping bentgrass on greens
No efficacy trial was conducted on mixtures of annual bluegrass and creeping bentgrass maintained at greens height. Primo MAXX is proposed for use at 49 g a.i./ha on greens for 50% growth inhibition. In the one trial conducted on fairway-height annual bluegrass and in which this rate was tested, clippings were reduced by a maximum of 38%. As previously discussed, application of this rate of Primo 1EC reduced fairway-height creeping bentgrass growth by a maximum of about one-third. Growth reduction on greens would be expected to be similar to or greater than that on fairways at any given rate. Therefore, a claim that Primo MAXX applied at 49 g a.i./ha could be expected to suppress growth of a mixture of annual bluegrass and creeping bentgrass on greens by one-third is acceptable.

Mixture of Kentucky bluegrass, perennial ryegrass and tall fescue at golf course rough canopy height
The rate proposed for this tank mixture, 291 g a.i./ha, is the same as that proposed for tall fescue, less than that proposed for perennial ryegrass (388 g a.i./ha), and greater than that proposed for Kentucky bluegrass (230 g a.i./ha). No data were submitted for this turf mixture. Therefore, data generated for each turf species individually were considered in support of the proposed use.

Data submitted from trials in which Kentucky bluegrass was treated with 230 g a.i./ha Primo 1EC or Primo MAXX were considered in support of the proposed use on this turf mixture. Additionally, data were available from nine field trials conducted over 3 years in which 280–286 g a.i./ha Primo 1EC was applied to Kentucky bluegrass mowed to 5.1–7.6 cm. Clippings biomass, evaluated in all eight trials, was reduced by a maximum of 50–88%. Canopy height was reduced by a maximum of 31 and 18% after the first and second application in one trial, and by 26% after a single application in a second trial.

The effect of a single application of a one-half rate near 145 g a.i./ha was evaluated in three field trials. Following application of this rate, clippings biomass was reduced by a

maximum of 47 and 79% vs. 66 and 84% after application of 291 g a.i./ha. In the third trial, height was reduced by a maximum of 23 and 26% after application of 145 and 291 g a.i./ha, respectively.

Data were submitted from three field trials conducted over 2 years in which Primo 1EC was applied to perennial ryegrass at or near the rate proposed for use on this mixture. Leaf extension was reduced by a maximum of 24–25% and clippings biomass was reduced by a maximum of 51–55% in two trials in which turf was maintained at a canopy height of 3.8 cm. In a third trial conducted on fairway-managed turf, height was reduced by 16%.

Field data have shown that a rate of 291 g a.i./ha applied to tall fescue can be expected to provide approximately 50% or more growth suppression of tall fescue.

Primo MAXX applied to solid swards of Kentucky bluegrass, tall fescue, or perennial ryegrass at the proposed rates of 230, 291, and 388 g a.i./ha, respectively, can be expected to result in at least 50% growth reduction. The rate proposed for the mixture is intermediate; therefore it would be expected to result in at least 50% growth reduction. Application of a one-half rate of 145 g a.i./ha every 2 weeks (or later) is also acceptable.

Multiple applications

It is proposed that up to 7 sequential applications of Primo MAXX can be made to turf at proposed rates 4 weeks apart, or that up to 14 applications of one-half rates can be made 2 weeks apart in any one year. In field trials in which Primo 1EC was applied five times to golf course rough-height Kentucky bluegrass at 229 g a.i./ha, six times to fairway-height creeping bentgrass at 48 and 96 g a.i./ha (2 trials), and four times to fairway-height perennial ryegrass at 192 g a.i./ha, the degree of growth reduction, assessed as canopy height (2 trials) and clippings biomass (3 trials), did not diminish or increase with successive applications.

Post growth suppression period

Turf treated with Primo 1EC sometimes experienced a growth resurgence after a period of suppressed growth. For tall fescue, a growth resurgence was observed following a period of growth suppression for turf treated with Primo 1EC in two trials. The canopy height of turf treated with 202–403 g a.i./ha was up to 9% greater than that of untreated turf at 70 days after application in one trial. The clippings biomass of turf treated with 286–382 g a.i./ha was about 57% greater than that of the untreated check in a second trial at 85 days after treatment. The growth of Primo 1EC-treated turf was numerically greater than that of the untreated control in several other trials after application of Primo 1EC beginning at 6 weeks after treatment or later. For Kentucky bluegrass, a period of increased growth was observed after a growth suppression period for turf treated with Primo 1EC. The canopy height of turf treated with 202–403 g a.i./ha was up to 13% greater than that of untreated turf at 57 days after application in one trial. In a second trial, the clippings biomass of turf treated with 143–573 g a.i./ha was 33–53% greater than that of the

untreated check 63 days after treatment. The growth of Primo 1EC-treated turf was numerically greater than that of the untreated control in several other trials after application of Primo 1EC beginning at 5 weeks after treatment or later. In two trials, growth of fairway-height creeping bentgrass treated with 48–229 g a.i./ha was numerically greater than that of the untreated control beginning at about 5–7 weeks after application. Similarly, the growth of perennial ryegrass was numerically greater for turf treated with 229 and 366 g a.i./ha Primo 1EC than the untreated control in two trials beginning at about 5 weeks after application.

Overall conclusions on efficacy of Primo MAXX for turf growth suppression

The data indicated that application of proposed rates of Primo MAXX can be expected to result in a peak growth reduction of 50% or more, except for greens and Kentucky bluegrass or perennial ryegrass fairways, where an approximate one-third reduction in growth can be expected. Data were insufficient to consider use of Primo MAXX on creeping bentgrass at canopy heights typical of golf course roughs. Use of a one-half rate at a frequency of every 2 weeks or later (except on greens) can be expected to reduce turf growth, but to a lesser degree than at full rates. The data support use of Primo MAXX on golf course roughs (and other golf course property turf, other than fairways and greens) maintained at a minimum of 3.8 cm for Kentucky bluegrass and perennial ryegrass and 5 cm for tall fescue. While Primo MAXX was proposed for use on fairways at canopy heights of 1.3 cm or less, data indicated that Primo MAXX could be expected to reduce growth of fairway turf maintained at canopy heights of up to 1.9 cm. Use of Primo MAXX on sod farms would be expected to provide a similar degree of growth reduction of turf maintained at canopy heights typical of golf course roughs and fairways.

Spray volume

Syngenta has proposed that application of Primo MAXX be made in a spray volume of 200–1500 L/ha. The effect of spray volume was assessed in one field trial conducted on Kentucky bluegrass turf. Spray volumes of 187, 561, and 1683 L/ha did not differentially affect the efficacy of 287 g a.i./ha Primo 1EC, when assessed as clippings biomass 21 days after application to Kentucky bluegrass turf maintained at canopy heights of 5–7.5 cm. For turf maintained at a height of 10 cm, application in 561 or 1683 L/ha resulted in a greater reduction in clippings biomass than where application had been made in 187 L/ha, and this was probably due to better coverage of the increased leaf area. The proposed spray volume range was supported by the data.

Kentucky bluegrass and annual bluegrass seedheads

Syngenta has proposed that foliar application of Primo MAXX to annual bluegrass and Kentucky bluegrass turf will reduce emergence of seedheads, when application is made prior to seedhead formation, at the proposed rates of 48 g a.i./ha (annual bluegrass on golf course greens), 97 and 194 g a.i./ha (annual bluegrass and Kentucky bluegrass on golf course fairways) and 230 or 291 g a.i./ha (Kentucky bluegrass on golf course roughs).

Data submitted from five U.S. field trials (two for annual bluegrass and three for Kentucky bluegrass) showed that Primo 1EC had an inconsistent effect on seedhead cover. In one trial, annual bluegrass seedheads were suppressed by 82% when assessed 26 days after application of 191 g a.i./ha Primo 1EC. In a second trial, however, seedhead cover of annual bluegrass treated with 98, 196, and 295 g a.i./ha Primo 1EC was greater than that of the untreated check 35 days after application. In two trials, Kentucky bluegrass seedheads in turf treated with 191 or 229 g a.i./ha Primo 1EC were slightly less on average than that of the untreated check when assessed 4 weeks after treatment in one trial and from 12–33 days after treatment in the other. In a third trial, Kentucky bluegrass seedhead cover was significantly greater in turf treated with 67 to 403 g a.i./ha Primo 1EC than that in the untreated check 36 and 41days after application. By 51 days after application, seedhead cover of turf treated with up to 280 g a.i./ha was similar to that of the untreated check.

The data submitted do not support the proposal that Primo MAXX provides partial seedhead suppression of annual bluegrass and Kentucky bluegrass.

Overseeding into turf infested with annual bluegrass

Syngenta has proposed that Primo MAXX can be used as part of an overseeding and turf renovation program for turf infested with annual bluegrass. It is proposed that application of Primo MAXX at greater than proposed rates (no upper limit was proposed) 1 to 5 days prior to overseeding permits better seedling growth of more desirable turf species. The following spring, application of the label rate of Primo MAXX would then be made.

In a trial conducted in Indiana over 3 years, creeping bentgrass was overseeded into a fairway consisting of mainly annual bluegrass after Primo 1EC had been applied at 191 and 382 g a.i./ha, which are twice and four times the rate proposed for use on fairways. Primo 1EC was applied prior to each overseeding in September of 1995, 1996, and 1997, and in April of 1996 and 1997. It was observed that there was no increase in creeping bentgrass establishment due to Primo 1EC at either rate over the time data were collected, from May of 1996 until November of 1997. The results of this trial do not support the proposal that Primo MAXX could be used as an integral part of a turf renovation and conversion program aimed at reducing annual bluegrass in favour of more desirable turf species, such as creeping bentgrass.

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

Trinexapac-ethyl inhibits the synthesis of the growth-promoting phytohormone, gibberellin. The development of resistance is not expected.

