Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Regulatory Decision Document PRDD2001-02

Primisulfuron-methyl

The active ingredient primisulfuron-methyl and the formulated end-use product Beacon 75 WG herbicide for control of quackgrass and specific broadleaf weeds in field corn 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 reviewed and the rationale for the proposed full registration of these products. The Pest Management Regulatory Agency (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. Please forward all comments to the Publications Coordinator at the address listed below.

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Foreword

The submission for the full registration of the active ingredient primisulfuron-methyl and the end-use product Beacon 75 WG, a herbicide developed by Syngenta Crop Protection Canada, Inc. for use on field corn against quackgrass, redroot pigweed, and lamb's-quarters, has been reviewed by the Pest Management Regulatory Agency (PMRA) of Health Canada.

The PMRA had previously issued a temporary registration (Regulatory Note 2000-12) for these products with the requirement that Syngenta Crop Protection Canada, Inc. (formerly Novartis Crop Protection Inc.) carry out additional rotational crop studies. These studies have now been completed.

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 the active ingredient primisulfuron-methyl and the end-use product Beacon 75 WG. The PMRA has concluded that the use of the active ingredient primisulfuron-methyl and the end-use product Beacon 75 WG 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 the active ingredient primisulfuron-methyl and the end-use product Beacon 75 WG is proposed for full registration, pursuant to Section 13 of the PCP Regulations.

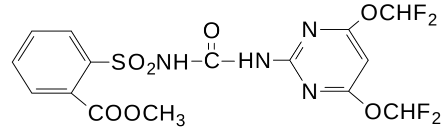
Methods of analysis of primisulfuron-methyl residues in various environmental media can be provided to monitoring agencies and research institutions upon request to the PMRA.

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 and its properties, uses, proposed classification, and labelling

1.1 Identity of the active substance and preparation containing the active substance

Active substance:	primisulfuron-methyl
Function:	herbicide
Chemical name (International Union of Pure and Applied Chemistry):	2-[4,6-bis(difluoromethoxy)-pyrimidin-2-ylcarbamoylsulfamoyl]benzoic acid, methyl ester
Chemical name (Chemical Abstracts Service [CAS]):	2-[[[[4,6-bis(difluoromethoxy)-2-pyrimidinyl]amino]carbonyl]amino]sulfonylbenzoic acid, methyl ester
CAS registry number:	86209-51-0
Nominal purity of active ingredient:	99% nominal
Identity of relevant impurities of toxicological, environmental, and (or) other significance:	nitrosamines were analyzed but were not detected at a limit of detection of <0.5 Fg/g; the product is not known to contain other microcontaminants known to be Toxic Substances Management Policy (TSMP) Track-1 substances
Molecular formula:	$C_{15}H_{12}F_4N_4O_7S$
Molecular mass:	468.3 Daltons
Structural formula:	

1.2 Physical and chemical properties of the active substance

Table 1.1 Technical product: CGA-136872

Property	Result	Comments
Colour and physical state	White crystals	Not applicable (N/A)
Odour	Odourless	N/A
Melting point range	194.8–197.4EC	N/A
Boiling point range	N/A	N/A
Density	1.64×10^3 kg/m^3 at 22EC	N/A
Vapour pressure	$<5 \times 10^{-6}$ Pa at 25EC	Low potential for volatilization
Ultraviolet (UV) – visible spectrum	No absorption maxima were observed between 290 and 750 nanometres (nm) in acidic, basic, or neutral solution	Phototransformation will not be an important route of transformation
Solubility in water at 25EC	pH / Solubility (mg/L) 5.0 / 3.7 7.0 / 390.0 8.5 / 11 000.0	Solubility increases with increasing pH; low solubility at pH 5; very soluble at pH 7 and pH 9 - potential for surface runoff and leaching to groundwater
Solubility in organic solvents at 25EC	Solvent / Solubility Acetone / 35.0 g/L Ethanol / 1000.0 mg/L Toluene / 570.0 mg/L *n*-Octanol / 7.7 mg/L *n*-Hexane / 1.5 mg/L	N/A
n-Octanol–water partition coefficient (K_{ow})	K_{ow} = 1.15 at 25EC	Will not bioconcentrate–bioaccumulate
Dissociation constant (pK_a)	pK_a = 3.47 at 20EC	Dissociates and exists as negatively charged ion at environmentally relevant pH values
Oxidizing properties	No thermal effect was found between room temperature and 150EC; no stability data with metals (the technical-grade active ingredient will not be for sale in Canada)	N/A
Storage stability	Not applicable to the technical product	N/A

Table 1.2 End-use product: Beacon 75 WG

Property	Result
Colour	Beige to light brown
Odour	Weak, uncharacteristic odour
Physical state	Granular solid
Formulation type	Water-dispersible granules
Formulants	All formulants used in the product are sodium salts and do not meet the TSMP criteria
Guarantee	75% weight per weight (w/w) nominal
Container material and description	Water-soluble bags in polyethylene packages with additional barrier material (polyethylene terephthalate)
Bulk density	0.667 g/mL
pH of 1% dispersion in water	6.5
Oxidizing or reducing action	Product does not contain any oxidizing and reducing agents
Storage stability	Stable for 2 years at 20EC in sale containers
Explodability	No explosive potential

1.3 Details of uses and further information

Primisulfuron-methyl is a group 2 herbicide belonging to the sulfonylurea family. Group 2 herbicides inhibit the enzyme, acetolactate synthase (ALS), which is required for the synthesis of branched chain amino acids. Beacon 75 WG is a wettable granule formulation containing 75% primisulfuron-methyl. Each polyethylene overpack bag will contain four 40-g water-soluble bags.

Beacon 75 WG may be applied to field corn in Eastern Canada at rates of 26.7 g/ha (20 g active ingredient [a.i.]/ha) or 40 g/ha (30 g a.i./ha) and must be applied with a nonionic surfactant at 0.2% volume per volume (v/v) spray volume. The lower rate of Beacon 75 WG is effective in controlling redroot pigweed and suppressing lamb's-quarters and quackgrass, whereas the higher rate is required for quackgrass control. Application may only be made once per year with ground equipment only. A minimum of 30, 45, and 88 days following application must pass before corn can be grazed (including the feeding of forage), harvested for silage, or harvested for grain, respectively.

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

Two reversed-phased high performance liquid chromatography (HPLC) methods were used for the determination of the active substance and the significant impurities (content $ 0.1%) in the technical product. The methods have been shown to have satisfactory specificity, linearity, precision, and accuracy.

2.2 Method for formulation analysis

An isocratic reversed-phased HPLC method was used for the determination of active substance in the formulation. The method has been shown to have satisfactory specificity, linearity, precision, and accuracy and is suitable for use as an enforcement method.

2.3 Methods for residue analysis

2.3.1 Multiresidue methods for residue analysis

Existing multiresidue methods of analysis were not found to be suitable for the determination of primisulfuron-methyl residues in corn because, in many cases, the residues did not come through the cleanup procedure.

2.3.2 Methods for residue analysis of plants and plant products

The residue of concern (ROC) was defined from the corn metabolism study as the parent compound, primisulfuron-methyl. The levels of any possible metabolites are expected to be below the limit of detection for most gas chromatography – HPLC methods (<0.01 parts per million [ppm]).

Residues of primisulfuron-methyl were determined by HPLC with UV detection (234 nm) in field corn (forage, fodder, grain) and its processed commodities (oil and presscake). The method limit of quantitation (LOQ) for primisulfuron-methyl was reported to be 0.01 ppm for field corn grain and its processed commodities (oil and presscake). This method was found to give good recoveries for the analysis of corn forage (91 ± 12%), silage-stage forage (86 ± 8%), fodder (97 ± 14%), grain (94 ± 15%), oil (89 ± 15%), and presscake (100 ± 35%). The standard deviations measured with respect to recoveries following spiking at the LOQ were indicative of the method having good repeatability. Representative chromatograms of control and spiked samples of corn matrices showed no background interferences from matrix coextractives, good peak shape, detectability, and sensitivity at the LOQ. Good linearity (correlation coefficient $r = 1.000$) was observed in the range of 0.01–0.5 ppm for primisulfuron-methyl. The interlaboratory validation supported the reliability and reproducibility of the Syngenta Crop Protection Canada, Inc. method for the determination of residues of primisulfuron-methyl in corn matrices.

2.3.3 Methods for residue analysis of food of animal origin

The ROC was defined from the goat and poultry metabolism studies as the parent compound, primisulfuron-methyl.

Residues of primisulfuron-methyl were determined by HPLC with UV detection (234 nm) in poultry tissues (lean meat, skin plus adhering fat, liver, and fat), eggs, dairy cow blood and tissues (round, loin, kidney, liver, perirenal fat, and omental fat), and whole milk. The method LOQ for primisulfuron-methyl was reported to be 0.01 ppm for milk and 0.05 ppm for all other matrices. This method was found to give excellent recoveries (91 ± 6.5%) for the analysis of poultry tissues, eggs, dairy cow tissues, and milk. The standard deviations measured with respect to recoveries following spiking at the LOQ were indicative of the method having good repeatability. Representative chromatograms of control and spiked samples of various tissues, milk, and eggs showed no background interference from matrix coextractives, good peak shape, detectability, and sensitivity at the LOQ. Good linearity (correlation coefficient $r = 0.9999$) was observed in the range of 0.01–1 ppm for primisulfuron-methyl. The interlaboratory validation supported the reliability and reproducibility of the Syngenta Crop Protection Canada, Inc. method for the determination of residues of primisulfuron-methyl in livestock and poultry matrices.

3.0 Impact on human and animal health

3.1 Effects having relevance to human and animal health arising from exposure to the active substance or to impurities in the active substance or to their transformation products

3.1.1 Absorption, distribution, metabolism, and excretion

From the various studies done on Sprague-Dawley (SD) rats, it appears that at a low oral dose (0.5 mg/kg body weight [bw]) females excrete more radioactivity in the urine (61–70%) and less in the feces (17–24%) than males (26–29% in urine and 61–67% in feces). At a high oral dose (55 mg/kg bw), both sexes excrete most of the radioactivity in the feces. Elimination in the feces and urine in all low-dose groups exhibits first-order kinetics during the slow phase (48–144 hours [h], post-dosing), with an average half-life of 20.3 h and with 94–103% of the dose being absorbed by the gastrointestinal (GI) tract. For the oral high-dose groups, only 23–32% of the dose is estimated to be readily absorbed. The highest ^{14}C residue levels, 7 days post-dosing, are found in the liver (<2.3 Fg/g tissue). Total radioactivity in the carcass and tissues is <0.2%, and there is no appreciable radioactivity in expired air. Total recovery is 88.5–102%, no matter which dosing regime is used. The metabolism of primisulfuron-methyl (CGA-136872) in rats involves hydroxylation of the pyrimidine ring followed by isomerization of the pyrimidinyl moiety. Bridge cleavage results in the formation of 2-carboxymethyl-benzene-sulfonamide in the feces and saccharin in the urine. The pyrimidinyl moiety is metabolized further to unidentified metabolites (11 metabolites, six of which were major [>10%]).

In a supplemental mouse study, two radiolabels were given to males at 1.064 mg/kg bw. Both the feces and urine had indications of two major metabolites, with one being more polar than the other. The parent did not appear to be present in any sample extracts.

3.1.2 Acute toxicity: technical and formulation

Technical primisulfuron-methyl (purity 94%) is considered to be of low acute toxicity via the oral (lethal dose 50% [LD_{50}] > 5050 mg/kg bw), dermal (LD_{50} > 2010 mg/kg bw), and inhalation (lethal concentration 50% [LC_{50}] > 4.81 mg/L) routes of exposure in the SD rat, New Zealand white (NZW) rabbit, and SD rat, respectively. It is nonirritating to the eye and skin of NZW rabbits and is not considered to be a dermal sensitizer in Hartley guinea pigs.

Beacon 75 WG, containing 75.8% primisulfuron-methyl technical, is considered to be of low acute toxicity via the oral (LD_{50} > 5050 mg/kg bw), dermal (LD_{50} > 2010 mg/kg bw), and inhalation (LC_{50} > 3.28 mg/L) routes of exposure in the SD rat, NZW rabbit, and SD rat, respectively. It is nonirritating to the eye and skin of NZW rabbits and is not considered a dermal sensitizer in Hartley guinea pigs.

Based on the results of the acute studies for the end-use product, no label signal words are required.

3.1.3 Genotoxicity

There is no evidence to support a mutagenic potential of primisulfuron-methyl in unscheduled deoxyribonucleic acid (DNA) synthesis tests, the *Salmonella*/Ames and the mammalian chromosomal aberration in vitro tests, and the in vivo micronucleus tests.

3.1.4 Subchronic and chronic toxicity

The subchronic and chronic toxicity of primisulfuron-methyl were investigated in mice, rats, and dogs. Initially, two 90-day studies (rat and dog) were conducted to establish appropriate dose levels to be used in the long-term studies. A 21-day dermal study was also carried out in rabbits.

3.1.4.1 Chronic toxicity in the mouse

In a carcinogenicity study, primisulfuron-methyl (purity 92.7–95.5%) was administered to 50 CD-1 mice per sex per dose in the diet at dose levels of 0, 10, 300, 3000, and 10 000 / 7000 (reduced during week 23) ppm (equal to 0, 1.35, 40.2, 408, and 1156 and 0, 1.72, 50.8, 512, and 1386 mg/kg bw/day for males and females, respectively) for 80 weeks. Males, starting at 3000 ppm, had increased mortality, absolute and relative liver weights, hypoplasia of the teeth, hepatocellular adenomas, hepatocellular carcinomas, chronic nephritis, and testicular degeneration. There was also a decrease in body-weight gain. Females, starting at 10 ppm, had increased absolute and relative liver weights but there was no apparent correlation between this weight gain and clinical chemistry. Starting at 3000 ppm, females had increased hepatocellular adenomas and hypoplasia of the teeth and at 10 000 / 7000 ppm they had increased mortality, hepatocellular carcinomas, and chronic nephritis, and decreased body-weight gain. The observed mortalities were considered to be related to toxicity and were not considered to be tumour-related. There was, at the 3000 and 10 000 / 7000 dose levels, an acceleration in the time to tumour for hepatocellular adenomas and adenomas–carcinomas combined. These doses, however, are considered to be beyond the maximum tolerated dose (MTD), and thus a no observed adverse effect level (NOAEL) can be established, since findings at 300 ppm are not considered to be adverse. Therefore, 300 ppm is considered to be the NOAEL, equal to 40.2 mg/kg bw/day.

Groups of 70 CD-1 mice per sex were exposed for 18 months to 0, 500, 1000, or 1500 ppm dietary concentrations of 98.2% pure primisulfuron-methyl (equivalent in males to 61, 122, or 185 mg/kg bw/day, respectively; equivalent in females to 77, 155, and 239 mg/kg/day, respectively). Beginning at 6 months and starting at 1000 ppm, both sexes had a statistically significant decrease in albumin and the females had a statistically significant decrease in total protein. At 1500 ppm, the only major, non-neoplastic, treatment-related effect, seen at 12 months in both sexes, was centrilobular hepatocellular hypertrophy. After 18 months, this effect was only statistically significant in females (32/70 for females and 27/70 for males). Incidences of liver tumours were similar among treated groups and controls. There was a treatment-related increase in the incidence of testicular degeneration and in the severity of nephropathy at 12 months in the 1500 ppm dose group. The oncogenic no observed effect level (NOEL) is 1500 ppm (185 mg/kg bw/day), and the chronic NOEL is 500 ppm (61 mg/kg bw/day). The MTD is near 1500 ppm, based on evidence of liver pathology, nephropathy, and testicular degeneration. This study verifies that the first study exceeded the MTD and that the established NOAEL of 40.2 mg/kg bw/day is valid.

3.1.4.2 Subchronic and chronic toxicity in the rat

In a 13-week short-term oral study, SD rats (15 per sex) were fed primisulfuron-methyl (purity 94%) in the diet at doses of 0, 10, 300, 3000, 10 000, and 20 000 ppm, equivalent to 0, 1, 30, 300, 1000, and 2000 mg/kg bw, respectively. At 10 and 300 ppm, all of the parameters monitored were comparable to those of the control group. Starting at 3000 ppm, males showed a statistically significant decrease in body weight. Starting at 10 000 ppm, both sexes had white discolouration of the incisors and (or) chipping of the incisors' enamel layer, and there was a statistically significant reduction in mean body weights and food consumption (g/animal/day). In both cases, the males were more severely affected. Feed efficiency was reduced in males during the first 3 weeks of treatment. Both sexes started to show statistically significant changes in hematological and clinical chemistry parameters, but these changes were within historical control levels, and remained within these levels even at the 20 000 ppm dose level. Microscopically, atrophy and degeneration of the testes were observed in one male, with another male only displaying degeneration. At 20 000 ppm, one female died during study week 12. Macroscopic findings included soft skull caps in three males and small testes in five males. Microscopically, atrophy and degeneration of the testes were observed in five males. The NOEL for this study is 30 mg/kg bw/day (300 ppm), based on the dose-related decrease in body weight starting at 300 mg/kg bw/day (3000 ppm).

