Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Note

REG2004-04

Iodosulfuron-methyl-sodium

The active ingredient iodosulfuron-methyl-sodium and associated end-use product Tribute™ Solo 32DF Herbicide, containing the technical grade active ingredients foramsulfuron and iodosulfuron-methyl-sodium as well as the safener isoxadifen-ethyl, for the control of quackgrass, annual grasses and broadleaf weeds in field corn, have been granted temporary registration under Section 17 of the Pest Control Products (PCP) Regulations.

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

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Foreword

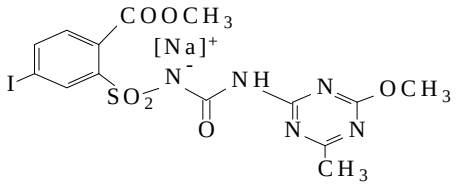
Health Canada's Pest Management Regulatory Agency (PMRA) has issued temporary registration for iodosulfuron-methyl-sodium and the associated end-use product (EP), Tribute™ Solo 32DF Herbicide (2% iodosulfuron-methyl-sodium, 30% foramsulfuron, and 30% of the safener isoxadifen-ethyl), for the control of quackgrass, annual grasses, and broadleaf weeds in field corn. These products were reviewed as a workshare within the North American Free Trade Agreement's Technical Working Group on Pesticides (NAFTA TWG) Joint Review Program by the PMRA and the United States Environmental Protection Agency (USEPA).

Bayer CropScience will be carrying out additional efficacy, storage stability, toxicology, and residue analytical method studies in environmental media as a condition of this temporary registration. Following the review of this information, the PMRA will publish a proposed registration decision document and request comments from interested parties before proceeding with a final regulatory decision.

Table of Contents

1.0 The active substance, its properties, and uses

1.1 Identity of the active substance and impurities

Active substance		Iodosulfuron-methyl-sodium
Function		Herbicide
Chemical name		
1.	International Union of Pure and Applied Chemistry	methyl 4-iodo-2-[3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)ureidosulfonyl]benzoate, sodium salt
2.	Chemical Abstracts Service (CAS)	4-iodo-2[[[[(4-methoxyl-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]benzoic acid methyl ester, monosodium salt
CAS number		144550-36-7
Molecular formula		$C_{14}H_{13}IN_5NaO_6S$
Molecular weight		529.2
Structural formula		
Nominal purity of active substance		91.9 (limits: 89.1–94.7)
Identity of relevant impurities of toxicological, environmental, or other significance		The technical grade iodosulfuron-methyl-sodium does not contain any impurity or microcontaminant known to be a Toxic Substances Management Policy (TSMP) Track 1 substance.

1.2 Physical and chemical properties of active substances and end-use product(s)

Technical product: Iodosulfuron-methyl-sodium technical

Property	Result	Comment
Colour and physical state	Beige crystalline powder	
Odour	Weak non-characteristic odour	
Melting point or range	152°C	
Boiling point or range	Not applicable	
Density	1.76 g/cm^3	
Vapour pressure at 20°C	Temp. (°C) — v.p. (Pa) 20 — 2.6×10^{-9} 25 — 6.7×10^{-9}	Not likely to volatilize from water and moist soil surfaces
Henry's Law constant	Temp. (°C) — Constant (Pa·m^3/mol) 20 — 2.29×10^{-11} 25 — 5.91×10^{-11}	
Ultraviolet-visible (UV-visible) spectrum	Solvent — λmax (nm) — ε [L/(mol × cm)] MeOH — 203 — 2.990×10^4 MeOH — 238 — 3.184×10^4 MeOH + NaOH (90/10, v/v) — 239 — 3.170×10^4 No observed absorption at λ 300–800 nm.	Not likely to undergo phototransformation in the environment
Solubility in water at 20°C	pH — Solubility (g/L) 7.6 (unbuffered) — 60.0 4 — 0.02 5 — 0.17 7 — 25.0 9 — 65.0 10 — 45.0	Soluble to very soluble Potential to leach

Property	Result	Comment
Solubility (g/L) in organic solvents at 20°C	Solvent — Solubility (g/L) acetone — >380.0 dichloromethane — >500.0 ethyl acetate — 23.0 n-hexane — ~ 1.2×10^{-3} methanol — 12.0 n-heptane — ~ 1.1×10^{-3} 2-propanol — 4.4 toluene — 2.1 acetonitrile — 52.0 dimethyl sulfoxide — >500.0 polyethylene glycol — 87.0	
n-octanol–water partition coefficient (K_{ow}) at 25°C	pH — log K_{ow} 4 — 1.96 5 — 1.07 6 — 0.07 7 — −0.70 9 — −1.22 10 — −1.15	Low potential to bioaccumulate
Dissociation constant (pK_a)	pK_a = 3.22 ± 0.06 at 20°C	Potential for mobility in soil
Stability (temperature, metal)	Data on stability to metals and metal ions are not applicable. AE F115008 TGAI is stored in steel drums with an inner polyethylene lining. Exposure to metal (stainless steel) is reduced to an insignificant minimum. The EP is packed in suitable plastic containers.	

End-use Product: Tribute™ Solo 32DF

Property	Result
Colour	Yellowish brown
Odour	Weak aromatic
Physical state	Fine-grained granule
Formulation type	Water-dispersible granule
Guarantee	Foramsulfuron: 30% (limits: 29.1–30.9%) Iodosulfuron-methyl-sodium: 2% (limits: 1.9–2.1%)

Property	Result
Formulants	The product does not contain any USEPA List 1 formulant or formulant known to be a TSMP Track 1 substance.
Container material and description	HDPE blow-moulded with injection-moulded closure and induction sealing disc in cardboard case
Bulk density	Tap density: 0.63 g/mL.
pH of 1% dispersion in water	6.7
Oxidizing or reducing action	No chemical incompatibility when in contact with reducing (zinc powder) or oxidizing (ammonium nitrate) agents
Storage stability	Tribute™ Solo 32DF is stable after storing in polyethylene bottles at room temperature for 2 years.
Explodability	Not explosive

1.3 Details of uses and further information

Iodosulfuron belongs to the general class of herbicides termed sulfonylureas (Group 2). Iodosulfuron inhibits the activity of acetolactate synthase (ALS), which is the key enzyme in the biosynthesis of the branch-chain amino acids isoleucine, leucine and valine. Although the actual sequence of phytotoxic processes is unclear, plant death results from events occurring in response to inhibition of the ALS enzyme.

Iodosulfuron behaves like both a contact and systemic herbicide when it is applied to weed species after their emergence. Uptake by the target plant is immediate upon application and phytotoxic effects within the plant are also immediate. The visible symptoms of herbicidal action are the almost immediate arresting of growth, followed by leaf yellowing, inhibition of anthocyanin production and finally, progressive shoot necrosis. Depending on the weed species and environmental conditions, plant death will usually occur between one and three weeks after herbicide application.

Iodosulfuron is present in one EP, Tribute™ Solo 32DF, which is formulated as a water-dispersible granule with a guarantee of 2% iodosulfuron and 30% foramsulfuron and must be applied with the surfactant Hasten. Foramsulfuron also belongs to the general class of herbicides termed sulfonylureas (SU) (Group 2) as described above.

Foramsulfuron is also found in other herbicide EPs, Tribute™ 2.25 SC and Tribute™ 35 DF. For information on the herbicide EPs containing foramsulfuron, please refer to the foramsulfuron regulatory document.

Tribute™ Solo 32DF also contains a built-in safener, isoxadifen-ethyl, which has no herbicidal activity when applied alone but, when applied in conjunction with iodosulfuron and foramsulfuron, encourages rapid inactivation of the herbicide in corn, without compromising the herbicide's effectiveness.

Tribute™ Solo 32DF is a selective herbicide for use as a post-emergence application to field corn grown in Eastern Canada, utilizing conventional tillage systems, for the control of specific broadleaf and grass weeds. Tribute™ Solo 32DF must be applied with the Hasten spray additive at 1.0% v/v (volume to volume) (i.e., 1 L Hasten per 100 L spray solution) and 2.5 L/ha of 28% liquid nitrogen fertilizer in a minimum total spray volume of 150 L/ha with a maximum of one application per year using ground equipment only.

Field corn, soybeans, spring barley, spring canola, spring oats, and dry common beans (kidney, navy, cranberry) may be planted 10 months after application of Tribute™ Solo 32DF.

2.0 Methods of analysis

2.1 Analytical methods for analysis of the active substance as manufactured

A reverse-phase high performance liquid chromatography–ultraviolet (HPLC-UV) method was provided for the determination of the active substance, iodosulfuron-methyl-sodium, in the technical product. Based on the validation data and the chromatograms provided, the method was assessed to be sufficiently specific, precise, and accurate.

2.2 Analytical methods for formulation analysis

A reverse-phase HPLC-UV method was provided for simultaneous determination of iodosulfuron-methyl-sodium and foramsulfuron present in Tribute™ Solo 32DF. Based on the validation data and the chromatograms provided, the method was assessed to be sufficiently specific, precise, and accurate for use as an enforcement analytical method.

2.3 Analytical methods for residue analysis

2.3.1 Methods for environmental residue analysis

For soil analysis, two chromatographic methods were submitted for the determination of the parent compound, iodosulfuron-methyl-sodium (AE F115008) and its major transformation products metsulfuron-methyl (AE F075736) and 2-amino-4-methoxy-6-methyl-1,3,5-triazine (AE F059411). Based on the validation data and the chromatograms provided, the methods were assessed to be sufficiently sensitive, precise, accurate and specific for the determination.