7.3 Effects on yield of treated plants or plant products in terms of quantity and quality

Primo MAXX contains trinexapac-ethyl, a growth-inhibiting plant growth regulator. The intended use of the product is to reduce turf canopy height and clippings biomass, thereby reducing the number of mowings over a given time period.

7.4 Phytotoxicity to turf

Data were submitted from field and greenhouse trials that were conducted in the U.S. from 1993 until 1999 in which the tolerance of turf to Primo 1EC was evaluated. Trials were conducted on turf that was maintained at canopy heights typical for fairways (usually 1–2 cm), greens (0.4–0.8 cm) or at heights typical for golf course roughs, (usually 5–7.5 cm). Tolerance was assessed as phytotoxicity, turf colour, overall quality and density. Phytotoxicity, density, colour, quality, and density were visually rated on scales of usually 0/1–9/10, with the highest number, respectively, representing severe injury, good density, dark green colour, and highest quality, i.e., turf that is dense, uniform, and dark green. Phytotoxicity and density were occasionally rated as percent injury and percent ground cover, respectively. The tolerance of turf to Primo MAXX and to Primo 1EC was compared in seven bridging trials conducted in 1998 and 1999 (the same trials in which efficacy of the two formulations were compared).

The tolerance of Primo EC and Primo MAXX were directly compared in trials conducted on annual bluegrass in 1998 (1 trial), Kentucky bluegrass in 1998 (2 trials), perennial ryegrass in 1998 (1 trial) and 1999 (2 trials), and tall fescue in 1999 (1 trial). The performance of these formulations were compared on annual bluegrass maintained at 1.6 cm height (96 and 192 g a.i./ha), Kentucky bluegrass maintained at approximately 3.8 cm (230 and 460 g a.i./ha), perennial ryegrass maintained at 1.3–1.9 cm (2 trials: 192 g a.i./ha) or 3.8 cm (1 trial: 290 g a.i./ha) and tall fescue maintained at 12.5 cm (385 and 770 g a.i./ha). No data were available for creeping bentgrass or any turfgrass species maintained at a canopy height typical for greens (0.4–0.5 cm), however, given the similarity in tolerance (colour [6 trials], quality [2 trials] and density [1 trial]) of turf to the two formulations in these trials, no difference in tolerance of greens turf or creeping bentgrass turf to these two formulations would be expected. Therefore, data generated with the Primo 1EC formulation were used in consideration of the application to register Primo MAXX.

Creeping bentgrass

The tolerance of fairway-height creeping bentgrass turf to Primo 1EC applied at 95 g a.i./ha or greater was visually evaluated in 14 field trials. Tolerance was assessed as phytotoxicity (3 trials), turf colour (9 trials), overall quality (5 trials) and density (2 trials). Colour and quality were rated on scales of usually 0/1–9/10, with the highest number representing dark green colour or highest quality, i.e., dense, uniform, dark green turf. Data from trials conducted on fairway-height turf are summarized below.

Phytotoxicity was slight in two trials at 27–28 days after application of Primo 1EC at 96–100 g a.i./ha (both trials) or 143 g a.i./ha (1 trial). In the one trial that included later evaluations, injury disappeared 10 days later. In a third trial, injury was very slight for 3 of 16 creeping bentgrass cultivars 10 days after application of 95 g a.i./ha.

The quality of turf treated with 95–293 g a.i./ha Primo 1EC was variable relative to that of the untreated check. In one trial in which Primo 1EC was applied at 98, 196, and 293 g a.i./ha, quality was initially reduced within 3 weeks of application, but increased afterwards, such that quality was rated higher than that of the untreated check by 4 weeks after treatment. The greatest reduction in quality of nearly 2 points (on a scale of 1–9) was observed for the highest rate. In the remaining four trials, quality after application of 95–100 g a.i./ha (3 trials) or 191 g a.i./ha (2 trials) was the same as or greater than that of the untreated check after up to 5 sequential applications. In two greenhouse trials, the quality of creeping bentgrass clipped to 2.5 cm height and treated with 280 g a.i./ha Primo 1EC was initially lower than that of the untreated control, but recovered by 28 and 56 days after treatment.

The colour response of turf treated with Primo 1EC was also variable. In five trials, turf of creeping bentgrass alone or in mixture with annual bluegrass that was treated with 95–96 g a.i./ha had colour ratings that were the same as or greater than that of untreated turf after up to six sequential applications. The colour rating of turf treated with higher rates of Primo 1EC was reduced relative to that of the untreated check in the remaining trials. In one trial conducted on a mixture of creeping bentgrass and annual bluegrass, the colour rating of turf treated with 100 g a.i./ha Primo 1EC and that had received no nitrogen was slightly lower than that of the untreated check at 4 weeks after treatment, but had later recovered. Primo 1EC did not affect colour of turf that had received nitrogen fertilizer. In another trial, turf treated with 152 and 229 g a.i./ha Primo 1EC was reduced when evaluated 7 days after treatment but had recovered to that of the untreated check by 24 days after application. In a third trial, the colour rating of turf consisting of a mixture with annual bluegrass and treated with 191 g a.i./ha was lower than that of the untreated check after the first and second applications. In a fourth trial, the colour rating of turf treated with 286 or 572 g a.i./ha was severely reduced after the first and second applications, by up to 2.5 points for the lower rate on a scale of 1–6.

Density was evaluated in two trials, including one trial that was conducted in lysimeters. The density of turf treated with 290 g a.i./ha Primo 1EC was similar to that of untreated turf in the lysimeter trial. The density of turf treated with 96 g a.i./ha Primo 1EC in a second trial was less than that of the untreated check after the first application but was greater than that of untreated turf after the second and third treatments.

The tolerance of golf course greens-height creeping bentgrass turf to Primo 1EC applied at 48 g a.i./ha or greater was visually evaluated in five field trials. In a trial conducted in North Carolina in which 48 g a.i./ha was applied monthly for 2 years to creeping bentgrass maintained at 0.4 or 0.48 cm, slight phytotoxicity of up to 2% was observed.

However, higher injury was observed to turf maintained at 0.32 cm in this trial, where up to 10 and 15% injury was observed in the untreated check and Primo 1EC treatments; much of the injury related to the low clipping height. In the latter trial, Primo 1EC did not affect overall turf quality or turf density at any mowing height, and turf colour was not affected by Primo 1EC at the two higher mowing heights, but the colour rating of turf clipped to 0.32 cm and treated with Primo 1EC was usually slightly lower than that of untreated turf. In a second trial, turf treated with 95 g a.i./ha was similar in colour to that of untreated turf. In a third trial, no injury was observed to creeping bentgrass following application of 96 g a.i./ha. Similarly no injury was noted to a mixture of creeping bentgrass and annual bluegrass after application of 115 g a.i./ha Primo 1EC in a fourth trial. In the latter trial, the quality of turf treated with Primo 1EC was similar to or greater than that of the untreated check after 2–4 applications. In a fifth trial, the colour rating of turf treated with 190 g a.i./ha was greater than that of untreated turf.

The data indicate that creeping bentgrass turf maintained at canopy heights typical for golf course fairways and greens can be expected to be tolerant to Primo MAXX when applied at 97 and 49 g a.i./ha, respectively. No tolerance data were submitted for creeping bentgrass maintained at mowing heights typical of golf course roughs. However, colour ratings data from one field trial in which Primo 1EC was applied to fairway-height creeping bentgrass at 286 g a.i./ha calls into question whether creeping bentgrass can be expected to be tolerant to the proposed rate of 291 g a.i./ha. Therefore, creeping bentgrass is not an acceptable host for sites where maintained canopy heights are over those typical for fairways.

Annual bluegrass

The tolerance of fairway-height turf consisting of annual bluegrass, or mixtures of it with Kentucky bluegrass, to Primo 1EC applied at 191 g a.i./ha or greater was visually evaluated in eight field trials. Tolerance was assessed as turf colour (4 trials), overall quality (4 trials), and density (2 trials).

In one trial, the colour rating of turf consisting of a mixture of annual bluegrass and Kentucky bluegrass was initially reduced after application of 229 g a.i./ha Primo 1EC, but was similar to that of the untreated check by 24 days after application. The colour rating of turf treated with 96 or 192 g a.i./ha Primo 1EC or Primo MAXX was reduced in one trial, but had recovered to that of the untreated check after approximately 4 weeks. The colour of turf treated with 192 g a.i./ha Primo 1EC was similar to that of the untreated check after each of two applications in a third trial. In a fourth trial in which 191 g a.i./ha was applied to a mixture of annual bluegrass and creeping bentgrass, colour was rated on a scale of 1–5 (5 = dark green). The colour was 0.6 and 1.0 points lower than the untreated check at 13 and 19 days after the second application, respectively. Evaluations were not conducted at about 4 weeks after application, so it is not known if turf colour rating recovered. In one additional trial conducted on a mixture of annual bluegrass and creeping bentgrass, turf treated with 100 g a.i./ha Primo 1EC had a slightly lower colour rating than that of untreated turf at 4 weeks after treatment, but only for turf that had not

received nitrogen fertilizer. The colour rating was similar to that of the untreated check 3 weeks later.

In three trials conducted on a mixture of annual bluegrass and Kentucky bluegrass, the quality rating of turf treated with 191–370 g a.i./ha Primo 1EC was greater than that of untreated turf at 3–4 weeks after the first application (1 of 2 trials), 4 weeks after the second application (2 of 2 trials), and 8 weeks after the third application (1of 1 trial). In a fourth trial, quality of annual bluegrass turf treated with 196 or 295 g a.i./ha Primo 1EC was lower than that of untreated turf 4 weeks after application. No later evaluations were conducted. In an additional trial conducted on a mixture of annual bluegrass and creeping bentgrass, the quality rating of turf treated with 100 g a.i./ha Primo 1EC was similar to that of untreated turf when assessed 60 days after application. Quality was not rated earlier in this trial.