In a combined chronic–carcinogenicity study, primisulfuron-methyl (purity 92.7–94%) was administered in the diet to Charles River CD rats. In the main study, 70 rats per sex were dosed at 0, 10, 300, 3000, 10 000 / 8000 (reduced after 13 weeks), and 20 000 ppm (equal to 0, 0.413, 12.4, 127, and 385 and 0, 0.526, 15.6, 160, and 470 mg/kg bw/day for males and females, respectively). An interim sacrifice was conducted with two sets of 10 rats per sex per dose for doses of 0, 3000, and 10 000 / 8000 ppm. The first set was sacrificed at the end of 12 months; the second set was placed in recovery at this time (fed a control diet) and sacrificed 1 month later. After 13 weeks, a dose of 20 000 ppm was severely depressing weight gain, so the group was terminated and the 10 000 ppm dose was reduced to 8000 ppm. At 3000 ppm, males had a 12% (overall) decrease in body-weight gain. At 10 000 / 8000 ppm, both sexes had reduced food consumption and the males had a moderate increase in soft testis at necropsy, correlating with an increase in testicular atrophy. Chipped teeth were more frequent in males and females receiving 10 000 / 8000 ppm than with controls. The recovery groups had similar results when compared to the 12-month sacrifice groups. The NOEL for chronic toxicity is 300 ppm, equal to 12.4 mg/kg bw/day. Primisulfuron-methyl was not oncogenic under the conditions of this study.

3.1.4.3 Subchronic toxicity in the dog

In a short-term (13-week) oral study, purebred beagle dogs (four per sex) were fed diets containing primisulfuron-methyl (purity 94%) at dose levels of 0, 25, 1000, and 10 000 ppm (equivalent to 0, 0.625, 25, and 250 mg/kg bw, respectively). At 1000 ppm, females had a non-adverse, but statistically significant increase in mean platelet values, one female had thickened mucosa of the gallbladder, and, microscopically, a few dogs had trace to mild epithelial hyperplasia of the gallbladder (trace in one male and one female, mild in two females). The gallbladder effects do not appear to be adverse because these pathological findings were not evident in the 1-year study of dogs. At 10 000 ppm, both sexes had decreased body weight, food consumption, and food efficiencies; decreased erythrocyte, haemoglobin, and hematocrit values; decreased absolute and relative thyroid weights; thickened and distended mucosa and trace to mild hyperplasia of the gallbladder; and small follicles with depleted colloid and parafollicular hyperplasia of the thyroid. Also, males had increased prothrombin time, and the females had increased urinary calcium and creatinine values. The NOAEL for this study is 1000 ppm (equivalent to 25 mg/kg bw/day), based on macroscopic and microscopic effects seen in the gallbladder and increased platelet values.

In a 1-year dietary toxicity study, primisulfuron-methyl (purity 94%) was administered to four beagle dogs per sex per dose at dose levels of 0, 25, 1000, and 10 000 / 5000 ppm (reduced to 5000 during week 11). At 10 000 ppm (weeks 1–11), both sexes had decreased body weight and body-weight gain, slight anemia, increased platelets, lower cholesterol, and microscopic changes in the liver and thyroid. Females at 5000 ppm (weeks 12–52) continued to have decreased body weight and body-weight gain. The NOEL is 1000 ppm (equal to 28.1 mg/kg bw/day).

3.1.4.4 Subchronic toxicity in the rabbit

In a 21-day dermal toxicity study, primisulfuron-methyl (purity 98.2%) was administered to five NZW rabbits per sex at dose levels of 0, 10, 100, and 1000 mg/kg bw/day. There were no treatment-related effects on any of the parameters examined (e.g., histopathology, clinical chemistry, haematology). The NOEL is ≥1000 mg/kg bw/day.

3.1.5 Reproductive and developmental toxicity

In a two-generation reproduction study, primisulfuron-methyl (purity 94%) was administered via the diet to 30 Charles River COBS® CD rats per sex per dose at dose levels of 0, 10, 1000, and 5000 ppm (actual mg/kg bw/day not provided). There was one litter per generation. At 5000 ppm, there were effects on reproduction (decrease in testicular–spermatic function), and there was a decrease in body-weight gain in F_1 males and body weight – growth in the offspring. The NOEL for systemic and reproductive toxicity, therefore, is 1000 ppm (equivalent to 50 mg/kg bw/day).

In a developmental toxicity study, primisulfuron-methyl (purity 94%) was administered to 24 Crl:COBS® CD (SD) BR female rats at dose levels of 0, 100, 500, and 1000 mg/kg bw/day from days 6 to 15 of gestation. A NOAEL was established at 1000 mg/kg bw/day. The developmental NOEL is 100 mg/kg bw/day, based on a statistically significantly increased litter incidence of skeletal variations, including incomplete ossification of the skull hyoid at 1000 mg/kg bw/day and bipartite vertebral centrum at 500 and 1000 mg/kg bw/day. There was no evidence of teratogenicity.

In a second rat developmental toxicity study, primisulfuron-methyl was administered by gavage to 26 Crl:COBS® CD (SD) BR female rats per dose from days 6 to 15 of gestation. Dose levels were 0, 10, 50, and 100 mg/kg bw/day. There were no treatment-related effects on any parameter examined and, thus, both the maternal and developmental NOELs are ≥100 mg/kg bw/day. Since the MTD was not reached, this study is classified as acceptable only in conjunction with the preceding rat developmental study.

In a rabbit developmental study, primisulfuron-methyl (purity 94%) was administered once daily by gastric intubation to 19 impregnated NZW rabbits at doses of 0, 10, 300, or 600 mg/kg bw/day during days 7–19 of gestation. Toxicologically significant maternal signs observed during treatment included two deaths at the high dose (on days 25 and 26 of gestation), three abortions at the high dose, two abortions at the mid-dose, salivation in the high dose (one doe), stool abnormalities in 6 of 19 does of the mid-dose and 8 of 19 does of the high dose, and decreased maternal body-weight gain in the high dose on days 7–20, 14–20, and 20–24 and in the mid-dose on days 7–14. Apart from the abortions in the mid- and high-dose groups, which decreased the number of viable litters examined, there were no compound-related fetal effects. Both the maternal and the fetal NOEL for this study is 10 mg/kg bw/day, based on maternal decreases in body-weight gains, stool alterations, and abortions (also considered fetotoxic) in the mid- and high-dose groups.

3.1.6 Neurotoxicity (acute, delayed, and subchronic)

Not applicable.

3.1.7 Integrated toxicological summary

A complete database was submitted for the new technical primisulfuron-methyl and the Beacon 75 WG formulation. The studies were in conformance with currently acceptable international testing protocols and are considered sufficient to clearly define the toxicity of this chemical.

The metabolism of primisulfuron-methyl in rats follows first-order kinetics, which involves the hydroxylation of the pyrimidine ring, followed by isomerization of the pyrimidinyl moiety. A subsequent bridge cleavage results in the formation of 2-carboxymethyl-benzene-sulfonamide in the feces and saccharin in the urine. The pyrimidinyl moiety is further metabolized to unidentified metabolites (11 metabolites, six of which were major [$10%]). Males and females present different excretion patterns at low oral doses. The females excrete 61–70% of the radioactivity in the urine and 17–24% in the feces. Males excrete 26–29% in the urine and 61–67% in the feces. At high oral doses, the excretion pattern is similar between the sexes, but only about 23–32% of the dose is absorbed. This low absorption indicates that primisulfuron-methyl has a metabolic threshold. Total recovery was 88.5–102%, no matter which dosing regime was used.

Acute dosing revealed that both the technical primisulfuron-methyl and the Beacon 75 WG formulation are of low acute toxicity via the oral, inhalation, and dermal routes of exposure in laboratory animals. They are nonirritating to rabbit skin and eyes and are not a skin sensitizer in the guinea pig.

In subchronic and chronic oral studies, toxicologically significant effects seen in the dog occurred at the MTD of 5000 ppm. The dogs presented with anemia, thyroid hyperplasia, decreased body weights and body-weight gains, and increased absolute and relative liver weights, with the liver showing vascular changes.

No apparent effects were noted in the rabbit (21 days) dermal study.

In the rat, males started showing a decrease in body weight and body-weight gain at 3000 ppm (equivalent to 124 mg/kg bw/day). At doses $8000 ppm (equivalent to 400 mg/kg bw/day) in the chronic study and $1000 mg/kg bw/day in the subchronic study, the animals had white discolouration of the incisors and (or) chipping of the incisors' enamel layer, with males being more affected than females. The males also presented with testicular atrophy–degeneration.

In the first chronic–oncogenicity mouse study, the two high doses exceeded the MTD and at 300 ppm (40.2 mg/kg bw/day) the females had increases in absolute and relative liver weights. In a second chronic–oncogenicity mouse study, at $1000 mg/kg bw/day, both sexes had decreased albumin and females had decreased total protein. This study also showed that 1500 ppm (185 mg/kg bw/day) is likely the MTD for the mouse. With the exception of the dose levels exceeding the MTD in the first study, there was no evidence of oncogenicity in either study.

In a battery of seven mutagenicity studies, technical primisulfuron-methyl was negative for genotoxicity. Taken together with the lack of evidence of carcinogenicity in both sexes of rats and mice, primisulfuron-methyl is not likely to pose a carcinogenic risk to humans.

There was no evidence of teratogenicity in either the rat or the rabbit developmental studies.

In the rat teratology study, there were no adverse maternal effects seen at the highest dose tested (1000 mg/kg bw/day). The only effect seen on the pups was a delay in ossification, occurring at $500 mg/kg bw/day. This delay is considered to be evidence of increased sensitivity of fetuses to *in utero* exposure to primisulfuron-methyl.

In rabbits at $300 mg/kg bw/day, there were stool abnormalities, abortions, and decreased body-weight gains during days 7–14 of gestation. The only effect seen on the pups was the abortions. A maternal and developmental NOEL, therefore, was set at 10 mg/kg bw/day.

In the two-generation reproduction study, primisulfuron-methyl affected the reproductive organs in male rats. At the highest dose tested (250 mg/kg bw/day), F1 parental males had tubular atrophy and aspermatogenesis, which is consistent with the testicular degeneration seen in the chronic and subchronic rat studies. The possibility exists, therefore, that at high doses ($250 mg/kg bw/day) primisulfuron-methyl causes endocrine effects.

3.2 Determination of acceptable daily intake

The most appropriate NOEL was in the rabbit developmental study at a level of 10 mg/kg bw/day for both maternal and fetal toxicity. At $300 mg/kg bw/day, the dams had stool abnormalities, abortions, and decreased body-weight gains during days 7–14 of gestation. The fetal NOEL is based on the abortions. The decrease in body-weight gain was also evident in male rats during the combined chronic–oncogenicity study (NOEL = 12.4 mg/kg bw/day).

For the calculation of acceptable daily intake (ADI), a safety factor (SF) of 100 is proposed. Although there was evidence of delayed ossification in the rat developmental study, the rabbit developmental NOEL is 10 times lower than the rat developmental NOEL (giving a margin of exposure [MOE] of 1000) and 15 times lower than the NOEL at which chipped teeth were seen in the rat (giving an MOE of 1500). With respect to testicular atrophy and aspermatogenesis seen in the rat at a NOEL of 50 mg/kg bw/day, the rabbit developmental NOEL is five times lower (giving an MOE of 500).

The proposed ADI is calculated according to the following formula:

$$\mathbf{ADI} = \frac{\mathbf{NOEL}}{\mathbf{SF}} = \frac{10}{100} = 0.1\ \mathbf{mg / kg\ bw / day\ \ of\ \ primisulfuron - methyl}$$

The maximum acceptable intake for a 60-kg person, calculated to the formula of ADI × 60 kg, is 6 mg/day.

3.3 Acute reference dose

For females of child-bearing age, the recommended acute reference dose (ARfD) = ADI (0.1 mg/kg bw/day). This ARfD, like the ADI, is derived from the rabbit teratology study and adequately compensates for the increased sensitivity of delayed ossification seen in the rat teratology study at ≥100 mg/kg bw/day.

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

Technical primisulfuron-methyl and the end-use formulation, Beacon 75 WG, are of low acute toxicity by the oral, dermal, and inhalation routes. Both were minimally irritating to the skin and eyes of rabbits and are not considered to be dermal sensitizers.

The general effects found in the short- and long-term studies included decreased body weight, discolouration and chipping of the enamel layer of the teeth (more prominent in the males), and testicular degeneration in the males.

There was no evidence of teratogenicity in either the rat or rabbit developmental studies. In the rat teratology study, there were no adverse effects on the dams. The only effect seen on the pups was a delay in ossification, occurring at ≥500 mg/kg bw/day. This delay is considered to be evidence of increased sensitivity of fetuses to *in utero* exposure to primisulfuron-methyl, and an additional safety factor of three for the NOEL of 100 mg/kg bw/day, set for delayed ossification, is warranted. In rabbits, at ≥300 mg/kg bw/day, maternal toxicity consisted of stool abnormalities, abortions, and decreased body-weight gain during days 7–14 of gestation. The only effect seen on the pups was the abortions. A maternal and developmental NOEL, therefore, was set at 10 mg/kg bw/day.

Given the short-term nature of occupational exposure, the maternal NOEL of 10 mg/kg bw/day in the rabbit developmental study was considered an appropriate study for the occupational risk assessment. Use of this NOEL will also provide adequate MOEs for the NOEL of 1000 mg/kg bw/day in the 21-day dermal toxicity study (i.e., a 20-fold higher MOE) and the NOEL of 50 mg/kg bw/day, based on testicular atrophy and spermatogenesis seen at the next dose level in the two-generation reproduction study (i.e., a fivefold higher MOE). An MOE of 100 is considered acceptable for these end points. Further, for female workers it was considered appropriate to ensure an MOE of 300 opposite the NOEL of 100 mg/kg bw/day, set for delayed ossification, in the rat developmental study. Use of the maternal NOEL of 10 mg/kg bw/day from the rabbit developmental study builds in a 10-fold safety factor for this end point.

3.5 Drinking water limit

Drinking water limit will be addressed in section 4.2.

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

3.6.1 Operator exposure assessment

Beacon 75 WG is an agricultural herbicide formulated as a water-dispersible granule and would be packaged in water-soluble bags of 40 g each. A storage-stability study with the water-soluble bags indicated that the packaging material is resistant to its contents. Beacon 75 WG is intended for selective weed control in field corn in Eastern Canada. Applications would be via groundboom and would be performed once per season post-emergent at the corn 2- to 6-leaf stage (up to 30 cm in height). Beacon 75 WG has a guarantee of 75% primisulfuron-methyl and a maximum application rate of 30 g a.i./ha, which is to be mixed in a minimum spray volume of 200 L/ha.

Dermal deposition and inhalation exposure
An occupational exposure study conducted with a similar end-use formulation was used as a surrogate study to assess exposure to Beacon 75 WG. In this study, 11 workers were monitored during mixing, loading, and application of Amber herbicide (triasulfuron) at 11 different sites. The sites were 32–40 ha in size and monitoring periods were 3–4 h. Each worker performed all tasks as part of his (her) typical work day including cleanup and minor repairs. Workers were monitored for dermal deposition by using cotton gauze patches attached to the outside of the inner clothing. Dermal deposition to the outside of the protective clothing was measured by analyzing sections cut from coveralls and hat patches. Neoprene gloves were worn for the handling and mixing of the product and during repair and cleanup activities. Hand washes before removing the gloves and then with bare hands provided estimates for deposition to the hands. To monitor inhalation

exposure, workers were equipped with personal air sampling pumps attached to a sampling tube. Adsorbent material inside the tube collected triasulfuron in the sampled air.

Field and laboratory recovery analyses were performed for all sampling media. Because some field recovery samples were <95%, some correction of data was necessary.

Although Amber is packaged in water-soluble bags, in the exposure study each operator was provided with the premeasured product in a glass jar. This was considered to adequately mimic workers handling water-soluble bags.

Dermal deposition was the major route of exposure (exposure by the inhalation route was very low). Unit exposure values from the surrogate study were adjusted for an application rate of 30 g a.i./ha and hectares treatable per day for both farmers and custom applicators (i.e., 80 and 140 ha, respectively) to derive estimates of exposure to primisulfuron-methyl. For farmers wearing gloves during mixing, loading, cleanup, and repair activities mean exposure (dermal deposition + inhalation) was 8.0 µg/kg bw/day. For custom applicators wearing gloves during mixing, loading, cleanup, and repair activities, mean exposure was 14 µg/kg bw/day.

Dermal absorption

Male Charles River SD rats were administered nominal doses of 0.002 and 0.02 mg/cm^2 of primisulfuron-methyl dermally and monitored up to 24 h post-dosing. The treated skin site was washed only at the 2-, 4-, 10-, or 24-h sacrifice intervals. Groups of four animals were treated at each dose level for each time interval. A single collection of urine, feces, and blood was obtained (separately) at sacrifice. Skin (treated skin and surrounding skin), carcass, skin wash, and the occlusive cover (stomahesive bandage, foil bridge, filter paper) were collected for analysis. Neither expired air nor individual tissues were collected for analysis. Total recovery of radioactivity for both dose levels and all time intervals was 95.38–100.31%.