The method used for the determination of the parent compound and the major transformation products in North American soil could be used for sediments. An HPLC-UV method was provided for the determination of the parent compound and the major hydrolysis product, metsulfuron-methyl (AE F075736) in drinking water. Based on the validation data and chromatograms provided, the method was assessed to be sufficiently sensitive, precise, accurate, and specific for the determination. An analytical method was provided for the determination of the parent compound in maize. It was extended to the residue method for plant matrix. A specific and sensitive method was not provided for animal matrix.

2.3.2 Multiresidue methods for residue analysis

Iodosulfuron-methyl-sodium (AE F115008) and the metabolite metsulfuron-methyl (AE F075736) were screened through multiresidue methods according to the *Pesticide Analytical Manual*, Volume I, Appendix II (1/94). Testing through Protocol A was not initiated since iodosulfuron-methyl-sodium or metsulfuron-methyl are fluorescent. Testing through Protocol B was not initiated as neither compound is a phenol. Testing through Protocol D was not conducted since neither compounds was recovered through the Florisil cleanup procedures, or because the NPD and FPD-S detectors lacked the necessary sensitivity to these compounds. As iodosulfuron-methyl-sodium and metsulfuron-methyl were not recovered through Florisil column cleanup procedures, testing through protocols E and F were terminated. Iodosulfuron-methyl-sodium and metsulfuron-methyl do not appear to be recoverable through the United States Food and Drug Administration (USFDA) multi-residue methods.

2.3.3 Methods for residue analysis of plants and plant products

An analytical method (BY/02/99) has been developed for the determination of residues of iodosulfuron-methyl-sodium and metsulfuron-methyl in crops, even though only iodosulfuron-methyl-sodium is the analyte of interest for enforcement purposes. Extractable residues of iodosulfuron-methyl-sodium and metsulfuron-methyl are removed from crops by blending it with acetonitrile. After blending, the extract is filtered, reduced in volume, and partitioned with hexane to remove oils. The partially cleaned extract is then evaporated to dryness under reduced pressure, then dissolved in dichloromethane, and further cleaned up through a series of solid phase extraction columns in the following order: silica gel, Bond Elut™ ENV and polyamide 6S. The extract is evaporated to dryness and reconstituted either in 70:30 deionized water:acetonitrile for analysis by HPLC-MS/MS (positive electrospray ionization mode) or in 50:50 deionized water:acetonitrile for analysis by HPLC-UV.

The limit of quantitation (LOQ) is 0.025 ppm in grain; 0.05 in forage and fodder. For matrices other than grain, MS/MS is more reliable and is the preferred technique. A successful independent laboratory validation (ILV) [BYR00R001] was conducted for Method No. BY/02/99 (LC-MS only).

The method BY/02/99 is suitable for the determination of the total extractable residues of iodosulfuron-methyl-sodium and metsulfuron-methyl in corn.

2.3.4 Methods for residue analysis of food of animal origin

Maximum Residue Limits (MRLs) are not required for livestock commodities when no detectable residue is observed in feed items from crop field trials that reflect the proposed use of the pesticide (DIR98-02, *Chemistry Residue Guidelines*, Section 2). Therefore, no enforcement method was conducted for the analysis of food of animal origin.

3.0 Impact on human and animal health

3.1 Integrated toxicological summary

A detailed review of the toxicological database available for the TGAI iodosulfuron-methyl-sodium has been completed. The following data are requested as confirmatory data to complete the toxicology database:

(1) acute neurotoxicity to confirm clinical signs of neurotoxicity noted in the database;
(2) rabbit developmental toxicity study with adequate high dose;
(3) mouse oncogenicity study with adequate high dose; and
(4) 21–28 day repeat-dose dermal toxicity study.

In rats, iodosulfuron was rapidly and extensively absorbed, greater than 93, 79, and 70% of the orally administered single low- (10 mg/kg bw), repeat mid- (100 mg/kg bw) and single high-doses (500 mg/kg bw), respectively. Maximal plasma concentrations (Cmax) were achieved within 3.6–6.0 and 7.3–7.6 hours following single low- and single high-dose administration, respectively. A comparison of the area under the curve (AUC) following oral and intravenous low-dose administration indicates a calculated absorption rate or bioavailability of approximately 86 and 63% of the administered dose for males and females, respectively. No significant tissue accumulation was evident, i.e., less than 0.5% of the administered dose remaining in the tissue/carcass at sacrifice (72 hours after dosing). The major route of excretion was via the urine with the majority of the administered dose being eliminated within 24 hours, and was generally complete within 72 hours. Elimination was biphasic showing a fast initial elimination followed by a slower terminal phase. Following single low-dose administration, approximately 93.9–97.6 and 4.3–7.3% of the administered dose was recovered in the urine and feces, respectively. Following high-dose administration, urinary excretion was reduced to 69.1–71.5% of the administered dose in males and approximately 78.4–85.5% of the administered dose in females. Fecal excretion was increased slightly to approximately 24.5–26.5% of the administered dose in males and approximately 14.9–17.0% of the administered dose in females. Radioactivity was not detected in exhaled air following dosing. Absorption, plasma kinetics, distribution, and elimination in dogs were comparable to those in rats. The majority of the administered dose was excreted as the

unchanged parent compound, accounting for approximately 48.7–86.3 and 1.1–11.1% of the administered dose in the urine and feces, respectively. Metabolites were identified as AE F145740 (approximately 0.9–4.5% of the administered dose), AE F148741 (approximately 1.5–8.2% of the administered dose) and AE F168532 (approximately 0.3–6.6% of the administered dose). Each of these metabolites were present in both the urine and feces. Unidentified metabolites were also isolated in the feces (approximately 0.6–1.2% of the administered dose). All other metabolites were each present at less than 0.6% of the administered dose. There was no significant difference in the metabolic profiles between sexes or dose levels, nor following repeated dosing in the rat or between the rat and the dog.

Iodosulfuron-methyl-sodium technical herbicide has low acute toxicity by the oral, dermal, and inhalation routes of exposure; it is moderately irritating to the eyes, minimally irritating to the skin, and is not considered to be a skin sensitizer. The metabolites of iodosulfuron-methyl-sodium tested have low acute toxicity by the oral and dermal routes of exposure. The formulation, Tribute™ Solo 32DF Herbicide, has low acute toxicity by the oral, dermal and inhalation routes of exposure; it is mildly irritating to the eyes, moderately irritating to the skin, and is considered to be a potential skin sensitizer. The formulants were on the USEPA Lists 3, 4A, or 4B, and were of no toxicological concern.

Iodosulfuron-methyl-sodium was tested in a battery of in vitro (bacterial and mammalian cell gene mutation assays, unscheduled DNA synthesis assay as well as mammalian cell chromosomal aberration assay) and in vivo (mouse micronucleus assay) mutagenicity studies. There was no evidence of genotoxicity potential in any of these assays; therefore, the weight of evidence suggests that iodosulfuron-methyl-sodium was not genotoxic under the conditions of the tests performed.

The subchronic and chronic toxicity of iodosulfuron-methyl-sodium was investigated in the mouse, rat, and dog. No repeat-dose dermal toxicity study was available.

In mice, treatment-related findings were noted in the liver in the 90-day and 80-week dietary studies. Increased liver weights, centrilobular hepatocellular hypertrophy, and centrilobular fat deposition were noted at 2100 and 7000 ppm in the 90-day dietary study and at 1750 ppm in the 80-week dietary study. In the 90-day dietary study, the hypertrophied cells exhibited lipofuscin deposition, possibly due to a degradation of the subcellular organelles in the cytoplasm. An increased incidence of focal necrosis was also noted at 7000 ppm in the 90-day dietary study. Centrilobular mononuclear infiltration and pigmentation of the centrilobular hepatocytes, possibly due to lipofuscin deposition, were also noted at 1750 ppm in the 80-week dietary study. In the 90-day dietary study, lower body weight (bw) and body-weight gains (bwg) were noted in males at 7000 ppm. The no-observed adverse effect level (NOAEL) for the 90-day dietary study was 700 ppm (equal to 119 mg/kg bw/d) for males and 2100 ppm (equal to 401 mg/kg bw/d) for females. The NOAEL for the 80-week dietary study was 350 ppm (equal to 54.2 and 57.6 mg/kg bw/d for males and females, respectively).

In rats, treatment-related findings were limited to lower bw and bwg in the 90-day and 2-year dietary studies. Lower bw and bwgs were noted at 5000 and 10 000 ppm (approximately 10–15 and 15–20%, respectively) in the 90-day dietary study and at 7000 ppm (approximately 25–33%) in the 2-year dietary study. Elevated alanine aminotransferase (ALAT) activity (approximately 11%) and slight centrilobular hepatocyte enlargement were noted in males at 10 000 ppm in the 90-day dietary study; however, in the absence of correlating findings in other liver function markers or changes in liver weight, these findings were considered to be an adaptive response and not treatment-related. The NOAEL for the 90-day dietary study was 1000 ppm (equal to 67 and 74 mg/kg bw/d for males and females, respectively). The NOAEL for the 2-year dietary study was 700 ppm (equal to 29.7 and 39.1 mg/kg bw/d for males and females, respectively).