In two of the three trials that were conducted on a mixture of annual bluegrass and Kentucky bluegrass, annual bluegrass density was lower for turf treated with 191, 280, and 370 g a.i./ha Primo 1EC than that of the untreated check when evaluated after the second application in one trial and after the third application in another. In these trials, the density of Kentucky bluegrass of treated turf had increased over that of the untreated check, particularly at the highest rate of 370 g a.i./ha.

The data collectively indicate that annual bluegrass can be expected to be tolerant of Primo MAXX when applied at up to 194 g a.i./ha.

The data support the proposed use of 194 g a.i./ha on fairway turf in which annual bluegrass is a component of a mixture with perennial ryegrass and Kentucky bluegrass. The data also support the use of 97 g a.i./ha on fairways in which annual bluegrass is a component of a mixture with creeping bentgrass.

Kentucky bluegrass

Data were submitted from 17 field trials over 5 years in which trinexapac-ethyl, applied as Primo MAXX (2 trials) or Primo 1EC (all trials) was applied near the proposed rate of 230 g a.i./ha or greater to Kentucky bluegrass turf maintained at canopy heights of 3.8–7.6 cm. Tolerance was assessed as phytotoxicity (5 trials), turf colour (11 trials), overall quality (10 trials), and density (2 trials).

The colour rating of turf treated with 230 g a.i./ha Primo 1EC or Primo MAXX was slightly lower than that of the untreated check from 12–30 days after application in two trials, but was greater than that of the untreated check in a third trial. The colour rating of treated turf was lower than that of untreated turf in 6 of the 10 trials that included treatments of Primo 1EC at rates of 280 g a.i./ha or greater. In one of the 6 trials, a reduction in colour rating was only observed 3 weeks after the second application, but had recovered to that of the untreated check by 2 weeks afterwards. The colour rating of

turf treated with 280–573 g a.i./ha Primo 1EC was greater than that of untreated turf in four trials.

The quality of turf treated with 229 g a.i./ha Primo 1EC was lower than that of the untreated check after each of five sequential applications in one trial, even though colour of turf treated with the growth regulator was enhanced and density of treated turf was similar to that of the untreated check for the first four applications. In a second trial, Primo 1EC applied at 224 g a.i./ha did not generally affect turf quality; however, where nitrogen fertilizer had been applied at a high rate (294 kg N/ha), turf quality was reduced 14–21 days after growth regulator application, after which quality recovered. In five trials, the quality of turf treated with Primo 1EC at rates of 286–291 (5 trials), 382 (2 trials), and 572 g a.i./ha (1 trial) was lower than that of the untreated check within 3 weeks of application, but in four trials, turf quality recovered to that of the untreated check by 4–5 weeks after treatment. Later assessments were not performed in the fifth trial. In three trials, the quality of turf treated with 280–286 (3 trials) and 403 g a.i./ha (1 trial) was greater than that of untreated turf.

The density of turf treated with 229 g a.i./ha Primo 1EC was similar to that of untreated turf following the first four applications of Primo 1EC made about 4 weeks apart. After the fifth and final application of Primo 1EC, the density of treated turf was lower than that of untreated turf. In one other trial, the density of turf treated with 286 or 572 g a.i./ha was 6% lower than that of untreated turf beginning at 3 days after application.

Phytotoxicity to Kentucky bluegrass turf was slight following application of 286 g a.i./ha in four of five trials, having reached maximum ratings of 0.8–2.0 from 14–36 days after application, after which injury diminished. In three of these trials that included treatments of Primo 1EC at higher rates, injury was greater after application of 403 (1 trial), 430 (1 trial), and 572 g a.i./ha (2 trials). In a fifth trial, phytotoxicity was assessed only once at 25 days after the second application of 286 g a.i./ha Primo 1EC. Injury to treated turf was rated as 3.3 on a scale of 1–5, where 5 denotes severe injury. No explanation was provided for this observation and later assessments were not conducted.

Tolerance trials were not conducted on solid stands of Kentucky bluegrass mowed at fairway heights. However, the tolerance of fairway-height turf consisting of a mixture of annual bluegrass and Kentucky bluegrass to Primo 1EC applied at 191 g a.i./ha or greater was assessed in four field trials conducted over 2 years. Tolerance was assessed as turf colour (2 trials), overall quality (3 trials), and density (3 trials).

The colour rating of turf treated with 192 g a.i./ha Primo 1EC was similar to that of untreated turf after each of two applications in one trial, but was lower after a second application in a second trial. In the latter trial, turf was stressed as indicated by the low quality ratings in all treatments (ratings of 2–3 on a 0–10 scale). The quality of turf treated with 191, 280, or 370 g a.i./ha was similar or greater than that of untreated turf after 1–3 applications in three trials. In the latter trials, the density of Kentucky bluegrass in the

mixture following treatment with Primo 1EC was either similar to or greater than that of the untreated check.

The data indicate that Kentucky bluegrass turf maintained at canopy heights typical for golf course roughs can be expected to be tolerant to Primo MAXX when applied at the proposed rate of 230 g a.i./ha. Kentucky bluegrass maintained at fairway canopy height can also be expected to be tolerant to either 194 g a.i./ha, the rate proposed for use on mixtures of Kentucky bluegrass, annual bluegrass and perennial ryegrass, or 97 g a.i./ha, the rate proposed for use on solid stands of Kentucky bluegrass.

Tall fescue

The tolerance of turf maintained at canopy heights of 5–12.5 cm to Primo 1EC applied at rates near or above the proposed rate of 291 g a.i./ha was evaluated in 11 field trials. Tolerance was assessed as phytotoxicity (3 trials), turf colour (3 trials), overall quality (9 trials), and density (5 trials).

In two trials, Primo 1EC applied at 280–286 g a.i./ha resulted in slight phytotoxicity, with a maximum rating of 1–2 on a scale of 0–10, which later diminished. In these trials, higher rates of 403 g a.i./ha or 572 g a.i./ha did not result in additional injury. In a third trial, phytotoxicity, assessed on a 0 (no injury)–100 scale, peaked at 23 when evaluated 25 days after application of 460 g a.i./ha, but turf recovered 9 days later.

Colour ratings were either similar or greater (i.e., darker green) after application of 286 g a.i./ha Primo 1EC than those of the untreated check in two trials. Colour of turf treated with either 381 or 572 g a.i./ha was similar to that treated with 286 g a.i./ha in these trials. In a third trial, turf colour rating was reduced by a maximum of 0.8, 1.9, and 2.6 points on a scale of 0–9, 42 days after application of 192, 385, or 770 g a.i./ha Primo 1EC or Primo MAXX.

Tall fescue turf quality was variably affected by trinexapac-ethyl. In one trial, quality ratings of turf treated with 280 or 403 g a.i./ha Primo 1EC were greater than those of untreated turf. In a second trial, the quality of turf treated with 270 or 370 g a.i./ha Primo 1EC was similar to that of untreated turf. In the remaining seven trials, quality was reduced from about 2–4 weeks after application of Primo 1EC at 286 (3 trials), 382 (1 trial), 400 (3 trials), 460 (1 trial), and 800 g a.i./ha (3 trials). Quality ratings recovered to those of the untreated check 5–8 weeks after application, except for the 800 g a.i./ha rate where quality had not recovered by 6–7 weeks after treatment.

The density values of tall fescue turf treated with 286 and 572 g a.i./ha Primo 1EC were 7 and 9% lower, respectively, than those of the untreated check 4 weeks after application. In three trials, density was reduced by 4–9% when assessed 5–7 weeks after application of 400 g a.i./ha, but density had recovered to that of the untreated check by 7–9 weeks after treatment. Density reductions were more severe after application of 800 g a.i./ha in these trials. Density was unaffected by 460 g a.i./ha Primo 1EC in an additional trial.

The data indicate that tall fescue can be expected to be adequately tolerant of Primo MAXX applied to turf maintained at canopy heights typical of golf course roughs at the proposed rate of 291 g a.i./ha.

Tall fescue may sustain slight injury, slight reductions in density, and reductions in quality and colour ratings; however, these effects are transient, and turf can be expected to recover if treated with the proposed rate of 291 g a.i./ha.

Perennial ryegrass

The tolerance of fairway-height perennial ryegrass turf to Primo 1EC applied at 191 g a.i./ha or greater was visually evaluated in eight field trials. Tolerance was assessed as phytotoxicity (2 trials), turf colour (3 trials), and overall quality (5 trials).

In two trials, phytotoxicity was not detectable or slight following application of Primo 1EC at or above 192–764 g a.i./ha.

Quality ratings of turf treated with 192–764 g a.i./ha Primo 1EC, relative to the untreated check, were variable, having been initially reduced within 3 weeks of application after which quality recovered to at least that of the untreated check (3 trials), unaffected (2 trials), or improved (1 trial). In one trial, turf quality ratings were reduced 7–21 days after application of 384 g a.i./ha Primo 1EC, after which quality recovered. Quality was again reduced 7 days after a second application of 192 g a.i./ha, but quality had recovered by 14 days after treatment. In a second trial, turf quality was rated slightly lower 7–21 days after application of 196 or 294 g a.i./ha, after which quality recovered to that of the untreated check. In a third trial, quality was reduced 12 days after the first application of 192 or 385 g a.i./ha, but quality of treated turf was greater than that of the untreated check beginning at about 26 days after application, and was greater after each of the remaining three applications applied 1–4 weeks apart. Quality was unaffected by Primo 1EC applied at 192 g a.i./ha in one trial, and by rates of up to 764 g a.i./ha in another. The quality of turf treated with three applications of 196 g a.i./ha Primo 1EC was greater than that of untreated turf in one trial. In a greenhouse study, quality of perennial ryegrass clipped to 2 cm and treated with 192 g a.i./ha Primo 1EC was greater than that of the untreated check.