Mean dermal absorption values (number of trials [*n*] = 4) were 22.95, 22.37, 20.86, and 27.05% after 2, 4, 10, and 24 h, respectively, for the low-dose group and 18.84, 21.55, 28.78, and 29.18% after 2, 4, 10, and 24 h, respectively, for the high-dose group. These absorption values include the percentage of dose retained in the skin site. Because the low dose was based on spray concentrations similar to those proposed for Beacon 75 WG, it was considered most appropriate to derive an estimate of dermal absorption based on the results from the low-dose (0.002 mg/cm^2) animals, which were sacrificed after 10 h. Mean dermal absorption for this group of animals was 21% (rounded from 20.86%).

Using the dermal absorption value of 21%, systemic exposure is 1.68 µg/kg bw/day for the farmer and 2.94 µg/kg bw/day for the custom applicator.

Using the maternal NOEL of 10 mg/kg bw/day from the oral rat developmental toxicity study and estimates of systemic exposure, an MOE of 6000 was obtained for the farmer and 3400 for the custom applicator. Margins of exposure are fivefold higher than this for the NOEL of 50 mg/kg bw/day in the two-generation reproduction study; 20-fold higher for the NOEL of 1000 mg/kg bw/day in the 21-day dermal toxicity study; and 10-fold higher for the NOEL of 100 mg/kg bw/day, set for delayed ossification in the rat developmental study. These MOEs are considered adequate.

3.6.2 Bystanders

Exposure and risk to bystanders should be minimal, given that application is by ground equipment only and given the proposed agricultural use scenario.

3.6.3 Workers

Re-entry exposure potential is considered negligible because application is early in the season (i.e., post-emergent at corn 2- to 6-leaf stage) and the rate of application is low (30 g a.i./ha).

4.0 Residues

4.1 Definition of the residues relevant to maximum residue limits

4.1.1 Definition of the residues in field corn relevant to maximum residue limits

Plant metabolism
In the metabolism study, ^{14}C-primisulfuron-methyl (formulated as a 5% a.i. wettable powder [5 WP], labelled in the phenyl and pyrimidinyl rings) was applied to 45 cm tall corn at an exaggerated rate of 160 g a.i./ha (about 5.3 × the proposed rate). Corn plants were sampled on days 20, 38, 66, and 106 after treatment. Mature corn plants were separated into stalks, grain, and cobs. Residues were quantified by scintillation counter.

The levels of ^{14}C in the various parts of the corn plants were still low regardless of the label position or the post-treatment sampling time. At maturity, the stalks contained 0.017–0.072 ppm, and the grain and cobs contained 0.004–0.008 ppm. The radiolabelled residues in the corn plants were below 0.08 ppm, and forage at silage stage and forage contained 0.014–0.056 ppm for both label positions.

The metabolic pathway of primisulfuron-methyl in field corn grown under field conditions was similar to that in greenhouse-grown field corn treated by either spray or stem injection and to that in corn cell culture. The metabolites identified suggested that there were three metabolic pathways in corn, i.e., hydroxylation and conjugation of the phenyl and the pyrimidinyl rings and cleavage of the sulfonylurea bridge. Based on the corn metabolism study, the ROC was defined as primisulfuron-methyl.

Confined crop rotation studies
In the confined crop rotation study, primisulfuron-methyl was applied to 45 cm tall field corn in loamy soil at 160 g a.i./ha. After the primary crop was harvested, wheat was planted 103 days after treatment (DAT), and corn, soybeans, sugar beets, and lettuce were planted at 334 DAT. The uptake of radioactivity was very low in the rotational crops. Residues of primisulfuron-methyl were below the limit of detection (<0.001 ppm) in all crops except winter wheat fall forage, which had levels below the LOQ (<0.002 ppm). Since secondary crops contained residues less than the LOQ, no further identification of the residues was required.

The confined crop rotation study supports the definition of the ROC, primisulfuron-methyl, as defined in the plant and animal metabolism studies.

Storage stability
In the freezer storage stability study, samples of chopped corn forage, fodder, and grain were spiked with primisulfuron-methyl at 0.2 ppm and stored at –15EC for 23 months. Under these conditions, residues of parent primisulfuron-methyl were stable and showed no degradation in any of the matrices tested. The method of analysis used to detect residues of primisulfuron-methyl was the same as that outlined in the analytical methodology. Plant metabolism and supervised residue trial samples were collected, stored, and analyzed within 23 months. It appears unlikely, therefore, that the integrity of the primisulfuron-methyl residues was affected during this storage period.

4.1.2 Definition of the residue in food of animal origin relevant to maximum residue limits

Animal metabolism
In the hen metabolism study, phenyl- and pyrimidinyl-labelled primisulfuron-methyl (as a formulation containing 75% a.i.) was administered orally to laying hens daily for eight consecutive days (3.0 mg/kg bw, equivalent to 50 ppm in feed rations). All samples (egg yolk, egg white, excreta, blood, skin and attached fat, breast and thigh muscle, liver, kidney, heart, and fat) were analyzed for total ^{14}C residue utilizing combustion of subsamples to $^{14}CO_2$ or solubilization and liquid scintillation counting. Results of this study indicated that, regardless of the dose level or label position, the majority of the radiolabelled residue was eliminated in the excreta (>86% of total radioactive residues). Primisulfuron-methyl and its 5-hydroxylated metabolite were the predominant residues in the excreta. Low levels (<0.2% of the total dose) of ^{14}C-primisulfuron-methyl residues were transferred to tissues of the body, and the highest levels of radioactivity were in the liver (1.9 ppm), kidney (0.4 ppm), blood (0.2 ppm), and fat (0.05 ppm). Less than 0.04% of the total dose of ^{14}C-primisulfuron-methyl residues was transferred to eggs. Volatiles and CO_2 were not found.

In the goat metabolism study, phenyl- and pyrimidinyl-labelled primisulfuron-methyl (as a formulation containing 75% a.i.) was administered orally to lactating goats daily for 10 consecutive days (3.0 mg/kg bw, equivalent to 5 ppm in feed rations). Most of the ingested dose was excreted in the urine (78% of the total dose) and feces (19%). The major compound identified in the goat urine was the parent compound primisulfuron-methyl, which was also a significant component of residues in feces, liver, and milk. The very low levels of tissue residues indicated that neither the parent compound nor its degradation products will accumulate in body tissues. Pyrimidinyl metabolites were identified in the liver and feces. The metabolites identified from the phenyl label were saccharin in liver, feces, and urine. The levels in milk plateaued within 2 days (-0.03 ppm), representing less than 0.22% of the dose.

The goat and hen metabolism studies suggest that primisulfuron-methyl was not extensively metabolized in the body but was rapidly excreted as the parent compound with negligible residues expected in meat, milk, or eggs. Based on the similarity of the goat, laying hen, and rat metabolic profiles, the ROC was defined as primisulfuron-methyl.

Storage stability

In the freezer storage stability study, samples of beef liver, poultry breast, eggs, and milk were spiked with primisulfuron-methyl at levels of 0.5, 0.5, 0.2, and 0.1 ppm, respectively, and stored at –15EC for a duration of 12 months. Under these conditions, residues of parent primisulfuron-methyl were stable and showed no degradation in any of the matrices tested. Residues were determined using the same method as that in the feeding studies. The method was assessed to be acceptable for use in determining residues of primisulfuron-methyl in beef and poultry tissues, eggs, and milk.

The data reviewed indicated that residues of primisulfuron-methyl were stable at –15EC for 12 months in beef liver, poultry breast, eggs, and milk. Animal metabolism and supervised residue trial samples were collected, stored, and analyzed within 12 months. It appears unlikely, therefore, that the integrity of the primisulfuron-methyl residues was affected during this storage period.

Livestock feeding study

In the dairy cattle feeding study, primisulfuron-methyl was administered by oral dosing with gelatin capsules to 11 Holstein and Jersey cows for a total of 28 days. The dosages were equivalent to 5, 25, and 50 ppm (Fg primisulfuron-methyl/g feed). Since the maximum anticipated dietary burden was estimated to be 0.12 ppm, these dosages were equivalent to 40, 200, and 400 times the maximum anticipated dietary burden, respectively. No detectable residues (<0.05 ppm) of the parent primisulfuron-methyl were found in tissues, fat, and blood when cows were treated at highly exaggerated rates (40×). Residues in milk were <0.01 ppm at all dosing levels (40–400×). Field corn constituted up to 50 and 80% of the diet of dairy cattle and beef cattle, respectively. Milled by-products accounted for 25 and 50% of the diet of dairy and beef cattle, respectively.

Residues in beef and beef by-products resulting from the feeding of animals with field corn or its processed commodities treated with primisulfuron-methyl at the proposed rate of 30 g a.i./ha were not expected to exceed 0.05 ppm. Consequently, a maximum residue limit (MRL) of 0.1 ppm should be established to cover residues of primisulfuron-methyl in beef and beef by-products. This proposed MRL is consistent with the United States (U.S.) tolerance of 0.1 ppm for these commodities.

Residues in milk resulting from the feeding of animals with field corn or its processed commodities treated with primisulfuron-methyl at the proposed rate were not expected to exceed 0.01 ppm. Consequently, an MRL of 0.02 ppm should be established to cover residues of primisulfuron-methyl in milk.

Poultry feeding study
In the poultry feeding study, primisulfuron-methyl was administered via treated commercial laying ration to 60 mature white Leghorn hens for 28 days. The dosages were equivalent to 0.1, 0.5, and 1.0 ppm (Fg primisulfuron-methyl/g feed). Since the maximum anticipated dietary burden was estimated to be 0.05 ppm, the dosages were equivalent to 2, 10, and 20 times this value. No detectable residues (<0.05 ppm) of the parent primisulfuron-methyl were found in eggs, poultry muscle, liver, or fat tissues when hens were treated at highly exaggerated rates. Field corn grain and its milled by-products constituted up to 80 and 60% of the total poultry diet, respectively.

Residues in poultry, poultry by-products, and eggs resulting from the feeding of field corn grain or milled by-products treated with primisulfuron-methyl at the proposed rate were not expected to exceed 0.05 ppm. Consequently, an MRL of 0.1 ppm should be established to cover residues of primisulfuron-methyl in poultry, poultry by-products, and eggs. This proposed MRL is consistent with the U.S. tolerance established at 0.1 ppm for these commodities.

4.2 Residues relevant to consumer safety

Supervised residue trials studies
The results from the supervised crop field trials study in field corn have shown that the maximum residues in grain collected 88–137 days following the last application of 40 g a.i./ha (1.3 × the proposed rate) Beacon 75 WG to corn from the 2- and 6-leaf stage were <0.01 ppm. Processed commodities (milled grain fractions) were not analyzed for this study because no residues (<LOQ) were found in the raw commodity at this exaggerated rate. Residues of primisulfuron-methyl in silage-stage forage, forage, and fodder were <0.05 ppm (LOQ) when treated at 40 g a.i./ha. An MRL of 0.02 ppm should be established to cover residues of primisulfuron-methyl in field corn grain. This proposed MRL is consistent with the U.S. tolerance of 0.02 ppm.

Residue decline
The results of the residue decline studies demonstrated that residues of primisulfuron-methyl in corn forage, silage, and grain dissipated within 20–32, 53–72, and 94–133 days, respectively, when treated with a single post-emergence application of the 75 WP formulation at the exaggerated rate of 160 g ai/ha (5.3 × the proposed Canadian application rate). Although these studies were not conducted according to the label

directions (30 g a.i./ha, one application per season), the data appear to support preharvest intervals (PHIs) of 30 days for forage, 45 days for silage, and 88 days for grain. Consequently, when treated at the label rate and harvested at the recommended PHIs, residues of primisulfuron-methyl are unlikely to exceed the proposed MRLs.

Processing study
In the processed food–feed study, primisulfuron-methyl, formulated as Beacon 75 WG, was applied to corn at 40, 120, or 200 g a.i./ha, equivalent to 1.3, 4, and 6.7 times the proposed rate, respectively. Mature corn grain (133 days) samples were processed into steepwater concentrate, coarse gluten, hulls (corn bran), gluten, starch, presscake – crude oil (expeller and solvent extracted), and refined oil. No residues were detected in the processed fractions (<0.01 ppm) of corn produced from crops treated at or below 40 g a.i./ha. Residues of primisulfuron-methyl in processed corn fractions will be covered under the raw agricultural commodity MRL of 0.02 ppm.

Freezer storage stability
In the freezer storage stability study, samples of the processed commodities corn oil and presscake were spiked with primisulfuron-methyl (0.1 ppm) and stored at –18EC for 14 months. Under these conditions, residues of parent primisulfuron-methyl were stable and showed no degradation in either corn oil or presscake. Residues of primisulfuron-methyl were determined using methods found to be acceptable for quantifying residues in the matrices tested.

Dietary risk assessment
The potential daily intake (PDI) was determined using the proposed MRLs on plant and animal commodities. A chronic dietary risk assessment was conducted using the USDA 1994-1996 Continuing Survey of Food Intake for Individuals as part of the Dietary Exposure Evaluation Model (DEEM™) software. The PDI was 10% of the ADI (ADI = 0.1 mg/kg bw) for the total population, including infants and children. For females of child-bearing age (13+ years), an ARfD (ARfD = 0.1 mg/kg bw/day) was recommended. The acute dietary risk assessment, conducted for this specific age group, indicated that the PDI represented only 1% of the ARfD (99.9 percentile).

The proposed domestic use of primisulfuron-methyl on field corn does not pose an unacceptable dietary (both food and water) risk to any segment of the population, including infants, children, and adults.

4.3 Residues relevant to worker safety

This issue has been addressed in section 3.6.3.

4.4 Proposed maximum residue limits and compliance with existing maximum residue limits

4.4.1 Compliance with existing maximum residue limits in Canada

Since this active ingredient is a new chemical, there are no existing MRLs.

4.4.2 Proposed maximum residue limits

On the basis of the residue data generated in Canada and the U.S., it is evident that residues of primisulfuron-methyl in field corn grain will likely not exceed 0.01 ppm. Data for field corn forage, fodder, and silage indicated that residues would likely not exceed 0.05 ppm when primisulfuron-methyl is used according to the proposed label directions.

Based on the submitted field trial residue data, and in light of the established U.S. tolerance of 0.02 ppm for field corn grain, it is proposed that an MRL of 0.02 ppm be established for residues of primisulfuron-methyl in (on) field corn grain.

Based on the supervised residue field trials and the processing studies, residues of primisulfuron-methyl in edible livestock commodities resulting from field corn treated at the proposed rate of 30 g a.i./ha were not expected to exceed 0.05 ppm. Data from the dairy cattle and poultry feeding studies suggested that residues of primisulfuron-methyl in beef, beef by-products, poultry, poultry by-products, and eggs resulting from the feeding of field corn treated with primisulfuron-methyl at the proposed rate of 30 g a.i./ha would not be expected to exceed 0.05 ppm. Consequently, an MRL of 0.1 ppm should be established to cover residues of primisulfuron-methyl in meat and meat by-products of cattle and poultry and eggs. This proposed MRL is consistent with the U.S. tolerance of 0.1 ppm for these commodities.

Residues in milk, resulting from the feeding of animals with field corn or its processed commodities treated with primisulfuron-methyl at the proposed rate, would not be expected to exceed 0.01 ppm. Consequently, an MRL of 0.02 ppm should be established to cover residues of primisulfuron-methyl in milk. This proposed MRL is consistent with the U.S. tolerance of 0.02 ppm for milk.

4.5 Proposed import tolerances

The proposed MRLs for domestic use of primisulfuron-methyl in (on) field corn grain are the same as the U.S. tolerances.

4.6 Basis for differences, if any, between established and proposed maximum residue limits

The Codex Alimentarius Commission has not established MRLs for residues of primisulfuron-methyl in (on) plant or animal commodities.

5.0 Fate and behaviour in the environment

5.1 Fate and behaviour in soil

The environmental chemistry and fate of primisulfuron-methyl in soil were investigated under laboratory and field conditions. Studies were performed using primisulfuron-methyl with a ^{14}C label in the phenyl and (or) pyrimidyl rings. Hydrolysis is not an important route of dissipation in neutral and alkaline soils, but would be increasingly more significant in acidic soils approaching pH 5. Phototransformation is not an important route of transformation. Biotransformation of primisulfuron-methyl in soil under aerobic and anaerobic conditions is an important transformation route. Laboratory studies indicated that primisulfuron-methyl has a potential for mobility in soil; however, the results of studies on terrestrial field dissipation indicated that there is a low potential for leaching.

5.1.1 Phototransformation on soil

The phototransformation of primisulfuron-methyl was studied with an acidic sandy loam soil at rates equivalent to 10.6 and 11.0 kg a.i./ha. The results obtained with the phenyl and pyrimidyl ring labelled compounds were similar. The phototransformation half-life of primisulfuron-methyl on soil was 24.1 and 24.2 days for the irradiated samples and 24.1 and 26.0 days for the dark control samples.

The total CO_2/volatile compounds amounted to 3.1 and 6.9% of the applied radioactivity in the irradiated and control samples, respectively. The major transformation products were 2-carboxymethyl-benzene sulfonamide (CGA-120844) (43.9% of the applied radioactivity) and 2-amino-4,6-bis(difluoromethoxy)-pyrimidine (CGA-171683) (37.9%). Unknowns made up 1.1% of the applied radioactivity.

Phototransformation of primisulfuron-methyl will not be an important route of transformation in the environment.