Dogs appear to be the most sensitive species tested. Dietary concentrations of 1200 and above caused dose-dependent hematological and histopathological findings indicative of anaemia in the 90-day and 1-year dietary studies. Hematological findings were generally characterized by lower red blood cell (RBC) count, hemoglobin (HGB), and hematocrit (HCT) at 1200 ppm and above. At 7200 ppm, the decreased RBC parameters were noted throughout treatment with the decrease gradually developing and becoming more severe as treatment progressed. Peripheral anaemia appeared to develop gradually, probably by natural turnover of erythrocytes since there was no evidence of hemolytic processes or hemorrhaging. Examination of the bone marrow smears revealed decreased late normoblasts at 1200 ppm and above, decreased erythroblasts at 7200 ppm, and increased myeloid to erythroid ratio (M:E) at 7200 ppm. Histopathological findings were characterized by severe generalized hematopoietic hyperplasia in the bone marrow at 1200 ppm and above, and extramedullary hematopoiesis in the spleen and liver at 7200 ppm. Hematopoietic hyperplasia was evident in sections of the stifle joint in which the epiphyseal medullary cavities of the femur and tibia were filled with cells of the myeloid and erythroid series as well as developing megakaryocytes. This correlated with increased incidences of juvenile forms of both the myeloid and erythroid series as indicated by an increase in the number of immature granulocytes present, a reduction in the number of erythroblasts present and an increase in the M:E ratio noted at 7200 ppm. There was no clinical chemistry or histopathological finding to indicate peripheral blood loss via hemolysis or hemorrhaging to account for the hematological and histopathological findings indicative of anemia; this suggests that these findings may be due to interference of the test substance with cell maturation in the hematopoietic tissue. In the 90-day dietary study, increased ALAT and aspartate aminotransferase (ASAT) activity, and increased liver weights were noted at 1200 and 7200 ppm; however, there was no correlating histopathological finding in the liver. Increased creatine phosphokinase (CPK) activity was also noted at 1200 ppm and above in the 90-day dietary study. At 7200 ppm, the increased creatine phosphatase kinase activity correlated with lower creatinine levels and may be due to muscle loss/injury. This would

also correlate with lower bw, bwg, and food efficiency noted at 7200 ppm. Other treatment-related findings noted at 7200 ppm in the 90-day dietary study included the following:

- unsteady gait,
- hunched posture and prostration,
- increased liver, spleen and kidney weights,
- pigmentation of the Kupffer cells and slight centrilobular congestion in the liver,
- subscapular tubular necrosis with cyst formation,
- interstitial nephritis and hyaline droplets in the kidney and
- atrophy of the lymphoid tissue in the spleen.

The NOAEL for the 90-day dietary study was 200 ppm (equal to 8.1 and 8.4 mg/kg bw/d for males and females, respectively). The NOAEL for the 1-year dietary study was 1200 ppm (equal to 41.8 mg/kg bw/d) for males and 200 ppm (equal to 7.3 mg/kg bw/d) for females.

In the 80-week dietary study, there was no evidence to indicate that iodosulfuron-methyl-sodium was oncogenic in mice at dose levels up to and including 1750 ppm (the highest dose tested [HDT]); however, the maximum tolerated dose (MTD) was not achieved in this study. Therefore, the dose levels were considered to be inadequate for evaluation of carcinogenicity in the mouse. In the rat 2-year dietary study there was no evidence to indicate that iodosulfuron-methyl-sodium was oncogenic in rats at dose levels up to and including 7000 ppm, the HDT. Dosing was considered to be adequate, based on decreased bw and bwgs (greater than 10%). Iodosulfuron-methyl-sodium was negative for mutagenicity in various in vitro and in vivo assays. Furthermore, registered sulfonyl urea compounds (structurally similar compounds) have been found to be non-carcinogenic. The weight of evidence suggests that iodosulfuron-methyl-sodium is not carcinogenic in mice or rats; however, with regard to its potential as a human carcinogen it is not classifiable, based on inadequate dosing in the mouse oncogenicity study.

There was no evidence in the toxicology database to suggest a significant increase in toxicity with increased duration of exposure in mouse, rat, or dog, or to indicate a significant difference in gender sensitivity.

In the rat 2-generation reproduction (one litter per generation) study, reproduction function, reproductive parameters, and litter parameters were not influenced by treatment in the first and second parental generations (P_1 and P_2) at dose levels up to and including 5000 ppm (equal to 346 and 390 mg/kg bw/d in males and females, respectively), the HDT. In addition, there was no treatment-related systemic finding in the P_1/P_2 animals. In the offspring, decreased pup survival and mean litter size were noted in the second-generation offspring (F_2) pups on lactation days 0 and 4. There was no treatment-related finding in the F_1 pups. The NOAEL for parental toxicity was 5000 ppm (equal to 346 and 390 mg/kg bw/d in males and females, respectively). The NOAEL for offspring toxicity was 500 ppm (equal to 34.2 and 39.7 mg/kg bw/d in males and females, respectively).

On the basis of the parental and offspring NOAELs, neonates appear to be both qualitatively and quantitatively more sensitive than adults to the toxic effects of iodosulfuron-methyl-sodium.

In the rat developmental toxicity study, increased salivation was noted in the dams at 1000 mg/kg bw/d throughout treatment (gestation days 8–17). This may suggest a neurotoxicity potential; however, data to confirm this were not provided. In the fetuses, increased incidence of weakly or non-ossification of sacral vertebral arch, individual skull bones, sternebrae, metacarpal 5 in the forepaw and phalanx III of the 1st to 5th toes were noted at 1000 mg/kg bw/d. These findings were generally within the historical control range; however, when considered collectively, they may indicate delayed skeletal development at this dose level. The NOAEL for maternal and developmental toxicity was 315 mg/kg bw/d. In the rabbit developmental toxicity study, there was no adverse treatment-related maternal or developmental finding at dose levels up to and including 400 mg/kg bw/d, the HDT. The NOAEL for maternal and developmental toxicity was 400 mg/kg bw/d. On the basis of the maternal and developmental NOAELs noted in the rat developmental toxicity study, there was no quantitative evidence to indicate an increased susceptibility of the fetus to in utero exposure to iodosulfuron; however, based on the severity of the findings noted at the respective NOAELs, there appears to be an increased qualitative susceptibility of the fetus to in utero exposure to iodosulfuron-methyl-sodium. In the rabbit, susceptibility of the fetus to in utero exposure could not be assessed since the dose levels tested were inadequate for assessing developmental toxicity; however, the rat appears to be more sensitive. In the rat, there was no evidence of any treatment-related irreversible structural change; therefore, iodosulfuron-methyl-sodium was not considered to be teratogenic in rats. In the rabbit, there was no evidence of any treatment-related irreversible structural change; however, the dose levels were inadequate for evaluation of teratogenicity.

In the rat, clinical signs suggest a neurotoxic potential, including squatting posture, ataxic and uncoordinated gait, increased salivation, and prone position, following acute exposure at dose levels of 2000 mg/kg bw and above. In the dog, effects suggestive of a neurotoxic potential, including unsteady gait, hunched posture, and prostration, were noted at 7200 ppm (301 and 317 mg/kg bw/d for males and females, respectively) in the 90-day dietary study. In the rat developmental toxicity study, increased salivation was noted in the dams throughout treatment (gestation days 8–17) at 1000 mg/kg bw/d, which may suggest a neurotoxic potential. There was no treatment-related change in brain weight nor histopathological finding in the nervous system in mice, rats, or dogs following subchronic or chronic dietary exposure or abnormalities in the development of the fetal nervous system in rats or rabbits to suggest a developmental neurotoxicity potential.

3.2 Determination of acceptable daily intake

The recommended acceptable daily intake (ADI) is 0.024 mg/kg bw/d, as calculated in the following equation:

$$ADI = \frac{NOAEL}{SF} = \frac{7.3 \text{ mg/kg bw/d}}{300} = 0.024 \text{ mg/kg bw/d}$$

The most appropriate NOAEL recommended to calculate the ADI is 7.3 mg/kg bw/d as determined in the 1-year dog dietary study. Treatment-related findings at the LOAEL (43.7 mg/kg bw/d) included gross and histopathological changes to the hematopoietic system. A safety factor (SF) of 300-fold is recommended – 100-fold to account for intra- and inter-species variations as well as an additional three-fold to account for the following:

- the inadequate mouse oncogenicity study and rabbit developmental toxicity study,
- increased qualitative susceptibility of the fetus to in utero exposure as indicated by delayed ossification in the fetus at a dose level that exhibited minimal maternal toxicity (increased salivation) in the rat developmental toxicity study, and
- increased quantitative and qualitative susceptibility of the neonate as indicated by decreased pup viability in the F_2 pups on lactation days 0 and 4 in the absence of maternal toxicity in the rat 2-generation reproduction study.

Margins of Exposure (MOEs) for other critical end point(s), calculated as NOAEL ÷ ADI, are as follows:

- The MOE for developmental toxicity is 13 125 – The rabbit developmental toxicity study was considered to be inadequate; however, based on the NOAELs for developmental toxicity, the rat appears to be more sensitive. Therefore, the most appropriate NOAEL for developmental toxicity is 315 mg/kg bw/d, based on delayed skeletal development at the LOAEL of 1000 mg/kg bw/d (next-highest dose), in the rat developmental toxicity study.
- The MOE for offspring toxicity is 1425 – The most appropriate NOAEL for offspring toxicity is 34.2 mg/kg bw/d, based on decreased pup survival and mean litter size in the F_2 pups on lactation days 0 and 4 in the absence of any maternal toxicity at the LOAEL of 346 mg/kg bw/d, in the rat 2-generation reproduction study.
- The MOE for reproductive toxicity is 14 416 – The most appropriate NOAEL for reproductive toxicity is 346 mg/kg bw/d (HDT), based on absence of any adverse treatment-related effect at this dose level in the rat 2-generation reproduction study.

3.3 Acute reference dose

An acute reference dose (ARfD) was not established since iodosulfuron-methyl-sodium was considered unlikely to present an acute hazard. There was no significant treatment-related findings in the acute, short-term, 2-generation reproduction, or developmental toxicity studies to indicate a concern in acute dietary risk assessment.