The colour of turf treated with 192–229 g a.i./ha Primo 1EC was similar to that of the untreated check in one trial, improved over that of the check in a second trial, and in a third trial, colour was rated slightly less for treated than untreated turf 1 week after application, but by 3 weeks after application, colour of treated turf was rated higher than that of untreated turf.

The tolerance of perennial ryegrass turf maintained at canopy heights of 3.8–7.6 cm, typical of golf course roughs, to Primo 1EC applied near the proposed rate of 388 g a.i./ha or greater, was visually evaluated in three field trials. In one trial, the quality of turf treated with 366 g a.i./ha was greater than that of the untreated check. In a second trial, the quality

of turf treated with 572 g a.i./ha Primo 1EC was rated lower than that of the untreated check by 1.5 points on a scale of 1–9 when assessed 4 weeks after application. The colour rating of turf treated with Primo 1EC at 366 g a.i./ha in one trial and 572 g a.i./ha in another was greater than that of the untreated check. Colour was not affected by 366 g a.i./ha in a third trial.

The data collectively indicate that perennial ryegrass turf maintained at canopy heights typical for golf course roughs and golf course fairways can be expected to be tolerant to Primo MAXX when applied at 388 and 194 g a.i./ha, respectively.

Turf mixtures

Data submitted for individual turf species was considered in support of the proposed turf mixtures, specifically mixtures of 1. Kentucky bluegrass, tall fescue and perennial ryegrass (golf course roughs, canopy height); 2. Kentucky bluegrass, annual bluegrass and perennial ryegrass (fairway canopy height); and 3. creeping bentgrass and annual bluegrass (fairway and greens canopy height). A review of the data indicated that solid stands of each of the turf species in any of the proposed turf mixtures could be expected to be tolerant of primo MAXX applied at the rate proposed for the turf mixture.

Multiple applications

It is proposed that up to 7 sequential applications of Primo MAXX can be made to turf at proposed rates 4 weeks apart, or that up to 14 applications of one-half rates can be made 2 weeks apart in any one year. In field trials in which Primo 1EC was applied five times to golf course rough-height Kentucky bluegrass at 229 g a.i./ha, six times to fairway-height creeping bentgrass at 48 and 96 g a.i./ha (2 trials), 24 times to greens-height creeping bentgrass at 48 g a.i./ha, and four times to fairway-height perennial ryegrass at 192 g a.i./ha, turf quality (3 trials), turf colour (4 trials), density (2 trials), and phytotoxicity (1 trial) did not change relative to that of the untreated control with successive applications. Therefore, turf can be expected to be tolerant to multiple applications of Primo MAXX at proposed rates.

Overall conclusions on tolerance of turf to Primo MAXX

It was proposed by Syngenta that in addition to growth suppression, increased turf density, colour and quality are frequently observed after Primo MAXX application. The data indicated that turf quality, colour and density were variably affected, and frequently reduced by Primo 1EC or Primo MAXX applied at proposed rates. However, reductions were usually transient, such that the quality, colour and density had usually recovered to at least that of the untreated check within 2–4 weeks of application. With the exception of creeping bentgrass at greater than fairway height, turf is expected to exhibit sufficient tolerance to the proposed rates of Primo MAXX. Due to risk of injury, application overlaps should be avoided.

Effect of trinexapac-ethyl on root growth (root mass and depth)
Primo MAXX is proposed to increase root and rhizome production by increasing root mass and root depth. This is contended to increase availability of soil moisture to turf, implying increased tolerance or avoidance of drought stress.

Primo 1EC did not usually have a significant effect on rootmass or root length. In two Kansas field trials, the root length density of perennial ryegrass treated with 192 g a.i./ha Primo 1EC was numerically reduced in the upper 10 cm of soil but was either unaffected or numerically increased at lower depths, such that total root length in the top 40 cm of soil was unchanged or slightly reduced. In one field trial conducted in North Carolina on greens turf, rootmass was usually not significantly affected by monthly applications of 48 g a.i./ha Primo 1EC over 2 years, but was numerically reduced at least as often as it was increased over the 2 years of the study. In greenhouse and growth chamber trials, rootmass was increased for Primo 1EC-treated perennial ryegrass but was usually reduced for creeping bentgrass and annual bluegrass.

Untreated and Primo 1EC-treated Kentucky bluegrass or tall fescue did not usually significantly differ in the force required to pull harvested sod pieces apart or to remove transplanted sod pieces from soil. For Primo 1EC-treated turf, numerically more force was usually required to pull apart harvested sod pieces than for those that were untreated. However, these data were not corroborated with root mass or root depth data.

The data submitted do not support a claim that application of Primo MAXX will increase root and rhizome production, or increase root depth of turf.

7.5 Observation on undesirable or unintended side effects

Undesirable or unintended side effects are not expected with the use of Primo MAXX, other than those discussed in Section 7.4.

7.5.1 Survey of alternatives

There is no registered chemical alternative. Mowing is presently the only option for maintaining a desired turf canopy height.

7.6 Economics

In 2000, the area of sod grown and sold nationally was 22 140 ha, 12.8% greater than that produced in 1998. During this period, the value of sod sold increased 30.6% from 60.1 to 78.6 million dollars.

7.7 Sustainability

7.7.1 Survey of alternatives

There is no control product registered for use as a growth retardant on sod farm and golf course turf.

7.7.2 Compatibility with current management practices including integrated pest management

Primo MAXX would only be applied to actively growing turf as required, but no more frequently than once every 4 weeks at proposed rates. Application of Primo MAXX would not preclude the sequential use of either fertilizers or other pest control products required for weed, disease, and insect control in turf that is typically intensively managed on sod farms and golf courses.

7.8 Conclusions

Data generated in field and greenhouse trials demonstrated that Primo MAXX applied at supported rates (Table 7.8-1) can be expected to effectively reduce turf growth with adequate margins of crop safety.

Table 7.8-1 Summary of supported uses for Primo MAXX

Crop	Turf (commercial sod farms and golf courses)
Pest inhibited	Excessive topgrowth (canopy height reduction)
Application timing	When turf is actively growing
Application method	Ground application only (hand sprayers, backpack sprayers, boom sprayers, and spraygun application devices)
Frequency of application	Every 4 weeks, or later as required, at rates shown below or every 2 weeks, or later as required, at one-half the rates shown below
Maximum number of applications per year	7 at rates shown below, or 14 at one-half the rates shown below

Rates (for approximately 50% growth inhibition, unless otherwise indicated)	Turf species	Commercial sod farms and golf courses, including rough areas[a]	Commercial sod farms and golf course fairways (height: 1.0–1.9 cm)	Golf course greens[b, c]
		mL/100 m^2 (equivalent rates in g a.i./ha)		
	Creeping bentgrass		8.0 (97)	4.0 (49)
	Tall fescue	24.0 (291)		
	Kentucky bluegrass	19.0 (230)	8.0 (97)[b]	
	Creeping bentgrass / annual bluegrass mixture		8.0 (97)	4.0 (49)
	Kentucky bluegrass / tall fescue / perennial ryegrass mixture	24.0 (291)		
	Kentucky bluegrass / perennial ryegrass / annual bluegrass mixture[d]		16.0 (194)	
	Perennial ryegrass	32.0 (388)	16.0 (194)[b]	

a Canopy height should be at least 3.8 cm for Kentucky bluegrass and perennial ryegrass, and at least 5 cm for tall fescue

b About one-third growth inhibition can be expected

c On greens, no data to support one-half rate

d Use 8.0 mL/100m^2 (97 g a.i./ha) on fairways consisting of annual bluegrass and Kentucky bluegrass

8.0 Toxic Substances Management Policy

During the review of trinexapac-ethyl, the PMRA has taken into account the federal Toxic Substances Management Policy and has followed the Regulatory Directive DIR99-03. It has been determined that this product does not meet TSMP Track-1 criteria.

8.1 Active ingredient

Trinexapac-ethyl does not meet the criteria for persistence. The values for half-life in water and sediment (5.5 days) and soil (25 days) are below the TSMP Track-1 cut-off criteria for water ($182 days), soil ($182 days) and sediment ($365 days). Because of low

volatility, a persistence in air study was not triggered. Trinexapac-ethyl does not bioaccumulate. Studies have shown that the *n*-octanol–water partition coefficient (log K_{ow}) is 2.1, 1.6, and –0.38 for pH 3, pH 5.3, and pH 7, respectively, which is below the TSMP Track-1 cut-off criterion of $5.0. Results from mammalian studies and two fish bioconcentration studies indicated a low potential for accumulation. The toxicity of trinexapac-ethyl is described in Chapters 3 and 6.

8.2 Transformation products

CGA-179500 is the primary transformation product in laboratory fate studies and the field dissipation study. This transformation product does not meet the TSMP Track-1 criteria because it does not bioaccumulate.

8.3 Formulants

All formulants in the formulated product, Primo MAXX, are either EPA list 3 or list 4. Known EPA list 1 or 2 formulants are not contained in this formulation.

8.4 By-products or microcontaminants

The formulated product does not contain by-products or microcontaminants that are known to be TSMP Track-1 substances. 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.

9.0 Proposed regulatory decision

The Pest Management Regulatory Agency (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 Trinexapac-ethyl Technical and Primo MAXX, proposed for registration by Syngenta Crop Protection Canada Inc. The PMRA has concluded that the use of Trinexapac-ethyl Technical and Primo MAXX in accordance with the label has merit and value consistent with Section 18.c of the PCP Regulations and does not entail an unacceptable risk of harm under Section 18.d. Therefore, based on the considerations outlined above, the use of Trinexapac-ethyl and Primo MAXX for growth inhibition of turf on commercial sod farms and golf courses is proposed for full registration, under Section 13 of the PCP Regulations.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed registration decision for this product.