5.1.2 Aerobic soil biotransformation

The biotransformation of primisulfuron-methyl was studied in sandy loam soils under aerobic conditions at application rates equivalent to 3.6 and 10.2 mg a.i./kg dry soil over a period of 1 year. The total CO_2 released amounted to approximately 2.1–11.7% of the applied amount of radioactivity. Primisulfuron-methyl was slightly to moderately persistent in soil, with 50% decline time (DT_{50}) values of 31–62 days.

The major transformation products were CGA-171683 (88.6% of the applied radioactivity), saccharin, *O*-benzoic sulfimide (CGA-27913) (23.1%), primisulfonic acid (CGA-191429) (14.6%), and CO_2 (11.7%). The minor transformation products were *O*-sulfonamide benzoic acid (CGA-177288) (6.7%), CGA-120844 (3.9%), and unknowns (6.9%).

At the end of the incubation period, 49.5 and 35.7% of the applied radioactivity for the phenyl label was present as bound and extractable residues, respectively. The corresponding amounts for the pyrimidinyl label were 7.4 and 79.8%.

Biotransformation is an important route of transformation of primisulfuron-methyl in soil under aerobic conditions.

5.1.3 Anaerobic soil biotransformation

The biotransformation of primisulfuron-methyl was studied in sandy loam soils under anaerobic conditions at rates of application equivalent to 3.6 and 10.2 mg a.i./kg dry soil over a period of 90 days. The initial 30 days of the study were under aerobic conditions, and the final 60 days under anaerobic conditions. Evolved CO_2 amounted to approximately 0.2% of the applied material. Primisulfuron-methyl is moderately persistent in soil under anaerobic conditions, with DT_{50} values of 50–88 days.

The major transformation products were CGA-171683 (71.1% of the applied radioactivity) and CGA-27913 (32.2%). Minor transformation products included CGA-120844 (9.0% of the applied radioactivity) and CGA-177288 (5.7%).

At the end of the incubation period, 6.5 and 89.2% of the applied radioactivity for the phenyl label was present as bound and extractable residues, respectively. Corresponding amounts for the pyrimidinyl label were 11.8 and 92.7%.

Biotransformation is an important route of transformation of primisulfuron-methyl in soil under anaerobic conditions.

5.1.4 Mobility

The adsorption–desorption characteristics of ^{14}C-labelled primisulfuron-methyl, phenyl-^{14}C-labelled CGA-120844, pyrimidinyl-^{14}C-labelled CGA-171683, phenyl-^{14}C-labelled CGA-177288, phenyl-^{14}C-labelled CGA-191429, and phenyl-^{14}C-labelled CGA-27913 were studied with four U.S. soils (sand, pH 6.5; clay, pH 5.9; sandy loam, pH 7.5; loam, pH 6.7). The adsorption coefficients K_d and K_{oc} for these six compounds ranged from 0 to 2.1 and from 0 to 74.5, respectively.[1]

The low adsorption values indicated that primisulfuron-methyl and five of its transformation products are weakly bound to sand, clay, sandy loam, and loam soils. In the soils tested, the mobility of primisulfuron-methyl, CGA-191429, CGA-177288, and CGA-27913 will be very high, the mobility of CGA-120844 will be high to very high, and the mobility of CGA-171683 will be moderate to high. Desorption K_d and K_{oc} values

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[1] The adsorption coefficient K_d is defined as the ratio of concentration in the soil phase to that in the aqueous phase under test conditions, and the adsorption coefficient K_{oc} relates K_d to the organic carbon content of the soil sample.

were higher than those obtained for adsorption, which indicated that, once adsorbed, these compounds are not readily desorbed.

The leaching behaviour of phenyl-^{14}C-labelled primisulfuron-methyl was studied with four unaged U.S. soils (sand, sandy loam, clay loam, loam) in 30-cm long soil columns. At the end of the 3-day leaching period, 50–100% of the applied radioactivity was found in the leachates. The radioactivity present was distributed throughout the column. Transformation products were not identified. The mass balance at the end of study amounted to 92.6%.

In an aged-soil study, the leaching behaviour of primisulfuron-methyl and its transformation products was studied with a U.S. sandy loam soil in 30-cm long soil columns. The soil was treated with 8.5 and 8.9 mg a.i./kg soil and aged for 30 days under aerobic conditions at 25EC and 75% moisture. The mass balance at the end of study was 96 and 99%.

At the end of the 3-day leaching period, 83.1% of the applied radioactivity for the pyrimidine label and 85.6% of the applied radioactivity for the phenyl label was found in the leachates. The amount of primisulfuron-methyl found in the leachates was 81.2% of the applied radioactivity for the phenyl label and 78.5% of the applied radioactivity for the pyrimidine label. Transformation products detected in the leachates were CGA-27913 (2.4% of the applied radioactivity), a co-elution of CGA-191429 and CGA-177288 (1.7%), CGA-120844 (0.2%), CGA-171683 (0.2%), and unknowns (2.3%).

Analysis of soil-column sections showed that most of the radioactive residues remaining in the column were found in the top soil layer, with 7.4% of the applied radioactivity for the phenyl label and 11.4% of the applied radioactivity for the pyrimidine label in the 0–2.5 cm depth. The amount of primisulfuron-methyl found in the upper soil layer was 0.23% of the applied radioactivity for the phenyl label and 8.96% of the applied radioactivity for the pyrimidine label. Transformation products detected in the top layer of soil were a co-elution of CGA-191429 and CGA-177288 (1.5% of the applied radioactivity), CGA-171683 (0.8%), CGA-120844 (0.5%), CGA-27913 (0.3%), and unknowns (0.2–0.5%).

The results indicate that primisulfuron-methyl, CGA-27913, and CGA-191429 and CGA-177288 have a very high potential to leach in sandy loam soils.

The results from the unaged and aged soil-column leaching studies indicated that primisulfuron-methyl residues have a high potential to leach in sand, sandy loam, clay loam, and loam soils. These findings are in agreement with the results of the adsorption–desorption studies.

5.1.5 Field soil dissipation studies

The results of the terrestrial field dissipation studies indicated that primisulfuron-methyl has a low potential to leach to groundwater and was slightly persistent. Laboratory adsorption–desorption studies and soil-column leaching studies, however, indicated that primisulfuron-methyl and its transformation products had a high potential to leach through the soils tested. The results of laboratory studies also indicated that primisulfuron-methyl was slightly to moderately persistent.

Soil dissipation–accumulation of primisulfuron-methyl was conducted on bare plots at three sites in southern Ontario (Springbank, Strathroy, and London) over a period of approximately 300 days. The soil textures at these sites were loam, loamy sand, and silty loam, respectively. Rainfall exceeded the 30-year average and temperatures were within normal ranges. Primisulfuron-methyl decreased from the maximum concentrations of 10.3–15.9 Fg a.i./kg soil (18.5–32.7% of the applied radioactivity) at 0 DAT (0–15 cm depth) to a maximum of 0.53 Fg a.i./kg soil (0.77%) at approximately 90 DAT, and to nondetectable levels at approximately 300 DAT (<0.05 Fg a.i./kg soil). At the end of the study, no carryover of primisulfuron-methyl was detected. Under field conditions in southern Ontario, primisulfuron-methyl was nonpersistent to slightly persistent (DT_{50} values of 9.5–21 days and 90% decline time [DT_{90}] values of 31.5–70.2 days). These results were not consistent with those from laboratory studies on biotransformation in soil which indicated that primisulfuron-methyl was slightly to moderately persistent. Although a mass accounting was not conducted, the results from the field studies indicated that up to 73% in excess of the nominal rate of 40 g a.i./ha was applied.

Two transformation products (formed via the cleavage of the sulfonyl-urea bridge; similar to hydrolysis) were detected, CGA-120844 (79% of the applied radioactivity) and CGA-171683 (13%). These findings were not consistent with the results of laboratory biotransformation studies, which indicated that CGA-171683 was the predominant major transformation product (88.6% of the applied radioactivity), with lesser amounts of CGA-27913 (23.1%), CGA-191429 (14.6%), and CO_2 (11.7%).

Primisulfuron-methyl and its major transformation products, CGA-120844 and CGA-171683, were primarily detected in the 0–10 cm soil depth (total residues detected in this layer were approximately 100% of the recovered amount), indicating little mobility.

These results indicate that primisulfuron-methyl and its transformation products have a very low potential to leach and to contaminate groundwater under Canadian field conditions.

Two field studies were conducted in Wisconsin, U.S. In the first study, the DT_{50} and DT_{90} values were approximately 11 and 150 days, respectively. Primisulfuron-methyl dissipated from a maximum concentration of 10.5–24 Fg a.i./kg soil (59–135% of the applied radioactivity) at 0 DAT (0–15 cm depth) to 0.8 Fg a.i./kg soil (4.8% of the applied radioactivity) at 274 DAT. At the end of the study (274 days), the total carryover of primisulfuron-methyl was 1.2% of the applied amount. Transformation products were not monitored. The residues of primisulfuron-methyl were primarily detected in the 0–15 cm soil depth (initially 93% of the expected environmental concentration [EEC] in soil). Over the course of the study, 10–33% of the primisulfuron-methyl applied was found in the 15–30 cm depth, and 7–9% in the 30–75 cm depth. These results indicated little mobility of residues. The low potential to leach under field conditions does not agree with the results of laboratory studies on mobility. Plant uptake was not measured. A mass accounting was not conducted, but the results indicated that approximately 93% of the nominal rate of 40 g a.i./ha was applied.

In the second U.S. study, the DT_{50} and DT_{90} values were approximately 2.5 and 20 days, respectively. Primisulfuron-methyl decreased from a maximum concentration of 17–41 Fg a.i./kg soil (95–229% of the applied radioactivity) at 0 DAT (0–15 cm depth) to 0.6 Fg a.i./kg soil (3.3%) at 92 DAT, and was nondetectable at 274 DAT. At the end of the study (274 days), the total carryover of residues was 0% of the applied amount. Transformation products were not monitored.

Primisulfuron-methyl was primarily detected in the 0–15 cm soil depth (approximately 100% of the recovered amount), with 9–11% of the applied radioactivity found in the 15–45 cm depth. These results indicated minimal mobility. Plant uptake was not measured. A mass accounting was not conducted, but the results indicated that up to 129% in excess of the nominal rate of 40 g a.i./ha was applied.

A prospective groundwater study was conducted in Indiana, U.S. Deficiencies were noted concerning detection and storage stability, and the results from the lysimeters for CGA-27913 and CGA-177288 indicated contamination prior to the day of application and in subsequent samples. The major transformation products from the laboratory hydrolysis study, CGA-120844 and CGA-171683, were not detected in water samples obtained from the lysimeters; however, CGA-171683 was detected in soil samples from the 0–15 cm depth. One transformation product that was identified in the laboratory studies on soil biotransformation, CGA-191429, was not detected in soil samples taken from the test site. Although primisulfuron-methyl and the transformation products were shown to have a high mobility in laboratory studies, these compounds were not detected below the 15-cm depth of soil. This may be attributed to the short half-life of primisulfuron-methyl (approximately 6 days in the 0–15 cm depth of soil); however, laboratory studies indicated that the DT_{50} values for aerobic soil transformation ranged from 31 to 62 days. Data on uptake of primisulfuron-methyl by plants were not collected. The uptake of primisulfuron-methyl by plants may have contributed to the lower DT_{50} value that was obtained in the field study.

5.1.6 Expected environmental concentration

The expected environmental concentration (EEC) of primisulfuron-methyl in soil was calculated assuming a soil bulk density of 1.5 g/cm^3, a soil depth of 15 cm, and a scenario in which the maximum Canadian label rate of 30 g a.i./ha is applied once to soil. The EEC for primisulfuron-methyl in soil was estimated to be 0.013 mg a.i./kg dry soil immediately following the application.

5.2 Fate and behaviour in aquatic systems

The environmental chemistry and fate of primisulfuron-methyl in aquatic systems were investigated under laboratory conditions. Studies were performed using primisulfuron-methyl with a ^{14}C label in the phenyl and (or) pyrimidyl rings. The results of these studies indicated that hydrolysis is not an important transformation pathway in water at neutral pH and alkaline pH, but increases in importance near pH 5. Phototransformation of primisulfuron-methyl in water is not an important route of dissipation in the environment. Biotransformation occurred in pond and river water, and primisulfuron-methyl is considered slightly to moderately persistent under aerobic aquatic systems. Significant amounts of applied radioactivity partitioned from the water to the sediment. This result was not consistent with studies on adsorption–desorption which indicated there should have been very little partitioning to sediment.

5.2.1 Hydrolysis

Hydrolysis of primisulfuron-methyl was studied in the dark at 25EC in sterile aqueous buffered solutions of pH 5, pH 7, and pH 9. The DT_{50} values of phenyl-labelled test material were 25 and 560 days for pH 5 and pH 7, respectively. Corresponding values for the pyrimidinyl-labelled material were 26 and 990 days. Primisulfuron-methyl did not undergo hydrolysis at pH 9. The major transformation products detected were CGA-120844 (46.8% of the applied radioactivity) and CGA-171683 (43.4%).

Hydrolysis is not an important route of transformation in the environment at neutral and alkaline pHs, but would be increasingly more significant approaching pH 5.

5.2.2 Phototransformation in water

The aqueous phototransformation of phenyl-^{14}C-labelled primisulfuron-methyl was studied at 23–24EC in sterile aqueous buffered solutions of pH 5, pH 7, and pH 9 at an initial concentration of 5–6.7 mg/L under natural sunlight conditions for 30 days. Aqueous phototransformation of pyrimidinyl-^{14}C-labelled test material was also studied at pH 9 at an initial concentration of 6.18 mg/L under similar natural sunlight conditions for 30 days. The half-life of primisulfuron-methyl was 20.6 and 248 days for pH 5 and pH 7, respectively, and could not be determined for pH 9. The rates of transformation in control and irradiated samples were similar at all pHs, and therefore transformation was attributed to hydrolysis, with photolysis playing a very minor role. The material balance was 98.7–105.4 and 99.5–103.6% for the irradiated and control samples, respectively.

Negligible amounts of CO_2 and volatile compounds were released from the samples. The major transformation products were CGA-120844 (54.6% of the applied radioactivity) and CGA-27913 (10.2%). Two minor transformation products detected were CGA-171683 (2.0% of the applied radioactivity) and CGA-191429 (0.7%). These results contrast with those of the hydrolysis studies in which CGA-120844 (46.8% of the applied radioactivity) and CGA-171683 (43.4%) were the major transformation products, with CGA-27913 (7.6%) being a minor transformation product.

Phototransformation is not an important route of primisulfuron-methyl transformation in the aquatic environment.

5.2.3 Aquatic aerobic biotransformation

The biotransformation of primisulfuron-methyl was studied in pond and river sediment–water systems under aerobic conditions at 20EC with application rates equivalent to 100 g a.i./ha. For the phenyl label, DT_{50} values for primisulfuron-methyl were 39 and 43 days for pond and river water, respectively, and 94 and 47 days for pond and river sediment, respectively. Corresponding DT_{90} values were 128 and 142 days and 311 and 155 days. For the pyrimidinyl label, DT_{50} values for primisulfuron-methyl were 15 and 50 days for pond and river water, respectively, and 20 and 57 days for pond and river sediment, respectively. Corresponding DT_{90} values were 65 and 167 days and 165 and 190 days.

The total CO_2/volatile compounds released during the 273-day incubation period amounted to 15.0% of the applied radioactivity for the pyrimidinyl label and 41.0% for the phenyl label in the river system. Corresponding values in the pond system were 18.1 and 48.5%. Mineralization to CO_2, therefore, is a major route of dissipation of primisulfuron-methyl in river and pond sediment–water systems.

In the river water, the major transformation products were CGA-191429 (32.0–44.0% of the applied radioactivity), CO_2/volatile compounds (15.0–41.0%), 2-urea-4,6-bis(difluoromethoxy)-pyrimidine (CGA-239771) (25.2%), and unknowns (6.7–12.8%). Minor transformation products were CGA-171683 (3.9% of the applied radioactivity), saccharin, *O*-benzoic sulfimide (CGA-147087) (2.4%), CGA-177288 (2.2%), and 3-(4,6-bis(difluoromethoxy)-pyrimidin-2-yl)-1-(2-methoxycarbonyl-5-hydroxy-phenylsulfonyl)-urea (CGA-219741) (4%).

In the pond water, major transformation products were CGA-191429 (52.4–54.1% of the applied radioactivity), CO_2/volatile compounds (18.1–48.4%), CGA-239771 (16.5%), and unknowns (11.1–12.7%). Minor transformation products were CGA-177288 (9.2% of the applied radioactivity), CGA-171683 (4.8%), CGA-147087 (4.0%), and CGA-219741 (0.9%).

Significant amounts of applied radioactivity (29.3 and 45.9% in the river and 37.6 and 55.7% in the pond) partitioned from the water to the sediment. The maximum ratio of phenyl-^{14}C-residues in sediment to those in water was 2.87 in the pond system and 0.598 in the river system. Corresponding values for the pyrimidinyl label were 2.79 and 1.10.

These values are not in agreement with the results of the adsorption–desorption studies that indicated limited partitioning to sediment.

In the river sediment, the major transformation product was CGA-239771 (33.0% of the applied radioactivity). Minor transformation products were CGA-171683 (2.3% of the applied radioactivity), CGA-147087 (2.3%), unknowns (1.5–1.9%), CGA-177288 (1.2%), and CGA-120844 (0.8%).