3.4 Toxicological end point selection: occupational and bystander risk assessment

Iodosulfuron-methyl-sodium technical herbicide has a low acute toxicity by the oral, dermal and inhalation routes of exposure; it is moderately irritating to the eyes, minimally irritating to the skin, and is not a potential skin sensitizer. The formulation, Tribute™ Solo 32DF Herbicide, also has low acute toxicity by the oral, dermal, and inhalation routes of exposure; however, it is mildly irritating to the eyes, moderately irritating to the skin, and is a potential skin sensitizer.

Iodosulfuron was rapidly and extensively absorbed, greater than 93, 79, and 70% of the orally administered single low- (10 mg/kg bw), repeat mid- (100 mg/kg bw), and high-doses (500 mg/kg bw), respectively. Maximal plasma concentrations (Cmax) were achieved within 6.0 and 7.6 hours following single low- and high-dose administration, respectively. No significant tissue accumulation was evident; less than 0.5% of the administered dose remained in the tissue/carcass at sacrifice (72 hours after dosing). The major route of excretion was via the urine with the majority being eliminated within 24 hours, and was generally complete within 72 hours. The majority was excreted as the unchanged parent compound, accounting for up to 86 and 11% of the administered dose in the urine and feces, respectively.

The subchronic and chronic toxicity of iodosulfuron-methyl-sodium was investigated in the mouse, rat, and dog. In mice, treatment-related findings were noted in the liver. The NOAEL for the 90-day dietary study was 119 mg/kg bw/d. The NOAEL for the 80-week dietary study was 54.2 mg/kg bw/d. In rats, treatment-related findings were limited to lower bw and bwg. The NOAEL for the 90-day dietary study was 67 mg/kg bw/d. The NOAEL for the 2-year dietary study was 29.7 mg/kg bw/d. Dogs appear to be the most sensitive species as indicated by hematological and histopathological findings indicative of anaemia noted at dose levels exhibiting minimal or no toxicity in mice or rats. Hematological findings were generally characterized by lower RBC count, HGB, and HCT. Histopathological findings were characterized by severe generalized hematopoietic hyperplasia in the bone marrow and extramedullary hematopoiesis in the spleen and liver. The decreased RBC parameters were noted throughout treatment with the decrease gradually developing and becoming more severe as treatment progressed. Examination of the bone marrow smears revealed decreased late normoblasts, decreased erythroblasts, and increased M:E ratio. The NOAEL for the 90-day dietary study was 8.1 mg/kg bw/d. The NOAEL for the 1-year dietary study was 7.3 mg/kg bw/d.

In mice, there was no evidence to indicate that iodosulfuron-methyl-sodium was oncogenic; however, the MTD was not achieved in the 80-week dietary study. In the rat 2-year dietary study, there was no evidence to indicate that iodosulfuron-methyl-sodium was oncogenic in rats. Iodosulfuron-methyl-sodium was negative for mutagenicity in various in vitro and in vivo assays. The weight of evidence suggests that iodosulfuron-methyl-sodium is not carcinogenic in mice or rats; however, with regard to its potential as a human carcinogen, it is not classifiable, based on inadequate dosing in the mouse oncogenicity study. There was no evidence in the toxicology database to suggest a significant increase in toxicity with increased duration of exposure in mouse, rat, or dog, nor to indicate a significant difference in gender sensitivity.

On the basis of the parental and offspring NOAELs in the rat 2-generation reproduction study, neonates appear to be both qualitatively and quantitatively more sensitive to exposure to iodosulfuron-methyl-sodium. Reproduction function, reproductive parameters, and litter parameters were not influenced by treatment. On the basis of the maternal and developmental NOAELs rat developmental toxicity study, there was no quantitative evidence to indicate an increased susceptibility of the fetus to in utero exposure to iodosulfuron; however, based on the severity of the findings noted at the respective NOAELs, there appears to be an increased qualitative susceptibility of the fetus to in utero exposure to iodosulfuron-methyl-sodium. In the rabbit, susceptibility of the fetus to in utero exposure could not be assessed since the dose levels tested were inadequate for assessing developmental toxicity; however, the rat appears to be more sensitive. In the rat, iodosulfuron-methyl-sodium was not considered to be teratogenic. In the rabbit, the dose levels were inadequate for evaluation of teratogenicity.

In rats and dogs, clinical signs suggesting a neurotoxic potential were noted. There was no treatment-related change in brain weight, nor histopathological finding in the nervous system in mice, rats, or dogs following subchronic or chronic dietary exposure, nor abnormality in the development of the fetal nervous system in rats or rabbits, to suggest a developmental neurotoxicity potential.

Occupational exposure is characterized as short-term and is predominantly by the dermal route. There was no 21/28-day repeat-dose dermal toxicity study available; however, to account for the treatment-related hematological and histopathological findings indicative of anaemia noted in dogs following 90-day and 1-year dietary administration, it is recommended that the 1-year dietary study in dogs be used for all proposed exposure scenarios. The recommended NOAEL is 7.3 mg/kg bw/d. A MOE of 300 is recommended, based on 100 to account for intra- and inter-species difference and an additional 3 to account for the inadequate mouse oncogenicity study and rabbit developmental toxicity study, increased qualitative susceptibility of the fetus to in utero exposure in the rat developmental toxicity study, and increased quantitative and qualitative susceptibility of the neonate in the rat 2-generation reproduction study.

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

3.5.1 Operator exposure assessment

Tribute™ Solo 32DF Herbicide is formulated as a wettable granule with a guarantee of 2% iodosulfuron-methyl-sodium, the active ingredient (a.i.). Tribute™ Solo 32DF Herbicide also contains the active ingredient foramsulfuron and the safener isoxadifen-methyl sodium.

Tribute™ Solo 32DF Herbicide is proposed for use on field corn as a post-emergence herbicide and would be applied by ground equipment. The proposed label for the EP calls for one application per season. Custom applicators or farmers could apply this product to field corn: custom applicators typically treat 140 ha/day and farmers typically treat 80 ha/day. The proposed maximum application rate for Tribute™ Solo 32DF Herbicide is 2 g of iodosulfuron-methyl-sodium per hectare. The EP, however, may be mixed with the Hasten spray additive at a rate of 1.75 L/ha.

From the proposed-use pattern, it is expected that farmers would be exposed one day per season and that custom applicators would be exposed up to 30 days per season (short-term exposure).

The proposed label for Tribute™ Solo 32DF Herbicide specifies that protective clothing, including goggles and chemical-resistant gloves, be worn when handling or mixing the products and that chemical-resistant gloves be worn while cleaning and repairing spray equipment. It also specifies a proposed re-entry interval of 12 hours and that, if workers enter fields within the 12-hour re-entry interval, they should wear long-sleeved shirts, long pants, protective eyewear, boots and chemical-resistant gloves.

Dermal absorption

A chemical-specific in vivo dermal absorption study entitled *(^{14}C)-AE F115008: Dermal Absorption in the Rat* was submitted. Sprague-Dawley (Crl:CD BR) rats were treated with (^{14}C)-AE F115008 (iodosulfuron-methyl-sodium) at nominal doses of 24 µg/cm^2 and 400 µg/cm^2 (20 animals/dose group). Rats were sacrificed at 3, 5, 8, 72 and 120 h (4 animals/sacrifice group/dose group). Skin washes took place before the animal was sacrificed, except for the 72- and 120-h sacrifice groups where a skin wash had taken place at 8 h. Urine, feces, cage wash, cage debris, carcass, skin, application site and adjacent areas, skin wash, and dressings were analysed for radioactivity. Recovery of the applied dose was acceptable and ranged from 96 to 108%.

One limitation in the study was the consistent high recovery of the administered dose in the dressings for both dose levels and all sacrifice groups (range of 17.17–29.93%). The amount of the administered dose retained by the protective dressings is not considered available for absorption. Therefore, the percentage of dermal absorption was recalculated based on the percentage of the dose available for absorption.

A dermal absorption value of 21% was established from the chemical-specific study. This value is based on the results obtained from the low-dose group at an exposure period of 8 h. This estimate is considered conservative since 15.42% of the applied dose is retained in the skin and is not considered likely to become systemically available in total.

Exposure assessment

The Pesticide Handlers Exposure Database (PHED) Version 1.1 assessments were conducted to derive estimates of occupational exposure for mixers, loaders and applicators (M/L/A). The data were based on high confidence PHED runs, adequate numbers of replicates, and A + B grade data. The generated PHED estimates conform with North American Free Trade Agreement (NAFTA) Guidelines for using and reporting PHED data, which neither provide exposure estimates for clean-up and repair activities, nor do they quantify the variability of exposure estimates. Exposure via the inhalation route was a minor component of overall exposure. Total systemic exposure was determined by summing dermal deposition estimates (adjusted for dermal absorption) and inhalation estimates.

Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e., summing the measure of central tendency for each body part most appropriate to the distribution of data for that body part. Exposure estimates were derived for individuals wearing a single layer of clothing (long-sleeved shirt and long pants) and gloves, with the exception of the ground boom applicator, for whom exposure was estimated without gloves (insufficient gloved replicates). Exposure estimates and margins of exposure (MOEs) derived for mixer/loader/applicators are presented in Table 3.5.1. These MOEs are acceptable.

Table 3.5.1 Exposure estimates and resulting MOEs for M/L/A

Occupational Scenario	Exposure [a] (mg/kg bw/day)	MOE (based on a NOAEL of 7.3 mg/kg bw/day [b])
Mixers/loaders + groundboom applicators (farmer)	9.9×10^{-5}	> 70 000
Mixers/loaders + groundboom applicators (custom)	1.7×10^{-4}	> 40 000

[a] Based on mixers/loaders wearing a single layer and gloves and groundboom applicators wearing a single layer and no gloves. Exposure refers to total systemic exposure and was determined by summing dermal deposition estimates (adjusted for 21% dermal absorption) and inhalation estimates.