List of abbreviations

ADI	acceptable daily intake
a.i.	active ingredient (does not contain impurities or formulation ingredients) [mg a.i.]
ARfD	acute reference dose
bw	body weight
bwg	body-weight gain
CAS	Chemical Abstracts Service
CD	caesarian derived
CNS	central nervous system
d	day(s)
DFR	dislodgeable foliar residue
DT_{50}	time required for 50% dissipation
dw	dry weight of diet
EC_{25}	concentration effective against 25% of test organisms
EC_{50}	median effective concentration
EEC	expected environmental concentration
EUP	end-use product
F	female(s)
F_0	1st generation parental animals
F_1	1st generation offspring
F_2	2nd generation offspring
GA	gibberellin
GC	gas chromatography
GSD	geometric standard deviation
H	Henry's Law Constant
HB	hemoglobin
HCT	hematocrit
HDPE	high-density polyethylene
HDT	highest dose tested
HPLC	high performance liquid chromatography
K_{oc}	organic carbon adsorption coefficient
K_{ow}	*n*-octanol–water partition coefficient
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LOQ	limit of quantitation
M	male(s)
MAS	maximum average score (for 24, 48 and 72 h)
MIS	maximum irritation score
MMAD	mass median aerodynamic diameter
MOE	margin of exposure
MOS	margin of safety
n	number

NOEC	no observable effect concentration
NOEL	no observable effect level
NOAEL	no observable adverse effect level
OC	organic carbon content
OM	organic matter content
PCP	pest control products
pH	$-\log_{10}$ hydrogen ion concentration
pK_a	$-\log_{10}$ acid dissociation constant
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
ppm	parts per million
RBC	red blood cell
SD	standard deviation
SG	specific gravity
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
UDS	unscheduled deoxyribonucleic acid synthesis
Fg	micrograms
FL	microlitre
U.S. EPA	United States Environmental Protection Agency

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Appendix 1 Summary of toxicology

METABOLISM: **Trinexapac-ethyl Technical (CGA 163935 Technical)**

Absorption: CGA-163935 (trinexapac-ethyl) was rapidly and extensively absorbed in both sexes following single or repeat low-dose (0.97 mg/kg bw) administration and single high-dose (166 mg/kg bw) administration. Greater than 95% of the administered dose was absorbed following single or repeat low-dose administration and single high-dose administration. Data suggests that there was very little or no biliary absorption.
Distribution: The highest residue levels were observed in the fat, lungs, kidneys and liver; however, mean recovery of radioactivity in tissues/carcass at sacrifice (at 168 h post-dosing) was less than 0.3% of administered dose for all dose groups indicating little potential for accumulation.
Metabolism: The major component in urine and fecal extracts was identified as CGA-179500 [4-cyclopropyl-"-hydroxy-methylene)-3,5-dioxo-cyclohexanecarboxylic acid], the free acid derivative of CGA-163935 resulting from hydrolysis of the ester bond of the parent compound accounting for approximately 82.0–91.6% of the administered dose. The only other residue found (found in fecal extract only) was identified as the parent compound, CGA-163935, accounting for less than 0.1% of the administered dose.
Excretion: Excretion was rapid, with the majority of radioactivity being eliminated within 12 h post-dosing via urine (greater than 85% of the administered dose at the low and high dose) and within 24 h post-dosing via feces (0.56–1.43 and 0.80–2.01% at the low and high dose, respectively). The major route of excretion was via urine, accounting for approximately 95% of administered dose at both dose levels. Fecal excretion accounted for approximately 1.0–2.4% of administered dose at both dose levels. By 72 h less than 0.01% of the administered dose was recovered in expired air. Data suggests that there was very little or no biliary excretion

Significant qualitative differences were not found in absorption, distribution, metabolism or excretion of CGA-163935 (trinexapac-ethyl) between the sexes, between single and repeat low-dose administration or between single low-dose and high-dose administration.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL (mg/kg bw/d)	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
ACUTE STUDIES: Trinexapac-ethyl Technical (CGA 163935 Technical)			
Oral	Sprague-Dawley rats 5 animals/sex/dose **Dose levels**: 3500 (F only), 4500 (M only), 4000 and 5050 mg/kg bw (both sexes)	**LD_{50} (95% confidence limits)** M: 4610 (4450–4790) mg/kg bw F: 4210 (3450–5140) mg/kg bw Sexes combined: 4460 (4180–4750) mg/kg bw	No mortality at 3500 mg/kg bw or in M at 4000 mg/kg bw; 3 F at 4000 mg/kg bw died by d 2; at 4500 mg/kg bw 1 M died by d 2; at 5050 mg/kg bw/d 5 M and 4 F died by d 2. No treatment-related clinical observation, necropsy finding or change in bw **LOW TOXICITY**
Dermal	SPF hybrid albino rats 5 rats/sex/dose **Dose level**: 4000 mg/kg bw	LD_{50} greater than 4000 mg/kg bw for both sexes	No mortality and no treatment-related necropsy finding or change in bw. Clinical signs included dyspnea, ruffled fur, abnormal body position and reduced spontaneous activity, completely resolved by d 10. **LOW TOXICITY**

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL (mg/kg bw/d)	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
Inhalation: Limit test (4-h nose-only)	Tif: RAI f (SPF) albino rats 5 rats/sex **Dose levels** Analytical concentration = 5.3 mg/L air Nominal concentration = 9.84 mg/L air (MMAD = 2.1 FM; GSD = 2.7)	LC_{50} greater than 5.3 mg/L air	No mortality and no treatment-related necropsy finding or change in bw. Clinical signs included slight dyspnea and ruffled fur, completely resolved by d 7. **LOW TOXICITY**
Eye irritation	New Zealand White rabbits 6 M and 3 F **Dose level**: 0.1 mL undiluted test substance	MIS: 5.33/110 at 1 h for unwashed and washed eyes. MAS (for 24, 48, and 72 h): 0.67/110 for unwashed eyes and 0.89/110 for washed eyes.	Minimal (grade 1) conjunctival redness, chemosis and discharge in all animals (unwashed and washed) at 1 h completely resolved by 72 h. **MINIMALLY IRRITATING**
Skin irritation	New Zealand White rabbits 3 M and 3 F **Dose level**: 0.5 mL undiluted test substance	MIS: 1.83/8 at 1 h MAS (for 24, 48, and 72 h): 1.0/8	Very slight erythema in all animals at 1 h, completely resolved by 72 h. Very slight edema in 5 of 6 animals at 1 h completely resolved by d 7. **MILDLY IRRITATING**

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL (mg/kg bw/d)	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
Skin sensitization (Optimization method)	Pirbright White guinea pigs 10 animals/sex in treatment and naive control group **Dose levels** Intradermal induction: 0.1 mL of 0.1% solution of test substance in physiological saline (week 1) or 0.1 mL of 0.1% solution of test substance in 1:1 formulation of physiological saline and Bacto Adjuvant (weeks 2–3) Intracutaneous challenge: 0.1 mL of 0.1% solution of test substance in physiological saline Epicutaneous challenge: 0.1 mL of 3% solution of test substance in vaseline	No dermal reactions observed at 24 or 48 h after intradermal or epidermal challenge treatment.	**NOT A DERMAL SENSITIZER**

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL (mg/kg bw/d)	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
ACUTE STUDIES: Primo MAXX Plant Growth Regulator			
Oral	Sprague-Dawley rats 5 animals/sex **Dose level**: 5050 mg/kg bw	LD_{50} greater than 5050 mg/kg bw for both sexes	One F found dead on day 1; no treatment-related necropsy finding or change in bw; clinical signs included decreased activity, piloerection and sensitivity to touch, completely resolved by d 3. **LOW TOXICITY**
Dermal	New Zealand White rabbits 5 animals/sex **Dose level**: 2020 mg/kg bw	LD_{50} greater than 2020 mg/kg bw for both sexes	No mortality and no treatment-related necropsy finding or change in bw; one F exhibited soft feces 2 h after dosing, completely resolved by d 2. **LOW TOXICITY**
Inhalation	Sprague-Dawley rats 5 animals/sex **Dose level** Analytical concentration = 2.57 mg/L air (MMAD = 2.7 FM; GSD = 2.3–2.4)	LD_{50} greater than 2.57 mg/L air for both sexes	No mortality and no treatment-related necropsy finding or change in bw; all animals exhibited fur coated with feces/ urine upon removal from chamber and piloerection on d 1, completely resolved by d 2. **LOW TOXICITY**
Eye imitation	New Zealand White rabbits 6 M and 3 F **Dose level**: 0.1 mL undiluted test substance	**Unwashed eyes**: MIS: 18.3/110 at 48 h. MAS (for 24, 48 and 72 h): 15.5/110 **Washed eyes**: MIS: 21.7/110 at 24 h. MAS (for 24, 48 and 72 h): 19.9/110	Mildly irritating to eye based on MIS/MAS for washed eyes; however, due to persistence of ocular irritation up to and including d 7 in both washed and unwashed eyes (not all d 7 scores equal 0), classification is upgraded to **MODERATELY IRRITATING**
Skin irritation	New Zealand White rabbits 3 M and 3 F **Dose level**: 0.5 mL undiluted test substance	MIS: 0.17/8 at 1 h. MAS (for 24, 48 and 72 h): 0/8	Very slight (grade 1) erythema noted in 1 animal at 1 h, dermal irritation completely resolved by 24 h. **MINIMALLY IRRITATING**
Skin sensitization (Buehler method)	Hartley albino guinea pigs 5 animals/sex in treatment and naive control group **Dose levels**: 0.4 mL of undiluted test substance for both the induction and challenge treatments	No dermal reactions observed at 24 or 48 h after challenge treatment	**NOT A DERMAL SENSITIZER**