In the pond sediment, the major transformation products were CGA-239771 (37.1% of the applied radioactivity) and CGA-191429 (13.4–17.0%). Minor transformation products were unknowns (4.2–6.8% of the applied radioactivity), CGA-177288 (3.1%), CGA-147087 (2.6%), CGA-171683 (1.8%), and CGA-120844 (1.0%).

Primisulfuron-methyl is considered to be slightly to moderately persistent in river and pond sediment–water systems. Biotransformation is an important route of transformation of primisulfuron-methyl under aerobic conditions in aquatic sediment–water systems.

5.2.4 Expected environmental concentration

Direct overspray
The EEC of primisulfuron-methyl in water immediately after application of Beacon 75 WG is 0.01 mg a.i./L water. This value is based on an application rate of 30 g a.i./ha and assumes a body of water with a 30-cm depth is directly oversprayed. This scenario is used as a first approximation of the EEC in aquatic systems. A further refinement of the assessment taking potential drift into consideration is utilized where necessary.

Runoff
The estimated seasonal losses from runoff following the application of a wettable formulation of primisulfuron-methyl (Beacon 75 WG) are expected to be 2–5% or less of the amount applied. Assuming a scenario in which a 100-ha watershed is treated once with Beacon 75 WG at the maximum Canadian label rate of 30 g a.i./ha, and 2–5% of the applied enters a 30 cm deep, 1-ha pond via runoff water, the EEC of primisulfuron-methyl is 0.02–0.05 mg a.i./L water.

6.0 Effects on nontarget species

6.1 Effects on terrestrial nontarget species

6.1.1 Wild birds

The effects of primisulfuron-methyl on 10- to 17-month-old bobwhite quail (*Colinus virginianus*) were assessed over 21 days. Primisulfuron-methyl was administered to the animals by single oral gavage at 1470 and 2150 mg a.i./kg bw. No mortalities or sublethal effects were observed at any of the dose levels. The NOEL and LD_{50} of primisulfuron-methyl to the bobwhite quail, based on mortality, were 2150 and >2150 mg a.i./kg bw, respectively. Primisulfuron-methyl is classified as practically nontoxic to bobwhite quail on an acute oral basis.

The acute oral toxicity of primisulfuron-methyl to 10-month-old mallard duck (*Anas platyrhynchos*) was assessed over 21 days. Primisulfuron-methyl was administered to the animals by single oral gavage at 1470 and 2150 mg a.i./kg bw. No mortalities or sublethal effects were observed at any of the dose levels. The NOEL and LD_{50} of primisulfuron-methyl to the mallard duck, based on mortality, were 2150 and >2150 mg a.i./kg bw, respectively. Primisulfuron-methyl is classified as practically nontoxic to mallard ducks on an acute oral basis.

The effects of primisulfuron-methyl to 13-day-old bobwhite quail (*C. virginianus*) were assessed over 8 days. Primisulfuron-methyl was administered to the animals in the diet at 312, 625, 1250, 2500, and 5000 mg a.i./kg diet. The no observable effect concentration (NOEC) and LC_{50} of primisulfuron-methyl to the bobwhite quail, based on mortality, were 2500 and >5000 mg a.i./kg diet, respectively. The NOECs for feed consumption and body-weight gain were 625 and 2500 mg a.i./kg diet, respectively. Primisulfuron-methyl is classified as practically nontoxic to bobwhite quail on a dietary basis.

The dietary toxicity of primisulfuron-methyl to 8-day-old mallard duck (*A. platyrhynchos*) was assessed over 8 days. Primisulfuron-methyl was administered to the animals in the diet at 312, 625, 1250, 2500, and 5000 mg a.i./kg diet. The NOEC and LC_{50} of primisulfuron-methyl to the mallard duck, based on mortality, were 2500 and >5000 mg a.i./kg diet, respectively. The NOECs for both feed consumption and body-weight gain were 5000 mg a.i./kg diet. Primisulfuron-methyl is classified as practically nontoxic to mallard ducks on a dietary basis.

The effects of technical primisulfuron-methyl on avian reproduction were assessed in a 20-week study with 24-week-old mallard ducks (*A. platyrhynchos*). Primisulfuron-methyl was administered to the animals in the diet at 20, 100, and 500 mg a.i./kg diet. An array of toxicological parameters were measured in the parent birds, eggs, embryos, and young chicks. The NOEC of primisulfuron-methyl to the mallard duck, based on parental toxicity and reproduction was 500 mg a.i./kg diet.

6.1.2 Bees

In an acute contact toxicity study, honey bees (*Apis mellifera*) were exposed to primisulfuron-methyl, administered topically at the rate of 13–100 Fg a.i./bee. The only mortality was a single bee in a negative control group. The NOEC and LC_{50} values were 100 and >100 Fg a.i./bee, respectively. Primisulfuron-methyl, therefore, is classified as relatively nontoxic to honey bees.

6.1.3 Earthworms

In an acute toxicity study, earthworms (*Eisenia foetida*) were exposed to primisulfuron-methyl at rates equivalent to 141–2250 kg a.i./ha in an artificial soil. The 14-day NOEC and LC_{50} values, based on survival, were 250 and >1000 mg a.i./kg soil, respectively. The 14-day NOEC and 50% effect concentration (EC_{50}) values, based on body-weight loss and flaccidity, were 125 and >1000 mg a.i./kg soil, respectively. Primisulfuron-methyl, therefore, is considered nontoxic to earthworms at concentrations up to 125 mg a.i./kg soil.

6.1.4 Nontarget plants

The results from a seed germination – seedling emergence study indicated that the treatment with primisulfuron-methyl resulted in a significant decrease in percent germination of lettuce, carrot, and tomato. Ryegrass and onion seeds did not germinate. Although some lettuce seed radicles emerged, their lengths were all less than 5 mm; therefore, seeds were not considered germinated. The percent reduction in the radicle length ranged from 29% in soybean to 100% in ryegrass.

For seedling emergence, the treatment resulted in a greater than 25% decrease in the number of emerged ryegrass seedlings. Many of the plants emerged at a slower rate in treated soil and were dead or dying 3 weeks after treatment. There was a greater than 25% decrease in shoot length and fresh weight of all plants tested. The effect on shoot length ranged from a 100% decrease in tomato to a 60% decrease in cucumber. The percent effect on fresh weight ranged from a 93% decrease in tomato to a 62% decrease in soybean.

As all plant species tested showed a greater than 25% detrimental effect compared with the control, a tier 2 study was triggered. The results from the tier 2 study indicated that different parameters showed different sensitivities to the herbicide. Seedling emergence was more sensitive to primisulfuron-methyl than seed germination. Among the parameters measured (percent seed germination, radicle length, percent emergence, phytotoxicity rating, seedling plant height, and emerged seedling dry weight), seedling dry weight was the most sensitive to this herbicide. The NOEC, 25% effect concentration (EC_{25}), and EC_{50} values were derived from probit analysis by plant species for seed germination and seedling emergence.

Seed germination was relatively insensitive to applications of primisulfuron-methyl compared to seedling emergence; the NOEC ranged from 4.6 g a.i./ha for onion to 148 g a.i./ha for soybean, cucumber, and corn. Among the species tested, soybean, cucumber, and corn were the plant species least sensitive to primisulfuron-methyl, and onion was the most sensitive. For seedling emergence, the NOEC ranged from 0.17 g a.i./ha for carrot and cabbage to 2.78 g a.i./ha for soybean, tomato, and corn. Soybean, tomato, and corn were the plant species least sensitive to primisulfuron-methyl, and carrot and cabbage were the most sensitive.

Nontarget phytotoxicity studies were conducted to determine the effect of primisulfuron-methyl on the vegetative vigour of six dicotyledon (soybean, lettuce, carrot, tomato, cucumber, and cabbage) and four monocotyledon (oat, ryegrass, corn, and onion) plant species. A single treatment of primisulfuron-methyl was applied at the maximum label (U.S. label) rate of 160 g a.i./ha. Treatment with this herbicide resulted in a greater than 25% detrimental effect on vegetative vigour, as measured by shoot length and fresh weight, in all plants tested. A tier 2 study, therefore, was triggered.

The tier 2 study statistical no-effect levels on plant-height gain, phytotoxicity ratings, and dry weight were determined and EC_{25} and EC_{50} values were derived from probit analysis. The first test, which evaluated response to doses ranging from 0 to 80 g technical substance/ha, had greater than 25% detrimental effect for all crops except soybean, oat, ryegrass, and corn. No-effect levels were achieved for the other plant species in the second test, which evaluated responses to doses ranging from 0 to 2 g technical substance/ha.

The NOEC values ranged from <0.12 g a.i./ha for carrot to 1.85 g a.i./ha for corn. Among the 10 plant species tested, carrot was the most sensitive species to primisulfuron-methyl. The most sensitive EC_{25} for terrestrial nontarget plants was 0.13 g a.i./ha for cucumber vegetative vigour.

6.2 Effects on aquatic nontarget species

6.2.1 Bioconcentration in fish

Based on the K_{ow} value, it is not anticipated that primisulfuron-methyl will bioconcentrate–bioaccumulate in fish. Data on bioconcentration–bioaccumulation in fish were not required.

6.2.2 Fish

In a 96-h acute toxicity study, rainbow trout (*Oncorhynchus mykiss*) were exposed to primisulfuron-methyl at mean measured concentrations of 67, 29, 20, 24, and 13 mg a.i./L. The 96-h LC_{50}, lowest observed effect concentration (LOEC), and NOEC values, based on mortality and nonlethal adverse effects, were 29 mg a.i./L (26–53 mg a.i./L), 20 mg a.i./L, and 13 mg a.i./L, respectively. Sublethal effects (e.g., darkened pigmentation, loss of equilibrium, lethargy) were observed in the groups exposed to 29 and 20 mg a.i./L of primisulfuron-methyl. Based on the results of this study, primisulfuron-methyl would be classified as slightly toxic to rainbow trout.

In a 96-h acute toxicity study, bluegill sunfish (*Lepomis macrochirus*) were exposed to primisulfuron-methyl at mean measured concentrations of 80, 68, 58, 48, and 17 mg a.i./L. The 96-h LC_{50}, LOEC, and NOEC values, based on mortality and nonlethal adverse effects, were >80, 58, and 48 mg a.i./L, respectively. Sublethal effects (e.g., darkened pigmentation, loss of equilibrium) were observed in the groups exposed to

80, 68, and 58 mg a.i./L of primisulfuron-methyl. No mortalities or sublethal effects were observed in the remaining mean measured concentrations, 48 and 17 mg a.i./L. Based on the results of this study, primisulfuron-methyl would be classified as practically nontoxic to bluegill sunfish.

6.2.3 Aquatic invertebrates

An acute 48-h toxicity study was conducted to determine the effects of primisulfuron-methyl on *Daphnia magna*. The 48-h EC_{50} and NOEC, based on mortality and sublethal adverse effects, were 260 and 110 mg a.i./L, respectively. Nonlethal effects (lethargy) were observed at 190 and 220 mg a.i./L. The maximum measured concentration of primisulfuron-methyl tested (530 mg a.i./L) was equivalent to 10 600 – 26 500 times the EEC in water (0.02–0.05 mg a.i./L). Based on the results of this study, primisulfuron-methyl would be classified as practically nontoxic to daphnids.

A chronic 21-day toxicity study was conducted to determine the effects of primisulfuron-methyl on *D. magna*. The 21-day LC_{50} and NOEC, based on mortality and nonlethal adverse effects, were 1.46 and 0.42 mg a.i./L, respectively. Sublethal effects (lethargy and reduced size compared to the controls) were observed in the group exposed to 2.8 mg a.i./L. Production of offspring in the treated groups indicated that primisulfuron-methyl had effects on reproduction at concentrations greater than 0.70 mg a.i./L.

6.2.4 Algae

An algal assay bottle test was conducted to determine the 7-day EC_{25} and EC_{50} values of primisulfuron-methyl to the freshwater green alga *Selenastrum capricornutum*. Increasing concentrations of test material had increasingly inhibitory effects on the population growth of *S. capricornutum.* Growth in the solvent control was somewhat reduced compared with the no-dose control. Effects of the test material day 7 relative to the solvent control ranged from 22.7 to 96.5% inhibition. As determined by inverse estimation least squares linear regression, the 7-day EC_{25} was 0.012 mg a.i./L (95% confidence limits 0.006–0.021 mg a.i./L) and the 7-day EC_{50} was 0.024 mg a.i./L (95% confidence limits 0.014–0.041 mg a.i./L). Based on the reduction of cell counts, the NOEC was determined to be 0.01 mg a.i./L nominal concentration.

6.2.5 Aquatic plants

A study on the toxicity of primisulfuron-methyl to duckweed (*Lemna gibba*) demonstrated that increasing test concentrations had increasingly inhibitory effects on the population growth. Growth in the solvent control was somewhat reduced compared with the control. Effects of the herbicide on day 14, relative to the solvent control, ranged from 8.5% stimulation to 98.4% inhibition. The 14-day EC_{50} value was 0.8 Fg a.i./L. The no-effect concentration was not determined.

The environmental toxicology end points are summarized in Appendix II.

6.2.6 Expected environmental concentration

Wildlife food sources

Based on a single application at the rate of 30 g a.i./ha, the EEC in food sources for wildlife was calculated as 3.6, 1.01, and 15.13 mg a.i./kg dry weight feed for the bobwhite quail, the mallard duck, and the rat, respectively.

6.3 Environmental risk assessment

6.3.1 Terrestrial organisms

Invertebrates

The 14-day NOEC for the earthworm (*E. foetida*), 125 mg primisulfuron-methyl/kg soil, was 9.6×10^3 times greater than the EEC in soil (0.013 mg/kg soil). Primisulfuron-methyl, therefore, is unlikely to have an adverse effect on earthworms following a single application at the label rate.

Primisulfuron-methyl is classified as relatively nontoxic to honey bees. Consequently, it is not anticipated that primisulfuron-methyl will have adverse effects on honey bees.

Wild birds

Acute risk assessment: The 14-day LD_{50} and NOEC derived from the results of the acute toxicity study conducted with bobwhite quail were >2150 and 2150 mg a.i./kg bw, respectively. Using an average body weight of 170 g and a daily intake of 15.2 g of food, the maximum number of days to intake by a bobwhite quail equivalent to the dose administered by gavage that had a no-observable effect on the laboratory population would be 6.7×10^3 days.

The 14-day LD_{50} and NOEC derived from the results of the acute toxicity study conducted with the mallard duck were >2150 and 2150 mg a.i./kg bw, respectively. Using an average body weight of 1200 g and a daily intake of 50 g of food, the maximum number of days to intake by a mallard duck equivalent to the dose administered by gavage that had a no-observable effect on the laboratory population would be 5.1×10^4 days.

Dietary risk assessment: The 8-day LC_{50} and NOEC, based on body-weight gain and feed consumption derived from the results of the dietary study with the bobwhite quail, were 2500 and 625 mg a.i./kg feed, respectively. The margin of safety, based on the NOEC, was calculated to be 174.

For the dietary study with the mallard duck, the 8-day LC_{50} and NOEC, based on mortality, were >5000 and 2500 mg a.i./kg feed, respectively. The margin of safety, based on the NOEC, was calculated to be 2480.

Reproductive risk assessment: The NOEC from the reproduction study with the mallard duck was 500 mg/kg diet. The margin of safety for reproduction is 495.

Wild mammals
Based on the results from studies conducted for human health evaluation, the margin of safety values calculated for primisulfuron-methyl indicate that it is not expected to pose a significant risk to small wild mammals.

Acute risk assessment: Results from the acute oral toxicity studies indicated that the maximum number of days of intake of primisulfuron-methyl by a wild rat equivalent to the dose administered by gavage that killed 50% of the laboratory population would be 6.68×10^3 days. The corresponding value for the formulated product was 5.00×10^3 days.

Short-term dietary risk assessment: The dietary margin of safety for the rat, based on the NOEL derived from the 90-day dietary study, is 19.8.

Chronic toxicity risk assessment: Based on the NOEL obtained from the reproduction study (1000 mg a.i./kg), the margin of safety is 66.

Plants
In the tier 2 vegetative vigour study, greater than 25% detrimental effect for all crops except soybean, oat, ryegrass, and corn was observed for application rates up to the equivalent of 80 g a.i./ha. The EC_{25} values ranged from 0.13 g a.i./ha for cucumber to 30.96 g a.i./ha for corn. There is a risk to nontarget terrestrial plants, therefore, resulting from the proposed use of primisulfuron-methyl on corn in Canada.

As the most sensitive EC_{25} value for terrestrial plants was for cucumber vegetative vigour (0.13 g a.i./ha), this value was used to determine the buffer zone for protection of sensitive wildlife terrestrial habitats (e.g., hedgerows and shelter belts).

6.3.2 Aquatic organisms

Invertebrates
For daphnids, the 21-day NOEC, based on mortality and nonlethal effects, was 0.42 mg a.i./L. Using an EEC of 0.01 mg a.i./L resulting from a direct overspray, the margin of safety for daphnids was calculated to be 42. Consequently, aquatic invertebrates are not expected to be adversely affected by a single application of primisulfuron-methyl at the label rate.