[b] Based on the 12-month dietary dog study.

3.5.2 Bystanders

For the proposed agricultural use scenario, bystander exposure during and after application was considered minimal compared to M/L/A and re-entry worker scenarios and, therefore, not quantified.

3.5.3 Workers

There is potential for short-term exposure to workers scouting or irrigating field corn treated with Tribute™ Solo 32DF Herbicide. Since the proposed product is to be applied at the 1–8 leaf stage of field corn, no other post-application activity is expected to coincide with application. The applicant did not submit chemical-specific data to address potential post-application exposure; therefore, a Tier 1 exposure assessment for workers was conducted using standard default assumptions. These standard defaults include an assumption that 20% of the application rate is dislodgeable and available for potential exposure on the day of application and workers spend eight hours per day scouting or irrigating treated field corn. Since the applicant is a member of the Agricultural Reentry Task Force (ARTF), the ARTF transfer coefficient for scouting and irrigation of corn plants of 1000 cm^2/hr was used for risk assessment purposes. Based on an exposure estimate of 9.6×10^{-5} mg/kg bw/day on the day of application and a NOAEL of 7.3 mg/kg bw/day from the 12-month dietary dog study, an acceptable MOE of >75 000 was obtained.

4.0 Residues

4.1 Residue summary

Nature of the residue in plants

Wheat plants at the tillering stage were treated with [^{14}C] iodosulfuron-methyl-sodium (triazinyl or phenyl label) at 20 g a.i./ha (10-fold) with the safener, mefenpyr-diethyl, in a 1:3 ratio. Mefenpyr-diethyl, however, was not the proposed safener with Tribute™ Solo 32DF. Samples of forage (0.1365–0.2487 ppm equivalents), hay (0.1292–0.1654 ppm equivalents), straw (0.2001–0.3698 ppm equivalents), and grain (0.0056–0.0109 ppm equivalents) were harvested and analysed. In wheat, metabolism of iodosulfuron-methyl-sodium proceeds via dehalogenation or demethylation followed by conjugation or ring separation. Iodosulfuron-methyl-sodium was a major residue component in forage, hay, and straw (13–68% of the total radioactive residues [TRRs] or 0.0484–0.0928 ppm). Metsulfuron-methyl (<1–2.9% of the TRRs or 0.0008–0.0476 ppm) and AE F145741 (3–15% of the TRRs or 0.0003–0.0251 ppm) were also detected in forage, hay, and straw. Residues in grain were minimal with iodosulfuron-methyl-sodium, metsulfuron-methyl, and AE F145741 detected at less than 4% of the TRRs (<0.004 ppm). The triazine metabolite AE 0031838 was detected in foliage matrices at 6–14% of the TRRs (0.0153–0.0432 ppm), and at 15% of the TRRs in grain (0.0016 ppm). The metabolite AE F059411 was detected in 20% of the TRRs in grain (0.0022 ppm). Metabolites containing only the phenyl ring were not detected in the [^{14}C-phenyl] labelled study. Therefore, the parent alone is the residue of concern (ROC) to be used in the risk assessment and expression of the maximum residue limit (MRL).

Confined rotational crops
Radiolabelled iodosulfuron-methyl-sodium was applied to bare soil in Germany at 20 g a.i./ha (10-fold). Wheat, spinach, and carrots were sown at 29, 120, and 365 days after treatment (DAT). Wheat was the only crop that developed normally at all treatment intervals. TRRs above 0.01 ppm were only observed in wheat straw at 29 DAT (0.52 ppm equivalents); 120 DAT (0.15 ppm equivalents) and 365 DAT (0.244 ppm equivalents) as well as at 365 DAT (0.055 ppm equivalents) in carrot foliage. The predominant residue identified in wheat straw at 29 DAT was AE F059411 (13.2% of the TRRs; 0.07 ppm). The only identified metabolites at 120 and 365 DAT were AE 0031838 (7.2–10.8% of the TRRs; 0.01–0.03 ppm) and AE F059411 (11.5–14.3% of the TRRs; 0.04 ppm). Iodosulfuron-methyl-sodium only appeared in wheat straw samples at 29 DAT. In the United States (U.S.), samples of soybeans (planted at either 7 or 14 DAT), and sugar beet (planted at 60 DAT) grown in bare soil treated at 5 g a.i./ha (approximately three-fold), and wheat (planted at 65 DAT) from soil treated at 8 g a.i./ha (four-fold), all had TRRs less than 0.01 ppm. Therefore, no detectable level of iodosulfuron-methyl-sodium is likely to occur in rotated crops under normal agricultural conditions, and thus the proposed rotational crop restrictions are adequate.

Field accumulation in rotational crops
Data were not submitted with the iodosulfuron-methyl-sodium petition for a field accumulation study in rotational crops, since residues in crops from the confined study were all less than the LOQ (DIR98-02, *Residue Chemistry Guidelines*, Section 14).

Nature of the residue in animals
Dairy cattle—in a dairy cow fed 14.23 ppm of [^{14}C] iodosulfuron-methyl-sodium in the diet for seven consecutive days, approximately 71% and 21% of the administered dose was excreted in urine and feces, respectively. Residue levels in milk reached a maximum concentration of 0.017 ppm equivalents at 103 hours post-dosage. The highest residues were seen in the kidney (0.1 ppm) and liver (0.061 ppm). Residues were lower in the renal fat (0.022 ppm), heart (0.008 ppm), subcutaneous fat (0.008 ppm), omental fat (0.007 ppm) and muscle (0.002–0.004 ppm). Iodosulfuron-methyl-sodium was the predominant residue in milk, liver, kidney, and fat (10 to 26% of the TRRs). Metsulfuron-methyl was found in kidney at 10% of the TRRs and in omental fat at 2% of the TRRs. Metabolites containing only the phenyl ring (AE F114368 and AE F143133) were identified in kidney (<1% of the TRRs). Minor amounts of oxidized, dehalogenated, hydroxylated, or de-methylated metabolites were present in the milk, kidney, fat, and liver.

Hens—when six laying hens were fed 10 ppm of [^{14}C-phenyl] iodosulfuron-methyl-sodium in the diet for 14 consecutive days, approximately 92% of the administered dose was excreted in the urine and feces. The highest residues were in the liver (0.029 ppm) and skin (0.014 ppm), followed by muscle (0.005 ppm) and subcutaneous fat (0.005 ppm). The TRRs reached a maximum concentration in egg whites (0.020 ppm) and in egg yolks (0.022 ppm) on days 2 and 10, respectively. Iodosulfuron-methyl-sodium was the predominant residue in egg yolks, egg whites, liver, and skin (11 to 33% of

the TRRs). AE F145741 was detected in egg whites at 13% of the TRRs and was also a minor metabolite in egg yolks, liver, and skin (<6% of the TRRs). Metabolites containing only the phenyl ring (AE F114368, AE F143628, and AE F143133) were found in eggs and liver (<8% of the TRRs). Insoluble residues accounted for 22 to 51% of the TRRs (<0.01 ppm) in eggs, liver, and skin.

The proposed metabolic pathway in animals is the 0-demethylation of iodosulfuron-methyl-sodium to AE F145741 or via hydroxylation to form AE F168532. Both AE F145741 and AE F168532 can lose the triazinyl group to form AE C627337/ AE F143628, which is hydrolysed to form AE F114368. This is in turn cyclised to AE F143133. AE F145741 can also be dehalogenated to produce AE F161778. Furthermore, in the cow, iodosulfuron-methyl-sodium can be deiodinated to form AE F075736 or demethylated to AE F145740. Therefore, the parent alone is the ROC to be used in the risk assessment and expression of the MRL.

Analytical methodology in plant and animal matrices
Both the data gathering method (HPLC-UV or HPLC-MS) and the enforcement method (HPLC-MS) are adequate to quantitate residues of iodosulfuron-methyl-sodium (AE F115008) and the metabolite metsulfuron-methyl (AE F075736) on corn grain, forage and fodder. The data-gathering method HPLC-MS has been successfully validated for iodosulfuron-methyl-sodium on corn grain and fodder. As MRLs are not required for livestock commodities, a livestock enforcement method is unnecessary at this time.

Storage stability
The submitted storage stability data are adequate and indicate that residues of iodosulfuron-methyl-sodium are stable in wheat grain (24 months), forage (26 months) and straw (28 months), stored at –18°C. Therefore, the storage stability of iodosulfuron-methyl-sodium in corn matrices can be inferred from the stability of the residues in wheat commodities.

Supervised residue trials
Twenty-one field corn trials were conducted in zones 1 (two trials), 2 (one trial), 5 (sixteen trials) and 6 (two trials) in the U.S.; however, field corn trials were not conducted in Zone 5B in Canada. In all zones examined, residues in field corn were less than the LOQ when treated at approximately four to five times the maximum recommended use rate. Consequently, it is unlikely that additional Canadian trials would provide any new information. Two sequential applications of iodosulfuron-methyl-sodium were made to field corn at 4.7–6.8 g a.i./ha (first application) and 2.3–2.6 g a.i./ha (second application), for total application rates of 7.2–9.3 g a.i./ha (three-fold to five-fold). Residues of iodosulfuron-methyl-sodium and metsulfuron-methyl were less than the reported LOQs of 0.025 ppm in corn grain, and 0.05 ppm in corn forage and stover. Therefore, the proposed MRL of 0.025 ppm on field corn grain is adequate.

Processing studies
The data indicate that residues of iodosulfuron-methyl-sodium and metsulfuron-methyl were below the respective method LOQs (< 0.025 ppm) in or on samples of the raw agricultural commodity (RAC), field corn grain. Therefore, no concentration factor was estimated.