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL (mg/kg bw/d)	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
SHORT TERM: Trinexapac-ethyl Technical (CGA 163935 Technical)			
90-d dietary: mouse	15 CD-1 [Crl: CD-1 (ICR)BR] mice/sex/dose **Dose level**: 0, 10, 100, 1000, or 10 000 ppm (equal to 0, 1.6, 15.4, 161, and 1552 mg/kg bw/d in M and 0, 2.0, 19.8, 194, and 1970 mg/kg bw/d in F)	**NOAEL**: 10 000 ppm (equal to 1552 and 1970 mg/kg bw/d in M and F, respectively) **LOAEL**: Not determined	There was no treatment-related finding in either sex at dose levels up to and including 10 000 ppm, the HDT **Control week 13 bw** M: 34.3 g F: 29.3 g **Control week 13 daily food consumption** M: 4.9 g/animal F: 5.2 g/animal
90-d dietary: rat	15 Sprague-Dawley rats/sex/dose **Dose level**: 0, 50, 500, 5000, or 20 000 ppm (equal to 0, 3, 34, 346, or 1350 mg/kg bw/d for M and 0, 4, 38, 395, and 1551 mg/kg bw/d for F)	**NOAEL** M: 500 ppm (equal to 34 mg/kg bw/d) F: 5000 ppm (equal to 395 mg/kg bw/d) **LOAEL** M: 5000 ppm (equal to 346 mg/kg bw/d) F: 20 000 ppm (equal to 1551 mg/kg bw/d)	5000 ppm: increased cytoplasmic accumulation of hyaline droplets in kidney (M) 20 000 ppm: lower bw, body-weight gain (bwg) and food consumption (M/F); lower urinary pH (M/F); increased urinary SG and urine volume (M); increased incidence of tubular basophilia, cytoplasmic accumulation of hyaline droplets and tubular casts in the kidney (M). Kidney histopathological findings considered to reflect early onset of spontaneous senile nephropathy (severity considered minimal). **Control week 13 bw** M: 557 g F: 318 g **Control week 13 daily food consumption** M: 25.4 g/animal F: 18.9 g/animal
90-d dietary: dog	4 beagle dogs/sex/dose **Dose levels**: 0, 50, 1000, 15 000 or 30 000 ppm (equal to 0, 2.0, 34.9, 516 and 927 mg/kg bw/d in M and 0, 1.9, 39.8, 582 and 891 mg/kg bw/d in F)	**NOAEL**: 15 000 ppm (equal to 516 and 582 mg/kg bw/d in M and F, respectively) **LOAEL**: 30 000 ppm (equal to 927 and 891 mg/kg bw/d in M and F, respectively)	30 000 ppm: lower bwg (M/F)

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL (mg/kg bw/d)	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
12-month dietary: dog	4 beagle dogs/sex/dose **Dose levels**: 0, 40, 1000, 10 000, or 20 000 ppm (equal to 0, 1.6, 31.6, 366, and 727 mg/kg bw/d in M and 0, 1.4, 39.5, 357, and 784 mg/kg bw/d in F)	**NOAEL**: 1000 ppm (equal to 31.6 and 39.5 mg/kg bw/d in M and F, respectively) **LOAEL**: 10 000 ppm (equal to 366 and 357 mg/kg bw/d in M and F, respectively)	10 000 ppm and above: mucoid or bloody feces, increased serum cholesterol and minimal focal bilateral vacuolation of the dorsal medial hippocampus and (or) lateral midbrain, considered to possibly reflect an interference with energy metabolism (energy deprivation syndrome) following prolonged exposure to high doses (M/F) 20 000 ppm: sporadic emesis (M/F); reduced RBC counts and HCT (M/F); reduced HB (F); lower bwg (M)
3-week dermal: rabbit (22 consecutive days)	5 New Zealand White rabbits/sex/dose **Dose levels**: 0, 10, 100, or 1000 mg/kg bw/d	**Systemic toxicity** NOAEL: 1000 mg/kg bw/d LOAEL: Not determined **Local dermal irritation** NOAEL: 10 mg/kg bw/d LOAEL: 100 mg/kg bw/d	No adverse treatment-related systemic finding in either sex. **Local dermal irritation**: marginal increased severity of acanthosis and minimal to moderate increased incidence of inflammation, hyperkeratosis and crust formation in both sexes at 100 and 1000 mg/kg bw/d
CHRONIC TOXICITY/ONCOGENICITY: Trinexapac-ethyl Technical (CGA-163935 Technical)			
78-week dietary: mouse	70 CD-1 [Crl:CD-1 (ICR)Br] mice/sex/dose **Dose levels**: 0, 7, 70, 1000, 3500, or 7000 ppm (equal to 0, 0.9, 9.0, 131, 451, and 912 mg/kg bw/d in M and 0, 1.1, 10.7, 154, 539, and 1073 mg/kg bw/d in F)	**Chronic toxicity** NOAEL: 7000 ppm (equal to 912 and 1073 mg/kg bw/d in M and F, respectively) LOAEL: Not determined	There was no treatment-related finding in either sex at dose levels up to an including 7000 ppm, the HDT No evidence to indicate any carcinogenic potential of trinexapac-ethyl at any dose level up to and including 7000 ppm, the HDT

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL (mg/kg bw/d)	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
2-year dietary: rat	80–90 Sprague-Dawley rats/sex/dose (10/sex/dose interim sacrifice; 10/sex interim sacrifice recovery group for control and 20 000 ppm groups only; 20/sex/dose chronic toxicity; 50/sex/dose terminal sacrifice) **Dose levels**: 0, 10, 100, 3000, 10 000, or 20 000 ppm (equal to 0, 0.4, 3.9, 116, 393, and 806 mg/kg bw/d in M and 0, 0.5, 4.9, 147, 494, and 1054 mg/kg bw/d in F)	**Chronic toxicity** NOAEL: 3000 ppm (equal to 116 and 147 mg/kg bw/d in M and F, respectively) LOAEL: 10 000 ppm (equal to 393 and 494 mg/kg bw/d in M and F, respectively)	10 000 ppm and above: decreased urinary pH (M/F) and brown pigmentation in renal tubular epithelium (F; partially reversible after recovery; not observed at 104 weeks). 20 000 ppm: lower bw, bwg and food consumption (M/F); increased incidence/severity hyaline droplets in kidneys and brown pigmentation in renal tubular epithelium (M; reversible after recovery; not observed at 104 weeks); bile duct hyperplasia (M); mammary gland galactoceles (F); acanthosis glandular stomach (F); low (2/80), but statistically significant, increased incidence of squamous cell carcinoma in fore-stomach (M), however, not considered toxicologically relevant to humans. Under conditions of this study, there was a possible treatment-related increased incidence of squamous cell carcinoma of the forestomach in M at 20 000 ppm (HDT); however, this is not considered toxicologically relevant to humans. No treatment-related difference detected in total number of animals with tumours or in the total number of benign or malignant tumours at 52 or 104 weeks. No treatment-related effect on the time-dependent occurrence of tumour-bearing animals.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL (mg/kg bw/d)	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
REPRODUCTION / DEVELOPMENTAL TOXICITY: Trinexapac-ethyl Technical (CGA-163935 Technical)			
Multi-generation: rat (1 litter/ generation)	30 Sprague-Dawley derived rats/sex/group **Dose levels**: 0, 10, 1000, 10 000, or 20 000 ppm (equal to 0, 0.6, 60, 594, and 1212 mg/kg bw/d in M and 0, 0.9, 76, 751, and 1484 mg/kg bw/d in F)	**Parental** NOAEL: 1000 ppm (M = 60 mg/kg bw/d F = 76 mg/kg bw/d) LOAEL: 10 000 ppm (M = 594 mg/kg bw/d F = 751 mg/kg bw/d) **Offspring** NOAEL: 10 000 ppm (M = 594 mg/kg bw/d F = 751 mg/kg bw/d) LOAEL: 20 000 ppm (M = 1212 mg/kg bw/d F = 1484 mg/kg bw/d) **Reproductive** NOAEL: 20 000 ppm (M = 1212 mg/kg bw/d F = 1484 mg/kg bw/d) LOAEL: Not determined	**Parental** 10 000 ppm: lower bw and bwg (F_0/F_1 M and F) 20 000 ppm: lower bw, bwg and food consumption (F_0/F_1 M and F) **Offspring** 20 000 ppm: lower pup body weight (F_1/F_2 pups) and slight decreased pup survival (F_1 pups) **Reproductive** No adverse treatment-related effect on reproductive parameters up to and including 20 000 ppm (HDT)
Teratogenicity: rat	24 sexually mature/nulliparous F Tif: RAIf (SPF) rats/dose **Dose levels**: 0, 20, 200 or 1000 mg/kg bw/d	**Maternal toxicity** NOAEL: greater than 1000 mg/kg bw/d LOAEL: Not determined **Developmental toxicity** NOAEL: 200 mg/kg bw/d LOAEL: 1000 mg/kg bw/d	**Maternal toxicity**: No treatment-related finding at any dose level up to and including 1000 mg/kg bw/d (HDT) **Developmental toxicity**: increased incidence of asymmetrically shaped vertebrae at 1000 mg/kg bw/d **Teratogenicity**: No evidence of teratogenicity at any dose level up to and including 1000 mg/kg bw/d (HDT); therefore, under the conditions of the study, trinexapac-ethyl was not teratogenic