Fish
The rainbow trout (*O. mykiss*) was the most sensitive fish tested by the applicant. The 96-h NOEC, 13 mg a.i./L, is 1.3×10^3 times the EEC in a 30-cm column of water which would result from a direct overspray. Consequently, fish are not expected to be adversely affected by a single application of primisulfuron-methyl at the label rate.

Plants
The 7-day EC_{25} for the freshwater green alga *S. capricornutum* was 0.012 mg a.i./L. As the EEC in water is 0.01 mg a.i./L, there is a potential risk for algae.

The 14-day EC_{25} for duckweed (*L. gibba*), 0.33Fg/L, indicated that duckweed was the most sensitive aquatic plant tested. As no NOEC value was determined, one-tenth of the EC_{50} value was used as an estimated NOEC (0.08 Fg a.i./L). The margin of safety for aquatic plants was determined to be 0.008. This value indicates that aquatic plants would be at risk from a single application of primisulfuron-methyl at the label rate.

The risk to nontarget organisms is summarized in Appendix III.

6.4 Environmental risk mitigation

To protect sensitive nontarget aquatic and terrestrial plants, buffer zones between the last spray swath and the edge of the sensitive areas are required.

Using the value of 0.08 Fg/L for the estimated NOEC for the most sensitive species, duckweed (*L. gibba*), it was determined that a buffer zone of 26 m is required between the last spray swath and the edge of sensitive aquatic habitats (e.g., wetlands, ponds, lakes, streams, and rivers).

Based on the EC_{25} for the vegetative vigour for cucumber (0.13 g a.i./ha), a buffer zone of 31 m is required between the last spray swath and the edge of sensitive terrestrial habitats (e.g., hedgerows and shelter belts).

To protect nontarget aquatic plant species from primisulfuron-methyl in surface runoff, the following label statement is required: *Do not spray if there is forecast of rain during or soon after application*.

7.0 Efficacy data and information

7.1 Effectiveness

7.1.1 Intended uses

Beacon 75 WG is a selective, post-emergent herbicide that is applied to field corn in Eastern Canada for control of specific weeds. It is effective in controlling redroot pigweed and suppressing lamb's-quarters and quackgrass when applied at 26.7 g/ha (20 g a.i./ha), and in controlling quackgrass when applied at 40 g/ha (30 g a.i./ha). Beacon 75 WG must be applied with a nonionic surfactant at 0.2% v/v spray volume. Field corn may be grown on fields treated with Beacon 75 WG in the previous year.

7.1.2 Mode of action

Primisulfuron-methyl is a member of the sulfonylurea family of herbicides. Sulfonylurea herbicides are systemic in the plant, moving through both the phloem and xylem, and inhibit ALS, also known as acetohydroxy acid synthase (AHAS), a key enzyme in the synthesis of the branched-chain amino acids valine, leucine, and isoleucine. The meristematic regions of susceptible plants cease growth shortly after application, which is followed by chlorosis and necrosis of the whole plant over a period of usually 2–3 weeks. The actual sequence of biochemical and physiological processes leading to death of plant tissues is not known, other than it is related to the inhibition of the ALS enzyme.

Selectivity is largely based on differential rates of metabolism among species. Field corn tolerance is based on rapid metabolic detoxification.

7.1.3 Crops

Field corn (*Zea mays*) is the only crop for which data were submitted and for which a label claim was made.

7.1.4 Effectiveness against pests

7.1.4.1 Post-emergent application (2- to 6-leaf stage of the corn crop)

Effectiveness against quackgrass (*Agropyron repens*, also known as *Elytrigia repens*)
Control of quackgrass was reported in 26 trials conducted over 4 years at 19 locations in Ontario, Quebec, New Brunswick, Prince Edward Island, and Nova Scotia. The average control of quackgrass at 27 or more days after application of Beacon 75 WG plus a nonionic surfactant at 0.2% v/v was 89% (n = 21) for the 30 g a.i./ha rate and 74% (n = 26) for the 20 g a.i./ha rate.

Effectiveness against redroot pigweed (*Amaranthus retroflexus*)
Control of redroot pigweed was reported in 12 trials conducted over 3 years (1987, 1989, and 1997) at nine locations in Ontario and Nova Scotia. Control averaged 90% at 44–51 days after application of Beacon 75 WG at 20 g a.i./ha plus a nonionic surfactant at 0.2% v/v. Higher rates did not result in additional control.

Effectiveness against lamb's-quarters (*Chenopodium album*)
Control of lamb's-quarters was reported in 18 trials at 13 locations in Ontario, Quebec, and Nova Scotia over 4 years (1987, 1989, 1996, and 1997). Control averaged 71% at 16–51 days after application of Beacon 75 WG at 20 g a.i./ha plus a nonionic surfactant at 0.2% v/v. Higher rates did not result in additional control.

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

Populations of redroot pigweed resistant to group 2 herbicides have been confirmed in Ontario.

Syngenta Crop Protection Canada, Inc. has included the following weed resistance–management information on the Beacon 75 WG label:

"Some weed populations may contain plants naturally resistant to Beacon 75 WG or other herbicides with the same mode of action (ALS/AHAS enzyme inhibitors, Group 2). Repeated use of herbicides with this mode of action may allow these plants to spread. Poor control may result.

To delay the selection of weeds:

- *Integrate tillage or other mechanical control methods into weed control programs wherever practical.*
- *Prevent movement of resistant weed seeds to other fields by cleaning harvesting and tillage equipment and planting clean seed.*
- *Maintain herbicide use records for each of your fields.*
- *Monitor fields regularly for resistant weed populations.*
- *For further information contact your local Syngenta Crop Protection Canada, Inc. representative."*

7.3 Effects on the yield of treated plants in terms of quantity and (or) quality

7.3.1 Post-emergent application (2- to 6-leaf stage of the crop)

A total of 16 trials evaluating performance of Beacon 75 WG at the requested rate of 30 g a.i./ha and recording yield data were conducted at 12 locations over 3 years (1989, 1996, and 1997). Grain yield averaged 159% that of the untreated and unweeded check over the 16 trials.

Grain yield of field corn cultivars treated with 40 g a.i./ha Beacon 75 WG was compared in two trials conducted in Ontario in 1996. A pre-emergent application of 1.92 kg a.i./ha Dual (metolachlor) plus 600 g a.i./ha Banvel (dicamba) was made in both trials for early season weed control. Cultivars were common to both trials and only the 13 cultivars not contraindicated on the Beacon 75 WG label were considered. Mean grain yield among cultivars ranged from 86 to 103% that of the check, and averaged 95% of the untreated check over all hybrids.

Grain yield among field corn cultivars treated with 50 g a.i./ha Beacon 75 WG was assessed in five trials conducted in Ontario in 1997. A pre-emergent application of 1.92 kg a.i./ha Dual (metolachlor) plus 600 g a.i./ha Banvel (dicamba) was made in all trials for early season weed control. Only those cultivars not contraindicated on the label were considered. Four trials included the same 13 cultivars that were included in the 1996 trials, and six cultivars were common among all five trials. Over the four larger trials, mean grain yield among hybrids ranged from 96 to 114% that of the untreated check, and averaged 105% of the untreated check over all hybrids. When the six cultivars common to all five trials were considered, mean grain yield ranged from 101 to 110% that of the untreated check and averaged 104% of the untreated check over the six hybrids.

7.4 Phytotoxicity to target plants

7.4.1 Post-emergent application (2- to 6-leaf stage of the crop)

Tolerance of field corn to Beacon 75 WG applied at the requested rate of 30 g a.i./ha was assessed in 24 trials conducted in 1996 and 1997 in Ontario, Quebec, Nova Scotia, New Brunswick, and Prince Edward Island. Field corn injury about 1 week following application averaged 6% (n = 20), but declined to 1% by 35–51 days after application (n = 17).

Relative tolerance among field corn cultivars to an application of 40 g a.i./ha Beacon 75 WG was assessed in six trials conducted in Ontario in 1996. Only those cultivars not contraindicated on the label were considered. Four trials included the same 13 cultivars, and two trials included the same seven cultivars. Six cultivars were common to all six trials. When averaged over the four larger trials, mean injury among cultivars ranged from 3 to 12% and averaged 7% over cultivars. When the six cultivars common to all six trials were considered, injury ranged from 4 to 16% among cultivars and averaged 8% over cultivars.

Relative tolerance among field corn cultivars to an application of 50 g a.i./ha Beacon 75 WG was assessed in five trials conducted in Ontario in 1997. Only those cultivars not contraindicated on the label were considered. Four trials included the same 13 cultivars as the four larger trials conducted in 1996. The fifth trial included the same cultivars as in the two smaller trials conducted in 1996. Six cultivars were common to all five trials. When averaged over the four larger trials, mean injury among cultivars ranged from 1 to 4% and averaged 2% over cultivars. When the six cultivars common to all five trials were considered, mean injury among cultivars ranged from 1 to 3% and averaged 2% over cultivars.

7.5 Observations on undesirable or unintended side effects

7.5.1 Impact on succeeding crops

Soybean

Seven trials were conducted in Ontario and Quebec over 2 years on a range of soil textures, including loamy sand, loam, and silt loam. Organic matter ranged from 2.7 to 5%, and pH from 6 to 7.6. Soybean was planted 11–12.5 months after Beacon 75 WG herbicide had been applied to corn at 25 and 50 g a.i/ha in three trials conducted in 1998, 25 and 30 g a.i./ha in one trial conducted in 1998, and 40 g a.i./ha in the remaining trials conducted in 1997. Maintenance herbicides, including 1.4 kg a.i./ha Embutox, 75 g a.i./ha

Pursuit, or 75 g a.i./ha Pursuit plus 720 g a.i./ha Basagran Forte, were applied over the entire trial area of six trials for weed control. Injury to soybean grown where 30–50 g a.i./ha Beacon 75 WG had been applied ranged from 0 to 12% and averaged 3.6% when assessed 45–53 days after planting. In the five trials in which injury was initially observed, injury had declined to an average of 1.2% (range 0–3%) when assessed from 69 to 83 days after planting. The latter five trials, each of which had been treated with a maintenance herbicide, were taken to yield. Yield of soybean grown where 30–50 g a.i./ha Beacon 75 WG had been applied 11–11.5 months earlier ranged from 90 to 122% and averaged 108% of the check.

White bean
Seven trials were conducted in Ontario and Quebec over 3 years on a range of soil textures including loamy sand, loam, and silt loam. Organic matter ranged from 2.7 to 5%, and pH from 6 to 7.4. White bean was planted 11–12.5 months after application of Beacon 75 WG herbicide (or a 5% wettable powder formulation in the earliest trial) to corn at 25 and 50 g a.i./ha in three trials conducted in 1998, 25 and 30 g a.i./ha in one trial conducted in 1998, 40 g a.i./ha in two trials conducted in 1997, and 40 and 80 g a.i./ha in the remaining trial conducted in 1987. In each of five trials, 75 g a.i./ha Pursuit and 1.1 or 1.4 kg a.i./ha Patoran were applied over the entire trial area for weed control. Injury to white bean grown in primisulfuron-methyl-treated plots ranged from 0 to 5% and averaged 1.9% when assessed 45–53 days after planting. Three trials conducted in 1998 and one in 1997, each of which had been treated with maintenance herbicides, were taken to yield. Yield of white bean grown where 40 or 50 g a.i./ha Beacon 75 WG had been applied 11–11.5 months earlier ranged from 102 to 113% and averaged 108% of the check.

Kidney bean
Five trials were conducted in Ontario over 2 years on a range of soil textures including loamy sand and silt loam. Organic matter ranged from 2.7 to 4.5%, and pH from 6 to 7.4. Kidney bean was planted 11–11.5 months after application of Beacon 75 WG herbicide to corn at 25 and 50 g a.i./ha in three trials conducted in 1998 and 40 g a.i./ha in two trials conducted in 1997. In each trial, 75 g a.i./ha Pursuit and 1.1, 1.2, or 1.4 kg a.i./ha Patoran were applied over the entire trial area for weed control. Injury to kidney bean grown in Beacon 75 WG treated plots ranged from 1 to 3 % and averaged 2% when assessed 46–53 days after planting. Four trials were taken to yield. Yield of kidney bean grown where 40–50 g a.i./ha has been applied 11–11.5 months earlier ranged from 97 to 128% and averaged 111% of the check.

Alfalfa
Five trials were conducted in Ontario over 3 years on silt loam soils. Organic matter ranged from 2.7 to 4.5%, and pH from 6.4 to 7.6. Alfalfa was planted 11–12.5 months after application of Beacon 75 WG herbicide (or a 5% wettable powder formulation in the earliest trial) to corn at 25 and 50 g a.i./ha in two trials conducted in 1998, 40 g a.i./ha in two trials conducted in 1997, and 40 and 80 g a.i./ha in the remaining trial conducted in 1987. In each trial except for that conducted in 1987, Embutox herbicide was applied at

1.4 kg a.i./ha over the entire trial area for weed control. Injury to alfalfa grown in primisulfuron-methyl-treated plots ranged from 1 to 8 % and averaged 3% when assessed 46–52 days after planting. Four trials were taken to fresh-weight yield. Fresh weight of alfalfa grown where 40–50 g a.i./ha had been applied 11–11.5 months earlier ranged from 83 to 166% and averaged 122% of the check.

Field corn
Twelve trials were conducted in Ontario at 10 locations over 3 years (1986, 1987, and 1997). Trials were conducted on a range of soil textures including loamy sand, sandy loam, and silt loam. Organic matter ranged from 3 to 4%, and pH from 6 to 7.6. Injury to field corn on plots treated with 40 g a.i./ha 10–11.5 months prior to planting averaged 3% (n = 12) when assessed 32–70 days after planting. Two trials conducted in 1997, in which 40 g a.i./ha Beacon 75 WG was applied 11 months prior to planting, were taken to grain yield. Each trial received a blanket pre-emergent maintenance treatment of 1.92 kg a.i./ha Dual plus 600 g a.i./ha Banvel. Yield of the cultivar Pioneer (P) 3897, for which the Beacon 75 WG label contraindicates use, averaged 93% that of the check and was 10% lower than that of cultivars P3820 and P3940, for which use is not contraindicated.

The following recropping directions were supported by the data: fields treated with Beacon 75 WG can be planted the following year to soybean, white bean, kidney bean, alfalfa, and field corn, except for field corn cultivars Funks G-4034, Funks G-4120, Funks G-4160, and P3897.

7.6 Economics

Corn is the most important grain crop in eastern Canada. In 1998, 6.02 million tonnes of grain corn was produced on 743 500 ha in Ontario and 2.65 million tonnes was produced on 333 000 ha in Quebec. In 1997, approximately 11 000 tonnes of grain corn was produced in Nova Scotia, with lesser amounts produced in Prince Edward Island and New Brunswick. Ontario and Quebec together account for approximately 98% of Canadian grain corn production. In 1997, Canada produced about 94% of its grain corn requirements.

In Ontario and Quebec, corn accounts for about 50% of feed grains consumed by livestock. Approximately 81% of Canadian grain corn is used as livestock feed while the remainder is channelled into the increasingly important food and industrial sectors situated mainly in Ontario. Production of fuel ethanol is expected to increase in Ontario and this in turn is expected to increase future demand for grain corn.

Corn does not compete well with weeds, particularly early in the season before the crop canopy has fully developed. Weed-control measures are normally necessary to maximize economic yield. Infestations of quackgrass and broadleaf weeds such as redroot pigweed can reduce grain yields by over 30% and negatively impact grain quality, such as by reducing grain weight.

Herbicide application to control a light weed infestation capable of causing less than a 10% yield loss is usually economically viable. Whether the cost of a herbicide and its application are recovered will depend on the actual weed infestation level and the associated yield loss potential, the efficacy of the herbicide to control the weeds present in the field, the cost of the herbicide itself, the yield and value of the harvested crop, and other items that factor into the cost of growing the crop, including tillage, seed, other pesticides, fertilizer, fuel, harvesting, drying, and trucking.

Through increased competition in the quackgrass post-emergence corn herbicide market, the introduction of Beacon 75 WG is expected to have a favourable impact on treatment costs borne by the grower.

7.7 Sustainability

7.7.1 Survey of alternatives

Many post-emergent herbicides are registered for weed control in field corn, many of which may be used alone or in tank mixtures. Of these, products containing glufosinate (for use on glufosinate-tolerant hybrids only), glyphosate (for use on glyphosate-tolerant hybrids only), nicosulfuron, or a combination of nicosulfuron and rimsulfuron are registered for post-emergence quackgrass control. Many other products are registered for post-emergence use in field corn for control of broadleaved weeds, including redroot pigweed and lamb's-quarters (Appendix IV).

7.7.2 Compatibility with current management practices including integrated pest management

Beacon 75 WG, as for other herbicides, may be used in conjunction with cultivation and does not exclude the use of other herbicides with different modes of action for preplant or pre-emergence weed control. While no products were proposed for tank mixing with Beacon 75 WG, other products may be applied sequentially with Beacon 75 WG for broader spectrum weed control.

Crop rotation is an important component of integrated pest management. The four legume crops, soybean, white bean, kidney bean, and alfalfa, may be grown in fields treated with primisulfuron-methyl during the preceding year.

7.7.3 Contribution to risk reduction

The amount of active ingredient applied per hectare with Beacon 75 WG is lower than most other herbicides registered for use in corn. As with other post-emergent herbicides, the product is only applied if weeds are present; it is not applied as a preventative measure.