Meat/Milk/Poultry/Eggs
Based on data from the ruminant and poultry metabolism studies, in which a cow and six hens were dosed at levels greater than the maximum theoretical dietary burden (MTDB) of 0.08 ppm and 0.02 ppm, respectively, there is no reasonable expectation that finite residues of iodosulfuron-methyl-sodium will occur in livestock commodities (DIR98-02, *Residue Chemistry Guidelines*, Section 2). Therefore, livestock feeding studies and MRLs for livestock commodities are not required at this time.

Dietary risk assessment
The proposed use of iodosulfuron-methyl-sodium (Tribute™ Solo 32DF Herbicide) on corn does not pose an unacceptable chronic dietary (both food and water) risk to any segment of the population, including infants, children, adults and seniors.

5.0 Fate and behaviour in the environment

5.1 Physical and chemical properties relevant to the environment

Physical and chemical properties relevant to the environment are presented for iodosulfuron-methyl-sodium in Appendix I, Table 7. The information presented was based on the results of the chemistry review by the Laboratory Services.

Iodosulfuron-methyl-sodium is soluble to very soluble in water over the range of pH 4 (0.02 g/L) to pH 9 (65 g/L), and the dissociation constant (pK_a) is 3.22 ± 0.06. Since these values indicate a potential for iodosulfuron-methyl-sodium to be mobile in soil, there is potential for leaching.

The vapour pressure of iodosulfuron-methyl-sodium was determined to be 2.6×10^{-9} Pa (20°C) and Henry's Law constant was 1.082×10^{14} (20°C). These values indicate that iodosulfuron-methyl-sodium is not likely to volatilize under field conditions from water or moist soil surfaces.

The log K_{ow} values were 1.96, 1.07, 0.07, −0.70, and −1.22 at pH 4, pH 5, pH 6, pH 7, and pH 9, respectively, indicating that there is a low potential for iodosulfuron-methyl-sodium to bioaccumulate.

The UV–visible absorption spectrum maximum of iodosulfuron-methyl-sodium is 239 nm and no absorption was observed at λ300–800 nm, indicating that iodosulfuron-methyl-sodium is not likely to undergo phototransformation in the environment.

5.2 Abiotic transformation

Using the Arrhenius equation, first-order hydrolytic half-lives at 25°C were estimated to be 2.5 days (pH 4), 18.4 days (pH 5), 197 days (pH 6), >365 days (pH 7), and 167 days (pH 9). The major transformation products detected were AE F149760, AE F114368 and AE F145741 (20–40°C), and AE F143133 (50–60°C). Hydrolysis of iodosulfuron-methyl-sodium was pH-dependent, with stability increasing with increasing pH. Hydrolysis is an important route of transformation for iodosulfuron-methyl-sodium under acidic conditions; however, under neutral to basic conditions, it is not.

The first-order phototransformation half-life of iodosulfuron-methyl-sodium on soil was 9.1 days (under test conditions of 12 hours light and 12 hours dark). One major transformation product detected was AE 0002166.

Phototransformation of iodosulfuron-methyl-sodium in aqueous solution occurred with first-order half-lives of 215–245 hours (equivalent to 9–10.2 days) of continuous irradiation. One major transformation product detected as AE 0002166.

Therefore, there is low potential for phototransformation of iodosulfuron-methyl-sodium in water and on soil.

5.3 Biotransformation

Iodosulfuron-methyl-sodium was non-persistent (first-order half-lives were 0.8–3.3 days) under aerobic soil conditions at a moisture content of 30% and 50% of the soil's maximum water holding capacity (MWHC). However, in dryer soils (25% MWHC) or soils tested at 10°C, the half-lives were 10–21.8 days, indicating that under these soil conditions, iodosulfuron-methyl-sodium is non-persistent to slightly persistent. The major transformation products detected included metsulfuron-methyl (AE F075736), AE F059411, AE F161778, and three unidentified compounds (M2, U1, and U2). The sulfonylurea bridge was preserved in all of the transformation products. Minor transformation products included AE F145741, AE F145740, AE 0000119, AE F161778, and the unidentified compounds U1, U2, and U4. Using the multi-compartment program TopFit 2, half-lives for the transformation products were estimated to be as follows:

- 20–99 days for metsulfuron-methyl (slightly to moderately persistent)
- 9.4–21.1 days for AE F161778 (non-persistent to slightly persistent) and
- 119–269 days for AE F059411 (moderately persistent to persistent).

Iodosulfuron-methyl-sodium was non-persistent to slightly persistent in aerobic water/sediment studies with first-order half-lives in the whole system ranging from 13.5 days to 23.3 days. The major transformation products included metsulfuron-methyl, AE F059411, AE 0000119, AE 0014966, and AE 0034855, while the minor transformation products were AE 0014965, AE F145740, and AE F161778. The sulfonylurea bridge was preserved in all the transformation products, with the exception

of AE 0000119. Up to day 150, the majority of radiolabelled residues (>50%) were recovered from the floodwater; however, after day 150, 29–46% of the residues were still detected in the water phase. Using the multi-compartment program TopFit 2, half-lives for the transformation products were estimated to be as follows:

- 34.4–55.2 days for metsulfuron-methyl
- 2.9–21.3 days for AE F161778
- 5.8–20.8 days for AE 0014966 and
- 87.6 days for AE F059411.

Thus, AE 0014966 is non-persistent to slightly persistent, and the persistence of each of the remaining transformation products was the same as reported in the aerobic soil biotransformation studies.

Iodosulfuron-methyl-sodium was non-persistent to slightly persistent in the anaerobic water/soil study with first-order half-lives of 14.3–28.1 days in the whole system. The only major transformation product detected was metsulfuron-methyl. The minor transformation products were AE 0014966, AE F059411, AE F161778, AE F145740, and AE F145741. The majority of radiolabelled residues (>72.7%) were recovered from the floodwater throughout the study. Using the multi-compartment program TopFit 2, the half-life for the transformation product metsulfuron-methyl was estimated to be 291 days in the whole system; thus, metsulfuron-methyl was persistent under anaerobic aquatic conditions.

All the studies indicated that iodosulfuron-methyl-sodium was fully transformed to bound residues and carbon dioxide.

5.4 Mobility

Based on the results from three adsorption/desorption studies, iodosulfuron-methyl-sodium and the transformation products, metsulfuron-methyl and AE F059411, do not adsorb strongly onto soil and can desorb readily. Therefore, iodosulfuron-methyl-sodium, metsulfuron-methyl, and AE F059411, are expected to be very mobile in soils, having the potential to leach or be transported to surface water by run-off and to predominantly partition into the water column. These results are supported by the biotransformation studies: the soil biotransformation study indicated that there was limited binding of the applied to the soil (<40% of radioactivity applied was soil-bound at study termination) and the aquatic biotransformation studies indicated that the majority of radiolabelled residues were recovered from the floodwater (>29–46% of applied throughout the duration of the studies).

Based on values for vapour pressure and Henry’s Law constant, data on the volatility of iodosulfuron-methyl-sodium are not required.

5.5 Dissipation and accumulation under field conditions

Laboratory biotransformation studies indicated that iodosulfuron-methyl-sodium is non-persistent (half-lives 0.8–3.3 days) under aerobic soil conditions with the formation of the major transformation products metsulfuron-methyl (slightly to moderately persistent), AE F059411 (moderately persistent to persistent), AE F161778 (non-persistent to slightly persistent), and three unidentified compounds (M2, U1, and U2). The Canadian field dissipation study (one Ontario site) reported a half-life for iodosulfuron-methyl-sodium of 4 days; thus, iodosulfuron-methyl-sodium would be classified as non-persistent in soil under field conditions. This was supported by the lack of residue carryover at the end of the study (98 days). The major transformation products detected in the field dissipation study were metsulfuron-methyl and AE F059411, which were below the level of detection at study termination (98 days). No residue was detected below the 0–7.5 cm soil depth for the parent compound or the transformation products. Although adsorption/desorption data indicated potential mobility of iodosulfuron-methyl-sodium residues, rapid transformation attenuated the potential for leaching under field conditions.

5.6 Bioaccumulation

The log K_{ow} (range of −1.22 to 1.96 at pH 9 and 4 respectively) indicated that there is a low potential for bioaccumulation of iodosulfuron-methyl-sodium; thus, a bioaccumulation study is not required. Studies were not submitted for review.

5.7 Summary of fate and behaviour in the terrestrial environment

The fate and behaviour of iodosulfuron-methyl-sodium in the terrestrial environment is outlined in Appendix I, Table 8. Laboratory studies of transformation in soil indicated that biotransformation is an important route of transformation for iodosulfuron-methyl-sodium, and that there is low potential for phototransformation on soil. Hydrolysis is not an important transformation route for iodosulfuron-methyl-sodium under neutral and basic conditions; however, it is an important route under acidic conditions. The major transformation products detected were AE F149760, AE F114368, and AE F145741 (20–40°C). The phototransformation study of iodosulfuron-methyl-sodium on soil indicated that the half-life on soil was 9.1 days (under test conditions of 12 hours of light and 12 hours of darkness), while iodosulfuron-methyl-sodium was essentially stable in the dark controls. One major transformation product detected was AE 0002166.

Based on the biotransformation half-life values (0.8–21.8 days), iodosulfuron-methyl-sodium was non-persistent under aerobic soil conditions at moisture contents of 30–50% of the soil's MWHC: however, iodosulfuron-methyl-sodium was slightly persistent under dry soil conditions (25% MWHC) or cooler temperatures (10°C). The major transformation products detected were metsulfuron-methyl (slightly to moderately persistent), AE F059411 (moderately persistent to persistent), AE F161778 (non-persistent to slightly persistent), and three unidentified compounds (M2, U1 and U2).