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL (mg/kg bw/d)	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
Teratogenicity: rabbit	16–17 sexually mature/ nulliparous F New Zealand White rabbits/dose **Dose levels**: 0, 10, 60 or 360 mg/kg bw/d	**Maternal toxicity** NOAEL: greater than 360 mg/kg bw/d LOAEL: Not determined **Developmental toxicity** NOAEL: 60 mg/kg bw/d LOAEL: 360 mg/kg bw/d	**Maternal toxicity**: No treatment-related finding at any dose level up to and including 360 mg/kg bw/d (HDT) **Developmental toxicity**: decreased live fetuses per litter and increased post-implantation loss at 360 mg/kg bw/d **Teratogenicity**: No evidence of any treatment-related irreversible structural change at any dose level up to and including 360 mg/kg bw/d (HDT); therefore, under the conditions of the study, trinexapac-ethyl was not teratogenic
GENOTOXICITY: Trinexapac-ethyl Technical (CGA 163935 Technical)			
STUDY	**Species or strain or cell type**	**Dose levels**	**Significant effects and comments**
Salmonella / Ames test	*Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537	0, 20, 78, 311, 1250, or 5000 Fg/plate. ± S9 metabolic activation	**NEGATIVE**
Mammalian chromosomal aberration (in vitro)	Mouse lymphoma L5178Y cells (at the thymidine kinase locus)	0, 7.5, 30.2, 120.6, or 1930 Fg/mL ± S9 metabolic activation	**NEGATIVE**
Mammalian cytogenetics (in vitro)	Human lymphocytes	0, 62.5, 125, 250, 500, or 1000 Fg/mL ± S9 metabolic activation	**NEGATIVE**
Micronucleus assay (in vivo)	M and F mouse bone marrow cells (erythrocytes)	0, 1000, 2000, or 4000 mg/kg bw (sacrifice at 16, 24, and 78 h)	**NEGATIVE**
Micronucleus assay (in vivo)	M and F mouse bone marrow cells (erythrocytes)	Initial assay: 0 or 3000 mg/kg bw (sacrifice at 16, 24, and 48 h) Confirmatory assay: 0, 750, 1500, or 3000 mg/kg bw (sacrifice at 48 h)	Significant increased frequency of micronucleated polychromatic erythrocytes in M and sexes combined at 48 h in the initial assay; however, values were within historical control range and not observed in the confirmatory assay at 3000 mg/kg bw at 48 h. In this study possible weak clastogen, however, weight of evidence suggests CGA-163935 not likely clastogenic.

STUDY	Species or strain or cell type	Dose levels	Significant effects and comments
UDS in vitro	Rat primary hepatocytes	Preliminary cytotoxicity assay: 0, 5, 10, 21, 41, 82, 164, 328, 656, 1313, 2625, or 5250 Fg/mL Initial UDS assay: 0, 0.8, 4, 20, 100, 200, or 400 Fg/mL Confirmatory UDS assay: 0, 4, 20, 100, 150, 200, 300, 400, or 500 Fg/mL	**NEGATIVE**
Compound-induced mortality: There was no significant increased incidence of treatment-related mortalities in any short-term, long-term or special studies.			
Recommended ARfD: An ARfD was not established, since trinexapac-ethyl is intended for turf use only (non-food use).			
Recommended ADI: An ADI was not established, since trinexapac-ethyl is intended for turf use only (non-food use).			

Appendix 2 Summary of residues

Not applicable.

Appendix 3 Summary of environmental assessment

Table 1 Physical and chemical properties of trinexapac-ethyl relevant to the environment

Property	Value	Comments
Water solubility (g/L) at 25EC	pH — Solubility 3.5 (distilled water) — 1.1 4.9 (buffer) — 2.8 5.5 (buffer) — 10.2 8.2 (buffer) — 21.2	Very soluble under all pH conditions
Vapour pressure	1.03×10^{-3} Pa at 20EC 2.16×10^{-3} Pa at 25EC (by extrapolation of curve from 38.0 to 170.2EC)	Low volatility under field conditions
H	5.27×10^{-10} atm m^3 /mole (pH 5.5) 2.54×10^{-10} atm m^3 /mole (pH 8.2)	Non-volatile from a water or moist soil surface Lab study on volatilization not required
pK_a	4.57	Likely mobile in soil at environmentally relevant pH
log K_{ow}	2.10 at pH 3 1.6 at pH 5.3 –0.38 at pH 7	Bioconcentration or bioaccumulation is unlikely
UV–visible absorption spectrum	Medium — 8 (nm) neutral — 240.2 — 277.4 acidic — 240.0 — 280.4 basic — 270.8 No absorption at 8 maxima of 340–750 nm	Low potential for phototransformation

Table 2 Physical and chemical properties of CGA-179500 relevant to the environment

Property	Value	Comments
Water solubility (g/L) at 25EC	pH / Solubility 5 / 13 6.8 / 200 8.4 / 260	Very soluble
Vapour pressure	1.0×10^{-6} Pa at 20EC 2.3×10^{-6} Pa at 25EC	Relatively non-volatile under field conditions
H	3.916×10^{-13} atm m^3/mole (pH 5) 2.546×10^{-14} atm m^3/mole (pH 6.8) 1.958×10^{-14} atm m^3/mole (pH 8.4)	Non-volatile from a water or moist soil surface Lab study on volatilization not required
pK_a in water (20EC)	1 = 5.32 2 = 3.93	Potentially mobile in environmentally relevant pHs
K_{ow}	1.8 at pH 2 and 25EC	Bioconcentration or bioaccumulation is unlikely
UV–visible absorption spectrum	8 (nm) 239.3 and 280.0 No absorption at 8 maxima of 340–750 nm	Low potential for phototransformation

Table 3 Fate and behaviour in the terrestrial environment

Property	Value	Comments
Abiotic transformation		
Hydrolysis	Stable for 30 d at pH 5 and pH 7 ($t_{1/2}$ of 228 and 455 d, respectively) First-order half-life = 8.1 d at pH 9	Hydrolysis may be an important route of transformation in basic media.
Phototransformation on soil	First-order half-lives = 43.7 d	Phototransformation is not an important route of transformation.
Biotransformation		
Biotransformation in aerobic soil	Half-lives = 3–6 h for parent compound and half-life of CGA-179500 = 16–18 d	Biotransformation is an important route of transformation. There would not be a concern of persistence of the parent and transformation products under aerobic conditions.
Biotransformation in anaerobic soil	Half-life of parent compound = 10–25 d CGA-179500 and the other major transformation product transform slowly and do not mineralize.	The major transformation products have potential to persist and accumulate and could contaminate ground water.

Property	Value	Comments
Mobility		
Adsorption or desorption in soil Trinexapac-ethyl adsorption CGA-179500 adsorption	Soil / K_{oc} Clay 635 Sand 283 Sandy loam 60 Loam 143 Clay 581 Sand 609 Sandy loam 144 Loam 328	Trinexapac-ethyl will be highly mobile in sandy loam and loam, moderately mobile in sand, and relatively immobile in clay. CGA-179500 will be highly mobile in sandy loam, moderately mobile in loam, and relatively immobile in sand and clay.
Soil leaching	For unaged, <1, 35, 45, and 87% of the applied was in the leachate for clay, sand, sandy loam, and loam, respectively. For aged (sandy loam), approximately 62% of applied was found in the leachate (57% CGA-179500, 2% parent and 3% polar transformation products).	Trinexapac-ethyl is mobile in sand, sandy loam, and loam soils, but it is relatively immobile in clay. CGA-179500 is also leachable.
Volatilization	No detectable trinexapac-ethyl was found to volatilize from dry or moist soil. Trinexapac-ethyl volatilized only slightly (1% of applied) from turf during 15 d of incubation at 15–25EC under continuous air flow	Volatilization will not be an important route of transport. Trinexapac-ethyl formulated as 2E product is slightly volatile from turf.
Field studies		
Field dissipation	DT_{50}s of trinexapac-ethyl and CGA-179500 are 1.1–1.4 d and 5.1–31.5 d, respectively	Trinexapac-ethyl is non-persistent and CGA-179500 is non-persistent to slightly persistent under field conditions. Carryover is not expected.
Field leaching	Trinexapac-ethyl and CGA-179500 are generally only detected in the top 0–15 cm soil	Neither the parent nor the transformation product leached under field conditions.

Table 4 Summary of transformation products formed in terrestrial fate studies

Study	Major transformation product	Minor transformation products
Hydrolysis (at pH 9)	CGA-179500	No minor transformation product
Phototransformation on soil	CGA-179500 and open-chain CGA-163935	Two unidentified minor transformation products
Aerobic biotransformation in soil	CGA-179500 and another unidentified polar compound that probably resulted from the cleavage of the CGA-179500 ring at the carbonyl group	No minor transformation product
Anaerobic biotransformation in soil	CGA-179500 and an unidentified compound that probably resulted from reduction of the exocyclic double bond	A number of unidentified minor transformation products
Field dissipation	CGA-179500	No minor transformation product

Table 5 Fate and behaviour in the aquatic environment

Property	Value	Comments
Abiotic transformation		
Hydrolysis	Stable for 30 d at pH 5 and pH 7 ($t_{1/2}$ of 228 and 455 d respectively) First-order half-life = 8.1 d at pH 9	Hydrolysis may be an important route of transformation in basic media
Phototransformation in water	At pH 7 under sterile conditions, first-order half-life = 63.5 h (equivalent to 5.3 d using intermittent light)	Phototransformation may be an important route of transformation
Biotransformation		
Biotransformation in aerobic water systems	In equilibrated water and sediment system, first-order half-lives = 3.9–5.5 d	Non-persistent in aerobic aquatic systems

Table 6 Summary of transformation products formed in aquatic fate studies

Study	Major transformation product	Minor transformation products
Hydrolysis	CGA-179500	No minor transformation product
Phototransformation in water	Ethyl ester of tricarballylic acid	Five minor transformation products including *cis*- and *trans*-isomers of trinexapac-ethyl, CGA-179500 and two unidentified transformation products
Biotransformation in aerobic water and sediment	CGA-179500	Two unidentified minor transformation products