7.8 Conclusions

A review of the submitted data indicates that field corn (except cultivars Funks G-4034, Funks G-4120, Funks G-4160, and P3897) grown in Eastern Canada is expected to be acceptably tolerant of 40 g/ha (30 g a.i./ha) Beacon 75 WG when applied according to label directions. Control of quackgrass can be expected following application of Beacon 75 WG at this rate. Application of Beacon 75 WG at 26.7 g/ha (20 g a.i./ha) can be expected to control redroot pigweed and suppress both lamb's-quarters and quackgrass.

Soybean, white bean, kidney bean, alfalfa, and field corn (except cultivars Funks G-4034, Funks G-4120, Funks G-4160, and P3897) may be grown in fields treated with primisulfuron-methyl during the preceding year.

7.8.1 Summary

Crop	Field corn (*Zea mays*)
Cultivars (hybrids)	Excluding Funks G-4034, Funks G-4120, Funks G-4160, and P3897
Product	Beacon 75 WG
Application timing and method	Apply post-emergence from the corn 2- to 6-leaf stage by ground equipment only
Number of applications per year	1
Rates of application	26.7 g/ha (20 g a.i./ha) or 40 g/ha (30 g a.i./ha)
Surfactant	Nonionic surfactant must be added at 0.2% v/v spray volume
Spray volume	Minimum 200 L/ha
Spray pressure	200–300 kPa

Weed species controlled or suppressed	
At 20 g a.i./ha	Redroot pigweed (*Amaranthus retroflexus*) (control), lamb's-quarters (*Chenopodium album*) (suppression), quackgrass (*Agropyron repens*) (suppression)
At 30 g a.i./ha	Quackgrass (control)
Rotational crops	Soybean, white bean, kidney bean, alfalfa, field corn (except cultivars Funks G-4034, Funks G-4120, Funks G-4160, and P3897)

8.0 Toxic Substances Management Policy

During the review of primisulfuron-methyl technical and Beacon 75 WG herbicide, the PMRA has considered the implications of the federal Toxic Substances Management Policy (TSMP) and the PMRA Regulatory Directive DIR99-03 (*The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*) and has concluded the following:

- Primisulfuron-methyl does not meet the criteria for persistence. Its half-life in water, soil, and sediment did not exceed 50, 88, and 94 days, respectively (see section 5.0 of this document), and is therefore below the TSMP Track-1 cutoff criteria for water ($182 days), soil ($182 days), and sediment ($365 days). Although a half-life in air was not submitted, primisulfuron-methyl is nonvolatile from moist soil and water surfaces.

- Primisulfuron-methyl will not bioaccumulate. The log K_{ow} of 0.06, which is below the TSMP Track-1 cutoff criterion of $5.0 did not trigger the fish bioaccumulation/bioconcentration study. The goat and hen metabolism studies indicated that primisulfuron-methyl was rapidly excreted as the parent compound and did not accumulate in body tissues.

- The toxicity of primisulfuron-methyl is described in detail in sections 3.0, 4.0, and 6.0 of this document.

- The technical grade of primisulfuron-methyl does not contain any by-products or microcontaminants and does not form any degradation products that meet the TSMP Track-1 criteria. Impurities of toxicological concerns are not expected to be present in the raw materials, nor are they expected to be generated during the manufacturing process.

The formulated product does not contain any formulants that are known to contain TSMP Track-1 substances.

9.0 Overall conclusions

Field corn (with the exception of cultivars Funks G-4034, Funks G-4120, Funks G-4160, and P3897) grown in Eastern Canada can be expected to be acceptably tolerant to Beacon 75 WG herbicide applied from the crop 2- to 6-leaf stage. Beacon 75 WG, when applied at 26.7 g/ha (20 g a.i./ha), can be expected to control redroot pigweed while suppressing lamb's-quarters and quackgrass. Control of quackgrass can be expected following application of 40 g/ha Beacon 75 WG (30 g a.i./ha).

The product chemistry data for primisulfuron-methyl in Beacon 75 WG herbicide is complete. The technical material was fully characterized and the specifications were supported by the analysis of five batches for the active substance and impurities using specific validated methods of analysis. The technical material is not known to contain any toxic microcontaminants identified as TSMP Track-1 substances. The required physical and chemical properties of the technical material and of the end-use product were determined using acceptable methods. A fully validated HPLC method for determination of the active substance in the formulation was submitted.

Acute dosing revealed that technical primisulfuron-methyl and Beacon 75 WG are of low acute toxicity via the oral, inhalation, and dermal routes of exposure in laboratory animals. They are nonirritating to rabbit skin and eyes and are not a skin sensitizer in the guinea pig.

In subchronic and chronic oral studies, toxicologically significant effects were seen at high doses in the rat. Males started showing a decrease in body weight and body-weight gain at 3000 ppm (equivalent to 124 mg/kg bw/day). At doses $8000 ppm (equivalent to 400 mg/kg bw/day) in the chronic study and $1000 mg/kg bw/day in the subchronic study, the animals had white discolouration of the incisors and (or) chipping of the incisors' enamel layer, with males being more affected than females. The males also presented with testicular atrophy–degeneration.

There was no evidence of teratogenicity in either the rat or the rabbit developmental studies. In the rat, there were no maternal effects at the highest dose tested (1000 mg/kg bw/day). The pups did have a delay in ossification, occurring at $500 mg/kg bw/day. This delay is considered to be evidence of increased sensitivity of fetuses to *in utero* exposure to primisulfuron-methyl. In rabbits, at $300 mg/kg bw/day, there were stool abnormalities, abortions, and decreased body-weight gain during days 7–14 of gestation. The only effect seen on the pups was the abortions. A maternal and developmental NOEL, therefore, was set at 10 mg/kg bw/day.

At the highest dose tested, primisulfuron-methyl affected the reproductive organs in male adult rats. The F_1 parental males had tubular atrophy and aspermatogenesis, which is consistent with the testicular degeneration seen in the chronic and subchronic rat studies. The possibility exists, therefore, that at high doses ($250 mg/kg bw/day), primisulfuron-methyl causes endocrine effects.

The recommended ADI was calculated to be 0.1 mg/kg bw/day, based on the most appropriate NOEL of 10 mg/kg bw/day established in the rabbit developmental study (primarily on the basis of abortions) and using a safety factor of 100. The ARfD, like the ADI, is derived from the rabbit teratology study and adequately compensates for the increased sensitivity of delayed ossification seen in the rat teratology study at $100 mg/kg bw/day.

A short-term oral toxicology study was deemed most relevant for the risk assessment for both farmers and custom applicators handling Beacon 75 WG. Margins of exposure, calculated on the basis of typical use patterns, are acceptable. Since the timing of application is early in the season, re-entry exposure and risk are considered negligible. The label should include the statement: *DO NOT re-enter treated areas for 12 hours*.

The plant metabolism study conducted on field corn demonstrated that primisulfuron-methyl is readily metabolized in corn. The metabolic pathway was similar for field- and greenhouse-grown corn, either by spray or injection treatment, and for corn cell cultures.

The goat and hen metabolism studies indicated that primisulfuron-methyl was rapidly excreted primarily as the unchanged parent compound. The major compound identified was the parent compound primisulfuron-methyl in the urine, feces, liver, and milk. Pyrimidinyl metabolites were also identified in liver and feces. The major metabolite identified from the phenyl label was saccharin in liver, feces, and urine.

The metabolic profile in plants and animals suggests three metabolic pathways: hydroxylation and conjugation of the phenyl and pyrimidinyl rings and cleavage of the sulfonylurea bridge. Based on the metabolism studies, the ROC in plants and animals was defined as the parent compound primisulfuron-methyl.

The confined crop rotation study showed that no significant residues of primisulfuron-methyl are expected in rotational crops planted in areas where Beacon 75 WG was used for weed control in corn. The confined crop rotation study, therefore, supports the definition of the ROC, primisulfuron-methyl, as defined in the plant and animal studies.

An HPLC method with UV detection (234 nm) was used to determine residues of primisulfuron-methyl in corn and animal matrices. The method LOQ for primisulfuron-methyl was 0.01 ppm for field corn grain and processed commodities (oil and presscake), including milk. The LOQ for animal tissues and eggs was 0.05 ppm. Good linearity (correlation coefficient $r = 1.000$) was observed in the range of 0.01–1 ppm for primisulfuron-methyl. The interlaboratory validation did support the reliability and reproducibility of the Syngenta Crop Protection Canada, Inc. (Novartis) method for the determination of primisulfuron-methyl residues in corn, livestock, and poultry matrices. The standard deviations measured with respect to recoveries following spiking at the LOQ were indicative of the method having good repeatability. Representative chromatograms of control samples showed no interferences from matrix components or from reagents, solvents, and glassware.

Submitted freezer storage stability studies indicated that residues of primisulfuron-methyl were stable for at least 23 months in corn matrices and 12 months in animal matrices, milk, and eggs, when stored at –15EC.

The results from supervised crop field trials demonstrated that maximum residues in field corn grain, collected 88–137 days following the last application of primisulfuron-methyl and treated at 40 g a.i./ha (1.3 × the proposed rate), were all <0.01 ppm. Residues of primisulfuron-methyl in silage-stage forage (45 days), forage (30 days), and fodder (88 days) were <0.05 ppm (LOQ) when treated at 40 g a.i./ha. Considering these results, the proposed MRL for primisulfuron-methyl in corn grain is 0.02 ppm, with a minimum PHI of 88 days, expressed in terms of the latest growth stage proposed for application, 6-leaf stage of growth for corn.

Residues in beef, beef by-products, poultry, poultry by-products, and eggs resulting from the feeding of field corn grain or milled by-products treated with primisulfuron-methyl at the proposed rate of 30 g a.i./ha were not expected to exceed 0.05 ppm (anticipated maximum dietary burden). Considering these results, the proposed MRL for primisulfuron-methyl residues in meat and meat by-products of cattle and poultry and eggs was 0.1 ppm.

Residues in milk resulting from the feeding of field corn grain or milled by-products treated with primisulfuron-methyl at the proposed rate were not expected to exceed 0.01 ppm. Considering these results, the proposed MRL for primisulfuron-methyl residues in milk is 0.02 ppm.

The PDI was determined using the proposed MRLs on plant and animal commodities. A chronic dietary risk assessment was conducted using the USDA 1994-1996 Continuing Survey of Food Intake for Individuals as part of the DEEM™ software. The PDI was 10% of the ADI (ADI = 0.1 mg/kg bw) for the total population, including infants and children. For females of child-bearing age (13+ years), an ARfD (ARfD = 0.1 mg/kg bw/day) was recommended. The acute dietary risk assessment, conducted for this specific age group, indicated that the PDI represented only 1% of the ARfD (99.9 percentile).

Consequently, the proposed domestic use of primisulfuron-methyl on field corn does not pose an unacceptable dietary (both food and water) risk to any segment of the population, including infants, children, and adults.

Biotransformation of primisulfuron-methyl under aerobic and anaerobic conditions is an important transformation route in soil. Laboratory studies indicated that primisulfuron-methyl has a potential for mobility in soil; however, the results of studies on terrestrial field dissipation indicated that there is a low potential for leaching. Hydrolysis is not an important transformation pathway in water at neutral pH and alkaline pH, but increases in importance near pH 5. Phototransformation of primisulfuron-methyl in water is not an important route of dissipation in the environment. Primisulfuron-methyl is considered slightly to moderately persistent under aerobic aquatic systems.

Terrestrial invertebrates, birds, fish, and wild mammals will not be at risk. It is not anticipated that primisulfuron-methyl will bioconcentrate–bioaccumulate in fish. Terrestrial and aquatic plants will be at risk from the proposed use of Beacon 75 WG.

To protect sensitive terrestrial habitats, a 31-m buffer zone is required between the last spray swath and the edge of the sensitive areas. To protect aquatic environments, a buffer zone of 26 m is required between the last spray swath and the edge of the sensitive areas.

To protect nontarget aquatic plant species from primisulfuron-methyl in surface runoff, the following label statement is required: *Do not spray if there is forecast of rain during or soon after application.*

10.0 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 primisulfuron technical and Beacon 75 WG herbicide, manufactured by Syngenta Crop Protection Canada, Inc. The PMRA has concluded that the use of primisulfuron technical and Beacon 75 WG herbicide 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 primisulfuron technical and Beacon 75 WG herbicide for the control of quackgrass and specific broadleaf weeds in field corn is proposed for full registration, pursuant to 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
AHAS	acetohydroxy acid synthase
a.i.	active ingredient
ALS	acetolactate synthase
ARfD	acute reference dose
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstracts Service
CD	cesarean-derived
CGA-120844	2-carboxymethyl-benzene sulfonamide
CGA-136872	primisulfuron-methyl: 2-[4,6-bis(difluoromethoxy)-pyrimidin-2-yl carbamoylsulfamoyl]benzoic acid, methyl ester, or 3-[4,6-bis-(difluoro methoxy)-pyrimidin-2-yl]-1-(2-methoxycarbonylphenylsulfonyl)-urea
CGA-171683	2-amino-4,6-bis(difluoromethoxy)-pyrimidine
CGA-177288	*O*-sulfonamide benzoic acid
CGA-191429	primisulfonic acid
CGA-219741	3-(4,6-bis(difluoromethoxy)-pyrimidin-2-yl)-1-(2-methoxycarbonyl-5-hydroxy-phenylsulfonyl)-urea
CGA-239771	2-urea-4,6-bis(difluoromethoxy)-pyrimidine
CGA-27913/147087	saccharin, *O*-benzoic sulfimide
DAT	days after treatment
DEEM™	Dietary Exposure Evaluation Model software
DNA	deoxyribonucleic acid
DT_{50}	dissipation half-life
DT_{90}	time to 90% dissipation
EC_{25}	25% effect concentration
EC_{50}	50% effect concentration
EEC	expected environmental concentration
GI	gastrointestinal
h	hour
Hb	hemoglobin
HPLC	high performance liquid chromatography
Ht	hematocrit
K_d	adsorption coefficient (ratio of concentration in the soil phase to that in the aqueous phase under test conditions)
K_{oc}	adsorption coefficient (relates K_d to the organic carbon content of the soil sample)
K_{ow}	octanol–water partition coefficient
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOEC	lowest observed effect concentration
LOEL	lowest observed effect level
LOQ	limit of quantitation
MOE	margin of exposure

MRL	maximum residue limit
MTD	maximum tolerated dose
n	number of trials
nm	nanometres
NOAEL	no observed adverse effect level
NOEC	no observable effect concentration
NOEL	no observed effect level
NZW	New Zealand white
PCP	Pest Control Products
PDI	potential daily intake
PHI	preharvest interval
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
PRDD	proposed regulatory decision document
r	correlation coefficient
RBC	red blood cell
ROC	residue of concern
SD	Sprague-Dawley
SF	safety factor
TSMP	Toxic Substances Management Policy
v/v	volume per volume
U.S.	United States
UV	ultraviolet
w/w	weight per weight

Appendix I Summary of the toxicology studies with primisulfuron-methyl

Metabolism

At a low oral dose, females excreted more radioactivity in the urine (61–70%) and less in the feces (17–24%) than males (26–29% in urine and 61–67% in feces). At a high dose, both males and females excreted most of the radioactivity in the feces. At the oral low dose, elimination follows first-order kinetics during the slow phase (48–144 h post-dosing), with an average half-life of 20.3 h and with 94–103% of the dose being absorbed by the GI tract. At the oral high dose, 23–32% of the dose is readily absorbed. Highest ^{14}C residue levels 7 days post-dosing were in the liver (less than 2.3 Fg/g tissue). Total radioactivity in the carcass and tissues is <0.2%, and there is no appreciable radioactivity in expired air. Total recovery, no matter which dosing regime was used, was 88.5–102%. Metabolism of CGA-136872 in rats involves hydroxylation of the pyrimidine ring followed by isomerization of the pyrimidinyl moiety; bridge cleavage results in formation of 2-carboxymethyl-benzene-sulfonamide in the feces and saccharin in the urine; the pyrimidinyl moiety is metabolized further to 11 unidentified metabolites (six of which were major [>10%]).

In a supplemental study, two radiolabels were given to male mice at a dose of 1.064 mg/kg bw. Both the feces and urine indicated two major metabolites, with one being more polar than the other. The parent did not appear to be present in any sample extracts.