The studies indicated that iodosulfuron-methyl-sodium is fully transformed to bound residues and carbon dioxide.

Based on the results from the adsorption/desorption studies, iodosulfuron-methyl-sodium and the transformation products, metsulfuron-methyl and AE F059411, do not adsorb strongly onto soil and can desorb readily. Therefore, iodosulfuron-methyl-sodium, metsulfuron-methyl, and AE F059411 are expected to be very mobile in soils, having the potential to leach or be transported to surface water by run-off, and to predominantly partition into the water column. These results are supported by the biotransformation studies, which indicated that there was limited binding of the applied to soil in the soil biotransformation study (<40% of applied was soil-bound at study termination) and the majority of radiolabelled residues were recovered from the floodwater in the aquatic biotransformation studies (>29–46% of applied throughout the duration of the studies). Based on values for vapour pressure and Henry's Law constant, data on the volatility of iodosulfuron-methyl-sodium are not required.

The Canadian field dissipation study (one Ontario site) reported a half-life for iodosulfuron-methyl-sodium of 4 days; thus, iodosulfuron-methyl-sodium would be classified as non-persistent in soil under field conditions. This was supported by the lack of residue carryover at the end of the study (98 days). The major transformation products detected in the field dissipation study were metsulfuron-methyl and AE F059411, which were below the level of detection at study termination (98 days). No residue was detected below the 0–7.5 cm soil depth for the parent compound or the transformation products. This indicated that iodosulfuron-methyl-sodium and the transformation products were relatively immobile, and leaching was not likely to be an important route of dissipation under field conditions.

5.8 Summary of fate and behaviour in the aquatic environment

The fate and behaviour of iodosulfuron-methyl-sodium in the aquatic environment is outlined in Appendix I, Table 9. Hydrolysis is not an important iodosulfuron-methyl-sodium transformation route under neutral and basic conditions; however, it is an important route under acid conditions. The major transformation products detected were AE F149760, AE F114368, and AE F145741 (20–40°C). There is low potential for phototransformation in surface waters. The aqueous phototransformation half-life was 9–10.2 days (under continuous irradiation) with the formation of the major transformation product AE 0002166.

Iodosulfuron-methyl-sodium was non-persistent to slightly persistent in aerobic water/sediment studies with first-order half-lives in the whole system ranging from 13.5 days to 23.3 days. The major transformation products included metsulfuron-methyl, AE F059411, AE 0000119, AE 0014966, and AE 0034855. Using the multi-compartment program TopFit 2, half-lives for some of the transformation products (metsulfuron-methyl, AE F161778, AE 0014966, and AE F059411) were estimated: the persistence for each were the same as reported in the aerobic soil biotransformation studies, with the

exception of AE 0014966, which is non-persistent to slightly persistent (was not detected in the soil biotransformation studies). Iodosulfuron-methyl-sodium was non-persistent to slightly persistent in the anaerobic water/soil study with first-order half-lives of 14.3–28.1 days in the whole system. The only major transformation product detected was metsulfuron-methyl. The half-life for metsulfuron-methyl was also estimated to be 291 days in the whole system; thus, metsulfuron-methyl was persistent under anaerobic aquatic conditions. The majority of radiolabelled residues in the aerobic and anaerobic studies were recovered from the floodwater, indicating that iodosulfuron-methyl-sodium and the transformation products do not readily bind to sediment in aquatic systems. All the studies indicate that iodosulfuron-methyl-sodium is fully transformed to bound residues and carbon dioxide.

5.9 Expected environmental concentrations

Owing to the presence of the safener compound in the EP, Tribute™ Solo 32DF, expected environmental concentrations (EECs) were calculated for the a.i. alone, as well as for the EP. The EECs in environmental compartments of concern (soil and water) were estimated by calculations made using simple scenarios. These concentrations were used as initial approximations for estimating the potential exposure to wildlife.

For the risk assessment, it was assumed that a single application was made at the maximum proposed Canadian label rate: for toxicity studies conducted with the a.i., the maximum rate of 2 g a.i./ha was used for the risk assessment, while for toxicity studies conducted with the EP, the maximum label rate of 100 g EP/ha was used for Tribute™ Solo 32DF. The scenarios assume that the concentrations in the various environmental compartments are obtained immediately following the single application.

5.9.1 Soil

The EEC of iodosulfuron-methyl-sodium on soil was calculated using a soil bulk density of 1.5 g/cm^3, a soil depth of 15 cm, and the maximum Canadian label application rate. The field dissipation half-life of 4 days (Ecoregion 8.1) was used to account for the dissipation of iodosulfuron-methyl-sodium between applications. When the half-life, the minimum application interval, the number of applications per year, and the highest application rate of iodosulfuron-methyl-sodium (2 g/ha) are considered, the EEC in soil would be 0.89 mg iodosulfuron-methyl-sodium/kg soil.

An EEC was also calculated for the EP Tribute™ Solo 32DF in soil: assuming the identical input parameters listed above, the EEC would be 0.044 mg EP/kg.

5.9.2 Aquatic systems

The EEC of iodosulfuron-methyl-sodium in water was calculated using the whole system half-life of 23.3 days from the aerobic water/sediment biotransformation study. Assuming a water density of 1.0 g/mL, a water depth of 30 cm, and a scenario in which a body of water is over-sprayed with the product, the EEC in water would be 0.67 mg iodosulfuron-methyl-sodium/L water.

An EEC was also calculated for the EP Tribute™ Solo 32DF in water: assuming the identical input parameters listed above, the EEC would be 0.033 mg EP/L.

Based on the potential use pattern of iodosulfuron-methyl-sodium in areas where corn is grown, residues in potential drinking water sources in these areas were calculated using the models PRZM/EXAM (for surface water) and LEACHM (for groundwater). The model was run using conservative scenarios, the environmental profile of iodosulfuron-methyl-sodium and an application rate of 2 g a.i./ha. The Level I estimated environmental concentration of iodosulfuron-methyl-sodium in drinking water sources is 0.172 mg a.i./L.

5.9.3 Vegetation and other food sources

Since data were not available on the residues of iodosulfuron-methyl-sodium or Tribute™ Solo 32DF in wildlife food sources immediately following application, the EECs of the above were estimated (Appendix I, tables 10, 11, and 12) using a standard scenario based on correlations of Hoerger and Kenaga (1972) and Kenaga (1973) as modified by Fletcher et al. (1994) using the maximum Canadian label rate for iodosulfuron-methyl-sodium (2 g/ha). No information was available on the dissipation of iodosulfuron-methyl-sodium on wildlife food sources; therefore, it was assumed that no dissipation occurred.

6.0 Effects on non-target species

6.1 Effects on terrestrial organisms

The effects of iodosulfuron-methyl-sodium and the EP Tribute™ Solo 32DF on terrestrial organisms are presented in Appendix I, Table 13. The acute (14-day) LC_{50} of iodosulfuron-methyl-sodium, the transformation products (metsulfuron-methyl and AE F059411), and Tribute™ Solo 32DF to the earthworm (*Eisenia fetida*) were all >1000 mg/kg soil. The NOECs for iodosulfuron-methyl-sodium and AE F059411 were both 1000 mg/kg soil, while the NOECs for metsulfuron-methyl and Tribute™ Solo 32DF were both 320 mg/kg soil.

The acute (48-hour) oral LD_{50} and NOEC of iodosulfuron-methyl-sodium to the honey bee (*Apis mellifera* L.) were >81.4 mg/bee and 22.7 mg/bee, respectively. The corresponding acute (48-hour) contact LD_{50} and NOEC were >150 mg/bee and 100 mg/bee, respectively. The acute oral and contact LD_{50} of Tribute™ Solo 32DF to the honey bee were >22.9 mg/bee and >159 mg/bee, respectively. Iodosulfuron-methyl-sodium is classified as practically non-toxic to the honey bee, according to the criteria of Atkins et al. (1981). The test material, Tribute™ Solo 32DF, is expected to pose a negligible risk to honey bees.

The effects on the beneficial capacity of beneficial arthropods (combined effect on lethal and sublethal parameters) as a result of contact exposure to residues on an inert substrate (glass or sand) were assessed for Tribute™ Solo 32DF. Tribute™ Solo 32DF is harmful to the parasitoid *Aphidius rhopalosiphi* in the field (1.5 times the maximum field rate in Canada), and moderately harmful in the field boundary as a result of spray drift. It is slightly harmful to the ground-dwelling predator *Aleochara bilineata* in the field (1.5 times the maximum field rate in Canada) and in the field boundary as a result of spray drift. However, Tribute™ Solo 32DF was harmless to the predatory mite *Typhlodromus pyri*, the ground-dwelling predator *Poecilus cupreus*, the ground-dwelling predator *Pardosa* spp., and the foliage-dwelling predator *Chrysoperla carnea*, at rates greater than 1.5 times the maximum field rate in Canada.

The acute (14-day) oral LD_{50} and NOEC of iodosulfuron-methyl-sodium to the bobwhite quail (*Colinus virginianus*) were >1744 mg/kg diet and 1744 mg/kg diet, respectively, while the corresponding subacute (8-day) dietary LC_{50} and NOEC were >4358 mg/kg diet and 4358 mg/kg diet, respectively. Similar results for subacute dietary LC_{50} (>4510 mg/kg diet) and NOEC (4510 mg/kg diet) of iodosulfuron-methyl-sodium to mallard duck (*Anas platyrhynchos*) were observed. The NOEC of iodosulfuron-methyl-sodium on reproduction in bobwhite quail, Japanese quail (*Coturnix coturnix japonica*), and mallard duck were 980, 984, and 905 mg/kg diet. Based on the results of the toxicity studies, iodosulfuron-methyl-sodium is classified as, at most, slightly toxic on an acute and dietary basis to both bobwhite quail and mallard ducks.