Table 7 Maximum EEC in vegetation and insects after a direct overspray

Matrix	EEC (mg a.i./kg fw)[a]	Fresh/dry weight ratios	EEC (mg a.i./kg dw)
Short range grass	153.14	3.3	505.37
Leaves and leafy crops	80.15	11	881.62
Long grass	70.13	4.4[b]	308.57
Forage crops	37.21	5.4[b]	200.94
Small insects	37.21	3.8[c]	141.4
Pods with seeds	7.66	3.9[c]	29.86
Large insects	6.37	3.8[c]	24.2
Grain and seeds	6.37	3.8[c]	24.2
Fruit	4.44	7.6[c]	33.72

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973)
[b] Fresh/dry weight ratios from Harris (1975)
[c] Fresh/dry weight ratios from Spector (1956)

Table 8 Maximum EEC in diets of birds and mammals

Organism	Matrix	EEC (mg a.i./kg dw diet)
Bobwhite quail	30% small insects 15% forage crops 55% grain	85.87
Mallard duck	30% large insects 70% grain	24.2
Rat	70% short grass 20% grain/seeds 10% large insects	361.02
Mouse	25% short grass 50% grain/seeds 25% leaves and leafy crops	358.85
Rabbit	25% short grass 25% leaves and leafy crops 25% long grass 25% forage crops	474.13

Table 9 Effects on terrestrial organisms

Organism	Study type	End point value	Degree of toxicity[a]
Invertebrates			
Earthworm	Acute	14-d LC_{50} > 93.1 mg a.i./kg NOEC = 93.1 mg a.i./kg (equivalent to 209.5 kg a.i./ha)	N.A.
Bee	Acute contact	48-h LD_{50} = 47 Fg a.i. per bee (52.6 kg a.i./ha)	Practically non-toxic
Birds			
Bobwhite quail	Dietary	LC_{50} > 5200 mg a.i./kg dw	Practically non-toxic
	Reproduction	NOEC = 200 mg a.i./kg dw	N.A.
Mallard duck	Oral acute	LD_{50} > 2000 mg a.i./kg bw	Practically non-toxic
	Dietary	LC_{50} > 5200 mg a.i./kg dw	Practically non-toxic
	Reproduction	NOEC = 600 mg a.i./kg dw	N.A.
Mammals			
Rat	Acute oral	LD_{50} = 4210 mg a.i./kg bw	Low toxicity
	90-d dietary	NOAEL = 500 mg a.i./kg dw (34 mg/kg bw/d)	N.A.
	Reproduction	**Parental** NOAEL = 1000 mg a.i./kg dw (60 mg a.i./kg bw/d for M and 76 mg a.i./kg bw/d for F) **Offspring** NOAEL = 10 000 mg a.i./kg dw (594 mg a.i./kg bw/d for M and 751 mg a.i./kg bw/d for F) **Reproductive** NOAEL = 20 000 mg a.i./kg dw (1212 mg a.i./kg bw/d for M and 1484 mg a.i./kg bw/d for F)	N.A.
Mouse	90-d dietary	NOAEL = 10 000 mg a.i./kg dw (1552 mg a.i./kg bw/d)	N.A.
Vascular plants			
Vascular plant	Seedling emergence	NOEC = 841 g a.i./ha for all species (highest rate tested) No EC_{25} was tested	N.A.
	Vegetative vigour	Most sensitive EC_{25} = 299 g a.i./ha on carrot plant dry weight	N.A.

[a] Atkins et al. (1981) for bees and U.S. EPA classification for others, where applicable; N.A., not applicable.

Table 10 Effects on aquatic organisms

Organism	Study type	Test substance	End point value	Degree of toxicity[a]
Freshwater species				
Daphnia magna	Acute 48-h	CGA-179500 Technical	EC_{50} = 111 mg/L NOEC = 58 mg/L	Practically non-toxic
	Chronic	Trinexapac-ethyl Technical	NOEC = 2.4 mg a.i./L	N.A.
Rainbow trout	Acute 96-h	Trinexapac-ethyl Technical	LC_{50} = 68 mg a.i./L NOEC = 30 mg a.i./L	Slightly toxic
		CGA-179500 Technical	LC_{50} > 100 mg/L NOEC = 100 mg/L	Practically non-toxic
Bluegill sunfish	Acute 96-h	Trinexapac-ethyl Technical	LC_{50} > 135.2 mg a.i./L NOEC = 48.3 mg a.i./L	Practically non-toxic
Fathead minnow	Early life stage	Trinexapac-ethyl Technical	NOEC = 0.89 mg a.i./L	N.A.
			NOEC = 0.41 mg a.i./L	N.A.
Carp	Acute 96-h	Trinexapac-ethyl Technical	LC_{50} = 57 mg a.i./L NOEC = 32 mg a.i./L	Slightly toxic
		CGA-179500 Technical	LC_{50} > 100 mg/L NOEC = 100 mg/L	Practically non-toxic
Channel catfish	Acute 96-h	Trinexapac-ethyl Technical	LC_{50} = 35 mg a.i./L NOEC = 20 mg a.i./L	Slightly toxic
Freshwater alga	Diatom 5-d growth and reproduction	Trinexapac-ethyl Technical	EC_{50} = 42 mg a.i./L NOEC = 6.2 mg a.i./L.	N.A.
	Diatom acute 96-h	CGA-179500 Technical	EC_{50} > 100 mg/L NOEC = 100 mg/L	N.A.
	Blue-green alga 5-d growth and reproduction	Trinexapac-ethyl Technical	EC_{50} = 0.35 mg a.i./L NOEC = 0.11 mg a.i./L	N.A.
	Green alga 5-d growth inhibition	Trinexapac-ethyl Technical	EC_{50} = 9.4 mg a.i./L NOEC = 3 mg a.i./L	N.A.
	Blue alga 96-h acute	CGA-179500 Technical	EC_{50} = 72 mg/L NOEC = 28 mg/L	N.A.
	Green alga 72-h growth inhibition	CGA-179500 Technical	EC_{50} > 97.6 mg/L NOEC = 97.6 mg/L	N.A.
Vascular plant	Duckweed 14-d growth and reproduction	Trinexapac-ethyl Technical	EC_{50} = 0.19 mg a.i./L NOEC = 0.018 mg a.i./L	N.A.

Organism	Study type	Test substance	End point value	Degree of toxicity[a]
Marine species				
Crustacean	Acute 96-h	Trinexapac-ethyl Technical	**Mysid shrimp** LC_{50} = 6.5 mg a.i./L NOEC < 3.4 mg a.i./L **Eastern oysters** EC_{50} = 89 mg a.i./L NOEC < 8.4 mg a.i./L	Slightly to moderately toxic
Sheepshead minnow	Acute 96-h	Trinexapac-ethyl Technical	LC_{50} = 180 mg a.i./L NOEC < 60 mg a.i./L	Practically non-toxic
Marine alga	Marine diatom 5-d growth and reproduction	Trinexapac-ethyl Technical	EC_{50} = 16 mg a.i./L NOEC = 3.7 mg a.i./L	N.A.

[a] U.S. EPA classification, where applicable

Table 11 Risk to terrestrial organisms

Organism	Exposure	End point value	EEC	MOS	Risk
Invertebrates					
Earthworm	Acute	NOEC = 93.1 mg a.i./kg	0.318 mg a.i./kg	292.8	No risk
Bee	Contact	LD_{50} = 52.6 kg a.i./ha	715.6 g a.i./ha	735	No risk
Birds					
Bobwhite quail	Reproduction	NOEC = 200 mg a.i./kg dw	85.87 mg a.i./kg dw diet	2.3	Low risk
Mallard duck	Acute	LC_{50} > 2000 mg a.i./kg dw	24.2	>73.4 d[a]	Low risk
Mammals					
Rat	Acute	LD_{50} = 4210 mg/kg bw (assuming NOAEL = 421 mg/kg bw)	361.02 mg a.i./kg dw diet	19.6 d	Low risk
	Dietary	NOAEL = 500 mg a.i./kg dw	361.02 mg a.i./kg dw diet	1.38	Low risk
	Reproduction	NOAEL = 1000 mg a.i./kg dw	361.02 mg a.i./kg dw diet	2.77	Low risk
Mouse	Dietary	NOAEL = 10 000 mg a.i./kg dw	358.85 mg a.i./kg dw diet	27.87	No risk
Vascular plants					
Vascular plant	Vegetative vigour	EC_{25} = 299 g a.i./ha	715.6 g a.i./ha	0.42	Moderate risk

[a] Number of days of intake to reach NOAEL.

Table 12 Risk to aquatic organisms

Organism	Exposure	End point value	EEC	MOS	Risk
Freshwater species					
Daphnia magna	Chronic	NOEC = 2.4 mg a.i./L	0.133 mg a.i./L	18.05	No risk
Rainbow trout	Acute	NOEC = 30 mg a.i./L	0.133 mg a.i./L	225.56	No risk
Bluegill sunfish	Acute	NOEC = 48.3 mg a.i./L	0.133 mg a.i./L	363.16	No risk
Fathead minnow	Early life	NOEC = 0.41 mg a.i./L	0.133 mg a.i./L	3.08	Low risk
Freshwater alga	Acute	NOEC = 0.11 mg a.i./L	0.133 mg a.i./L	0.83	Moderate risk
Vascular plant	Dissolved	NOEC = 0.018 mg a.i./L	0.133 mg a.i./L	0.14	Moderate risk
Marine species					
Crustacean	Acute	LC_{50} = 6.5 mg a.i./L	0.133 mg a.i./L	4.89	Low risk
Marine fish	Acute	LC_{50} = 180 mg a.i./L	0.133 mg a.i./L	135.34	No risk
Marine alga	Acute	NOEC = 3.7 mg a.i./L	0.133 mg a.i./L	27.82	No risk