Study	Species–strain and doses	NOEL–NOAEL and LOEL (mg/kg bw/day)	Target organ, significant effects, and comments
Acute studies			
Oral	Rat (SD), 5/sex, limit dose	LD_{50} > 5050 mg/kg bw	Clinical signs included piloerection, lacrimation, dilated–constricted pupils, polyuria, diarrhea, and exothalmos up to day 5 of treatment; based on the LD_{50}, this compound is of low acute oral toxicity in the rat
Dermal	Rabbit (NZW), 5/sex, limit dose	LD_{50} > 2010 mg/kg bw	Males showed diarrhea – no defecation, reduced activity, and emaciation up to day 14; based on the LD_{50}, this compound is of low acute dermal toxicity in the rabbit
Inhalation	Rat (SD), 5/sex, 4.81 mg/L	LC_{50} > 4.81 mg/L	Nominal concentration was 120 mg/L; males had piloerection, clear nasal discharge, lacrimation, salivation, constricted pupils, ptosis, and exophthalmos up to day 3; females had the same effects as the males, including polyuria, diarrhea, and constricted–dilated pupils up to day 7
Dermal irritation	Rabbit (NZW), 3/sex, 500 mg	Minimal dermal irritant	The maximum irritation score was 0.2/8
Eye irritation	Rabbit (NZW), 3/sex (unwashed), 3 males (washed)	Minimal eye irritant	The maximum average score was 3.7/110 for the nonwashed eyes
Skin sensitization (Buehler method)	Guinea pig (Hartley albino), 10 males, 500 mg	Negative	Challenge did not produce any irritation in the experimental group or naive control

Study	Species–strain and doses	NOEL–NOAEL and LOEL (mg/kg bw/day)	Target organ, significant effects, and comments
Short term			
21-day dermal	Rabbits (NZW), 5/sex; doses: 0, 10, 100, and 1000 mg/kg bw	NOEL $ 1000 mg/kg bw/day	No effect on any parameter examined
90-day dietary	Rats (SD), 15/sex; doses: 0, 1, 30, 300, 1000, and 2000 mg/kg bw	NOEL = 30 mg/kg bw/day	$300 mg/kg bw: males had a statistically significant reduction in body weight $1000 mg/kg bw: the animals had white discolouration and (or) chipping of the incisors' enamel layer; males were more affected than females; both sexes also had a statistically significant reduction in mean body weight and food consumption; males had reduced red blood cell (RBC) counts, hematocrit (Ht), glucose, and blood urea nitrogen (BUN) and increased mean cell volume, mean cell hemoglobin (Hb), and platelets; one male had atrophy and degeneration of the testes, and another displayed degeneration only; females had reduced BUN and cholesterol and increased platelets $2000 mg/kg bw: males had a reduction in albumin/globulin ratio; females had reduced RBC counts, Hb, and Ht; macroscopically, three males had soft skull caps and five males had small testes; microscopically, five males had atrophy and degeneration of the testes
90-day dietary	Dogs (purebred beagle), 4/sex; doses: 0, 0.625, 25, and 250 mg/kg bw	NOAEL = 25 mg/kg bw/day	$25 mg/kg bw/day: statistically significant increase in mean platelets in females; one female had thickened mucosa of the gallbladder, and three females had trace to mild epithelial hyperplasia of the gallbladder, but none of these effects at this dose level were apparent in the 1-year study of dogs. $250 mg/kg bw: both sexes had inappetence, thin appearance, weight loss, and reduced food consumption and feed efficiency, RBC counts, Hb, and Ht; males had an increase in prothrombin time, and females had increased urinary calcium and creatinine values; macroscopically, both sexes had a reduction in absolute and relative thyroid weight, thickened and distended mucosa of the gallbladder, trace to mild hyperplasia of the gallbladder, and small follicles with depleted colloid and parafollicular hyperplasia in the thyroid

Study	Species–strain and doses	NOEL–NOAEL and LOEL (mg/kg bw/day)	Target organ, significant effects, and comments
1-year dietary	Dog (beagle), 4/sex; doses: 0, 25, 1000, and 10 000 / 5000 ppm	NOEL = 1000 ppm (28.1 mg/kg bw/day); MTD = 5000 ppm	$10 000 / 5000 ppm dose level: both sexes had anemia, increased platelets, and increased absolute and relative liver weights, with vascular changes and thyroid hyperplasia; the animals also showed a negative effect on body weight and body-weight gain
Chronic toxicity–oncogenicity			
Lifetime chronic–oncogenicity dietary	Mice (CD-1), 50/sex; doses: 0, 10, 300, 3000, and 10 000 / 7000 ppm; supplemental study tested dose levels of 0, 500, 1000, and 1500 ppm	NOAEL = 40.2 mg/kg bw/day (300 ppm)	$10 ppm: females had increased absolute and relative liver weight $3000 ppm: males had increased mortality and liver (absolute + relative) weight and reduced body-weight gain; there were also increased incidences of chronic nephritis, testicular degeneration, and hypoplasia of the teeth, and a suggested increase in hepatocellular carcinomas $3000 ppm: females had hypoplasia of the teeth and increased hepatocellular adenomas $10 000 / 7000 ppm: females had increased mortality and hepatocellular carcinomas; also evident was reduced body-weight gain and an increase in chronic nephritis
Lifetime chronic–oncogenicity dietary (supplemental)	Mice (CD-1), 70/sex; doses: 0, 500, 1000, and 1500 ppm	Oncogenic NOEL = 1500 ppm (185 mg/kg bw/day); chronic NOEL = 500 ppm (61 mg/kg bw/day)	Designed to determine an MTD of CGA-136872 when administered to CD-1 mice for 18 months; the earlier study had doses that were beyond the MTD, and thus that study did not satisfy the guideline requirement for Organization for Economic Co-operation and Development 451 $1000 ppm: both sexes had decreased albumin at 6 months, and females had decreased total protein at the same time period $1500 ppm: the only non-neoplastic treatment-related effect in both sexes was centrilobular hepatocellular hypertrophy at 12 months; after 18 months, it was only significant in the females Since the liver weights are not statistically significantly high, this study also shows that in the first study tumours in the liver were likely skewing the data, giving artificially high liver weights in females
104-week chronic dietary (combined)	Rats (Charles River CD), 70/sex; doses: 0, 10, 300, 3000, and 10 000 / 8000 ppm	NOEL = 300 ppm (12.4 mg/kg bw/day)	$3000 ppm: males had a 12% reduction in body-weight gain $10 000 / 8000 ppm: females had increased body-weight gain; males and females had reduced food consumption and an increased incidence of chipped teeth; males had an increase in soft testis, correlating with an increase in testicular atrophy

Study	Species–strain and doses	NOEL–NOAEL and LOEL (mg/kg bw/day)	Target organ, significant effects, and comments
Reproduction – developmental toxicity			
Two-generation reproduction	Rats (COBS® CD), 30/sex; doses: 0, 10, 1000, and 5000 ppm	NOEL = 1000 ppm (50 mg/kg bw/day) parental + reproduction	$250 mg/kg bw (5000 ppm): testes of F_1 parental males had tubule atrophy and aspermatogenesis; also at this dose, offspring had reductions in body size and weight (reduction in physical growth)
Teratogenicity	Rats (CD[SD]BR), 24 females/dose; doses: 0, 100, 500, and 1000 mg/kg bw/day	Maternal NOAEL = 1000 mg/kg bw/day; developmental NOEL = 100 mg/kg bw/day	All dams had reduced body weight on day 8 of gestation and reduced body-weight gain during days 8–12 of gestation $500 mg/kg bw: there were increased incidences of delayed ossification There was no evidence of teratogenicity
Teratogenicity	Rats (SD), 26 females/dose; doses: 0, 10, 50, and 100 mg/kg bw/day	NOEL $ 100 mg/kg bw/day, maternal and fetal toxicity	No treatment-related effects at the highest dose tested; since this study did not reach the MTD, it is only considered acceptable in conjunction with the above study
Teratogenicity	Rabbits (NZW); doses: 0, 10, 300, and 600 mg/kg bw/day	NOEL = 10 mg/kg bw/day for both maternal and fetal toxicity	$300 mg/kg bw: stool abnormalities, abortions (2), and reduced body-weight gain during days 7–14 of gestation $600 mg/kg bw: the above effects were more pronounced (three abortions), and the reduction in body-weight gain occurred during days 7–20 of gestation
Mutagenicity			
Salmonella – Ames test	TA98, TA100, TA1535, and TA1537; doses: 20–5000 Fg/plate	Negative	Did not induce mutations in *Salmonella* strains TA1535, TA1537, TA1538, TA98, and TA100 with and without S9 activation
Micronucleus test	Chinese hamster bone marrow; doses: assay I, 0 and 5000 mg/kg bw; assay II, 0, 1250, 2500, and 5000 mg/kg	Negative for both assays	Both assays showed that the percentage of polychromatic erythrocytes with micronuclei was not statistically significantly different between the control and all dose groups

Study	Species–strain and doses	NOEL–NOAEL and LOEL (mg/kg bw/day)	Target organ, significant effects, and comments
Micronucleus test	Chinese hamster bone marrow; doses: 1250, 2500, and 5000 mg/kg bw	Negative	No significant increase in the frequency of micronucleated polychromatic erythrocytes in bone marrow after any treatment time; this study lacked Good Laboratory Practice and Quality Assurance statements; there was no information on the stability or purity of the test compound, the source of the animals was not given, and it was not stated if the animals were properly maintained; this study, therefore, is only supplemental to the above study
Mammalian chromosomal aberration (cytogenetics) (in vitro)	Chinese hamster V79 cells; doses: 20–100 Fg/mL	Negative	No evidence that the test article induced mutant colonies over background
Unscheduled DNA synthesis	Primary human hepatocytes; doses: 20–400 Fg/mL	Negative	In both the original and confirmatory DNA-repair tests, the mean number of silver grains per nucleus in the vehicle control and after treatment with CGA-136872 revealed no marked differences
Unscheduled DNA synthesis	Primary rat hepatocytes; doses: 1–500 Fg/mL	Negative	In both the original and confirmatory DNA-repair tests, the mean number of silver grains per nucleus in the vehicle control and after treatment with CGA-136872 revealed no marked differences
Chromosomal aberration (in vitro)	ATCC/CCL 61 Chinese hamster cells; doses: 75–600 Fg/mL	Negative	With a 21-h harvest time, without microsomal activation, there was a slight increase in aberrations at the high dose, but they were within historical controls; there was no evidence, therefore, of chromosomal aberrations induced over background

Appendix II Summary of environmental toxicology

Test organisms	Toxicity end-point value
Bees (contact study)	48-h LD_{50} > 100 Fg a.i./bee, 48-h NOEC = 100 Fg a.i./bee
Earthworms	14-day LC_{50} > 1000 mg a.i./kg soil, 14-day NOEC = 125 mg a.i./kg soil
Acute bobwhite quail	21-day LD_{50} > 2150 mg a.i./kg bw, 21-day NOEC = 2150 mg a.i./kg bw
Acute mallard duck	21-day LD_{50} > 2150 mg a.i./kg bw, 21-day NOEC = 2150 mg a.i./kg bw
Dietary bobwhite quail	8-day LC_{50} > 2500 mg a.i./kg bw, 8-day NOEC = 625 mg a.i./kg bw
Dietary mallard duck	8-day LC_{50} > 2500 mg a.i./kg bw, 8-day NOEC = 2500 mg a.i./kg bw
Reproduction mallard duck	NOEC = 500 mg a.i./kg bw
Terrestrial plants (most sensitive species)	
Seed germination	Carrot EC_{25} = 3.4 g a.i./ha
Seedling emergence	Cucumber EC_{25} = 0.137 g a.i./ha
Vegetative vigour	Cucumber EC_{25} = 0.13 g a.i./ha
Daphnia	
Acute	48-h EC_{50} = 260 mg a.i./L, 48-h NOEC = 110 mg a.i./L
Chronic	21-day EC_{50} = 1.46 mg a.i./L, 21-day NOEC = 0.42 mg a.i./L
Rainbow trout	96-h LC_{50} = 24 mg a.i./L, 96-h NOEC = 13 mg a.i./L
Bluegill sunfish	96 h LC_{50} = 80 mg a.i./L, 96-h NOEC = 48 mg a.i./L
Aquatic plants	
Freshwater green alga, *Selenastrum capricornutum*	7-day EC_{25} = 0.012 mg a.i./L, 7-day NOEC = 0.01 mg a.i./L
Duck weed, *Lemna gibba*	14-day EC_{25} = 0.33 Fg a.i./L, 14-day EC_{50} = 0.8 Fg a.i./L

Appendix III Summary of risk to nontarget organisms

Organisms	Risk assessment	Margin of safety
Bees (contact study)	Adverse effect unlikely	
Earthworms	Adverse effect unlikely	9600
Acute bobwhite quail	Adverse effect unlikely	
Acute mallard duck	Adverse effect unlikely	
Dietary bobwhite quail	Adverse effect unlikely	174
Dietary mallard duck	Adverse effect unlikely	2480
Reproduction mallard duck	Adverse effect unlikely	495
Mammals		
Dietary rat	Adverse effect unlikely	19.8
Reproduction rat	Adverse effect unlikely	66
Terrestrial plants	At risk	0.008
Daphnids	Adverse effect unlikely	42
Rainbow trout	Adverse effect unlikely	1300
Aquatic plants		
Duck weed, *Lemna gibba*	At risk	0.008

Appendix IV Active ingredients and examples of end products registered for post-emergence use in corn

Active ingredient and group number (in parentheses) to which herbicide belongs	Example of end-use products and registration numbers (in parentheses)	Types of weeds controlled	Control of weed species for which a claim of control is proposed for Beacon 75 WG
Flumetsulam (2), clopyralid (4), 2,4-D (4)	Striker (24909) + nonionic surfactant	Broadleaf	Redroot pigweed, lamb's-quarters
Bentazon (6)	Basagran (12221) + Assist oil or Basagran Forte (22006)	Broadleaf	Redroot pigweed (suppression), lamb's-quarters
Bentazon (6), atrazine (5)	Laddok Liquid Suspension (16641) + Assist oil	Broadleaf	Redroot pigweed, lamb's-quarters
Bromoxynil (6)	Pardner (14878)	Broadleaf	Redroot pigweed, lamb's-quarters
Prosulfuron (2)	Peak 75WG (25310) + nonionic surfactant	Broadleaf	Redroot pigweed, lamb's-quarters
Dicamba (4)	Banvel II Herbicide (23957)	Broadleaf	Redroot pigweed, lamb's-quarters
2,4-D (4)	2,4-D (several)	Broadleaf	Redroot pigweed, lamb's-quarters
MCPA (4)	MCPA amine (several)	Broadleaf	Lamb's-quarters
Bromoxynil (6), MCPA (4)	Buctril M Emulsifiable Selective Weedkiller (18022)	Broadleaf	Redroot pigweed, lamb's-quarters
2,4-D (4), dicamba (4), mecoprop (4)	Kil-Mor Liquid Herbicide (8885)	Broadleaf	Redroot pigweed, lamb's-quarters
Flumetsulam (2), clopyralid (4)	Fieldstar Corn Herbicide (24451) + nonionic surfactant	Broadleaf	Redroot pigweed, lamb's-quarters
Cyanazine (5)	Bladex 90DF Agricultural Herbicide (19159)	Broadleaf, annual grasses	Redroot pigweed, lamb's-quarters
s-Metolachlor (15)	Dual II Magnum Herbicide (25729)	Annual grasses	None
Glufosinate ammonium (10) for use on glufosinate-tolerant cultivars	Liberty 200SN Herbicide (25337)	Broadleaf, annual grasses, quackgrass	Redroot pigweed, lamb's-quarters, quackgrass
Diflufenzopyr (4), dicamba (4)	Distinct Herbicide (25811)	Broadleaf	Redroot pigweed, lamb's-quarters
Nicosulfuron (2), rimsulfuron (2)	Ultim 75DF Herbicide (24736) + nonionic surfactant	Annual grasses, quackgrass, redroot pigweed	Redroot pigweed, quackgrass
Nicosulfuron (2)	Accent 75% Dry Flowable (25116) + nonionic surfactant	Annual grasses, quackgrass	Quackgrass

Active ingredient and group number (in parentheses) to which herbicide belongs	Example of end-use products and registration numbers (in parentheses)	Types of weeds controlled	Control of weed species for which a claim of control is proposed for Beacon 75 WG
Rimsulfuron (2)	Elim EP 75DF Herbicide (25200) + nonionic surfactant	Annual grasses, broadleaf	Redroot pigweed, lamb's-quarters (suppression)
Dimethenamid (15)	Frontier Herbicide (23462)	Annual grasses	None
Linuron (7)	Lorox DF Herbicide (20193)	Annual grasses, broadleaf	Redroot pigweed, lamb's-quarters
Atrazine (5)	Aatrex Nine-O Agricultural Herbicide (14842)	Broadleaved, wild oats	Redroot pigweed, lamb's-quarters
Atrazine (5), 2,4-D (4)	Clean Crop Shotgun Flowable Herbicide (24608)	Broadleaf	Redroot pigweed, lamb's-quarters
MCPA (4), MCPB (4)	Tropotox Plus 400 Liquid Selective Herbicide (8211)	Broadleaf	Redroot pigweed, lamb's-quarters
2,4-DB (4)	Embutox 625 Emulsifiable Selective Weedkiller (19217)	Broadleaf	Redroot pigweed, lamb's-quarters
Pendimethalin (3), used only in tank mixture with atrazine or cyanazine or dicamba or atrazine plus dicamba	Prowl 60 WDG Herbicide (25137) in tank mixture with atrazine, Bladex, Banvel, or Marksman	Broadleaf, annual grasses	Redroot pigweed, lamb's-quarters
Atrazine (5), dicamba (4)	Marksman Herbicide (19349)	Broadleaf	Redroot pigweed, lamb's-quarters
Glyphosate (9) for use on glyphosate-tolerant cultivars	Roundup Transorb Liquid Herbicide (25344)	Broadleaf, annual grasses, quackgrass	Redroot pigweed, lamb's-quarters, quackgrass
Imazethapyr (2) for use on imazethapyr-tolerant cultivars	Pursuit Herbicide (21537)	Broadleaf, annual grasses	Redroot pigweed, lamb's-quarters