Iodosulfuron-methyl-sodium and Tribute™ Solo 32DF have low toxicity to rats on an oral, dermal and inhalation basis. Iodosulfuron-methyl-sodium was found to be moderately irritating to the eye and minimally irritating to the skin of rabbits, and non-sensitizing to the skin of guinea pigs. Tribute™ Solo 32DF was mildly irritating to the eye and moderately irritating to the skin of rabbits, and a potential skin sensitizer to the skin of guinea pigs.

In 90-day dietary tests, the NOAELs of iodosulfuron-methyl-sodium for rats, mice, and dogs were 67, 119 and 8.1 mg/kg bw/d respectively in males and 74, 401 and 8.4 mg/kg bw/d respectively in females. In a 12-month dietary study with dogs, the NOAELs were 41.8 and 7.25 mg/kg bw/d in males and females, respectively. In the rat dietary study, lower bw were observed for both sexes. In the mouse dietary study, increases in liver weight, centrilobular hepatocellular enlargement, lipofuscin and centrilobular fat deposition were observed. In the dog dietary study, effects were evident in blood cells and bone marrow; as well, increased ASAT, ALAT, and CPK activity was detected.

Oncogenicity studies with mice (NOAEL 54.2/57.6 mg/kg bw/d [M/F]) and rats (NOAEL 29.7/39.1 mg/kg bw/d [M/F]) indicated an increase in liver weight, centrilobular effects, lower bw and food consumption. There was, however, no evidence of oncogenicity. Iodosulfuron-methyl-sodium was not genotoxic and non-mutagenic in a standard battery of genotoxicity and mutagenicity tests such as bacterial reverse mutation, mammalian gene mutation, chromosomal aberration, mammalian cytogenetics (micronucleus assay), and DNA synthesis.

In a multi-generation reproduction study with rats (effects on pregnancy and fetuses), iodosulfuron-methyl-sodium did not cause adverse treatment-related effects in either generation (NOAELs 346 and 390 mg/kg bw/d for male and female reproductive effects, respectively). However, neonates appeared to be both qualitatively and quantitatively more sensitive than parental animals. In developmental toxicity studies with rats and rabbits, iodosulfuron-methyl-sodium effects included delay in skeletal development in rats (NOAEL 315 mg/kg bw/d, developmental), while no adverse treatment-related finding was detected in the rabbits (NOAEL 400 mg/kg bw/d, developmental). Iodosulfuron-methyl-sodium was non-teratogenic to rats, while results were inconclusive in rabbits.

Studies on the effect of the EP Tribute™ Solo 32DF on seedling emergence and vegetative vigour of monocot plants (corn *Zea mays*; oats *Avena sative*; onion *Allium cepa*; and wheat *Triticum aestivum*) and dicot plants (cabbage *Brassica oleracea*; cucumber *Cucumis sativus*; lettuce *Lactuca sativa*; radish *Raphanus sativus*; soybean *Glycine max*; and tomato *Lycopersicon esculentum*) were performed. The most sensitive EC_{25}s for seedling emergence and vegetative vigour were 14.1 g EP/ha (lettuce) and 16.1 g EP/ha (cucumber), respectively.

6.2 Effects on aquatic organisms

The effects of iodosulfuron-methyl-sodium and the EP Tribute™ Solo 32DF on aquatic organisms are presented in Appendix I, Table 14. The acute (48-hour) LC_{50} of iodosulfuron-methyl-sodium in the water flea (*Daphnia magna*) was >86.9 mg a.i./L, while the acute LC_{50} of the EP Tribute™ Solo 32DF was >100 mg EP/L. The chronic (21-day) NOEC of iodosulfuron-methyl-sodium in the water flea was 9.1 mg a.i./L, while the NOEC for Tribute™ Solo 32DF was 0.02 mg EP/L.

The acute (96-hour) LC_{50} of iodosulfuron-methyl-sodium to the rainbow trout (*Oncorhynchus mykiss*) and the bluegill sunfish (*Lepomis macrochirus*) were >88 mg a.i./L and >92 mg a.i./L, respectively, while the corresponding acute LC_{50} of Tribute™ Solo 32DF were 2.6 mg EP/L and 2.8 mg EP/L.

The acute (96-hour) EC_{50} of iodosulfuron-methyl-sodium in *Pseudokirchneriella subcapitata*, *Anabaena flos-aquae*, and *Navicula pelliculosa* were 0.041, 1.4, and >81.5 mg a.i./L, respectively, while the corresponding NOECs were 0.014, 0.63, and 81.5 mg a.i./L. The acute (96-hour) EC_{50} of the transformation products, metsulfuron-methyl and AE F059411, as well as the EP Tribute™ Solo 32DF to *P. subcapitata* were 0.12, >101, and 0.74 mg/L, respectively.

The acute (7- to 14-day) EC_{50} of iodosulfuron-methyl-sodium, AE F059411, and Tribute™ Solo 32DF to *Lemna gibba* were 0.83 mg/L, 101 mg/L, and 2.5 mg EP/L, respectively, while the corresponding NOECs were 0.39 mg/L, 57 mg/L, and 1.0 mg EP/L.

Based on the results of the freshwater toxicity studies, iodosulfuron-methyl-sodium is, at most, slightly toxic to *D. magna*, rainbow trout, and bluegill sunfish. Tribute™ Solo 32DF is practically non-toxic to *D. magna*, and moderately toxic to rainbow trout and bluegill sunfish. The most sensitive freshwater toxicity end point for iodosulfuron-methyl-sodium was the 14-day NOEC (8.3×10^{-4} mg a.i./L) for *Lemna gibba*.

Given the proposed use pattern (Use Site Category [USC] 7, 13, and 14 for use on corn), there is limited potential for marine/estuarine exposure and, therefore, a review of risk was not required.

6.3 Effects on biological methods of sewage treatment

Not applicable for the proposed use.

6.4 Risk characterization

Risk assessment integrates the exposure and ecotoxicology data to estimate the potential for adverse ecological effects. The PMRA currently conducts a deterministic risk assessment of pest control products. Environmental risk is characterized using the margin of safety (MOS) method, which is the ratio of the toxicity end point to the EEC. The end point used for both acute and chronic toxicity is the NOEC from the appropriate laboratory study. In those cases for which a NOEC was not reported, the value was estimated as $0.1 \times LD_{50}$ or $0.1 \times LC_{50}$. Risks were then classified based on the scheme presented in Appendix I, Table 15.

For birds and mammals, the number of days to intake the equivalent of a dose of a.i. by gavage by a wild species in order to kill 50% of the individuals in the lab population (number of days to LD_{50}) was also calculated. The number of days to LD_{50} was determined by calculating the LD_{50} of an individual (LD_{50} × body weight per individual [BWI]) and dividing it by the daily intake of a.i. (EEC in food × FC).

6.4.1 Environmental behaviour

Biotransformation in soil is an important route of transformation for iodosulfuron-methyl-sodium, and phototransformation on soil and in surface waters is a potential transformation route. Hydrolysis is not an important iodosulfuron-methyl-sodium transformation route under neutral and basic conditions; however, it is an important route under acidic conditions. Iodosulfuron-methyl-sodium is not expected to volatilize from water and moist soils; it is also non-persistent to slightly persistent in soil and in aerobic and anaerobic water/sediment systems. The major transformation products are metsulfuron-methyl (slightly to moderately persistent), AE F059411 (moderately persistent to persistent), and AE F161778 (non-persistent to slightly persistent). Iodosulfuron-methyl-sodium and the transformation products, metsulfuron-methyl and AE F059411, do not readily bind to soil or sediment, and under certain environmental conditions (heavy rainfall) are expected to be very mobile in soils, with the potential to leach or be transported to surface water by run-off and to predominantly partition into the water column. Since iodosulfuron-methyl-sodium is non-persistent in soil under field conditions, residues are not expected to carry over to the next growing season. Iodosulfuron-methyl-sodium did not leach under field conditions.

The transformation product, metsulfuron-methyl, is moderately persistent in the field and has the potential to leach, depending on the amount of rainfall and soil type. Metsulfuron-methyl is persistent under anaerobic aquatic conditions.

6.4.2 Terrestrial organisms

The risk of iodosulfuron-methyl-sodium, and the EP Tribute™ Solo 32DF to terrestrial organisms was presented in Appendix I, tables 16 and 17, respectively.

6.4.2.1 Earthworms

As the maximum EEC of iodosulfuron-methyl-sodium in soil is 0.89 mg a.i./kg soil, and the NOEC for earthworms is 1000 mg a.i./kg soil, iodosulfuron-methyl-sodium poses a negligible risk to earthworms at the proposed maximum application rate. The MOS (NOEC ÷ EEC) is >1000.

As the maximum EEC of Tribute™ Solo 32DF in soil is 0.044 mg EP/kg soil, and the NOEC for earthworms is 320 mg EP/kg soil, Tribute™ Solo 32DF poses a negligible risk to earthworms at the proposed maximum application rate. The MOS (NOEC ÷ EEC) is >1000.

6.4.2.2 Honeybees

The dietary LD_{50} for honey bees was >81.4 µg a.i./bee, which is equivalent to > 91.2 kg a.i./ha. The maximum seasonal application rate of 2 g a.i./ha is lower than the LD_{50}; therefore, iodosulfuron-methyl-sodium poses a negligible risk to honey bees at the proposed maximum application rate. The MOS (NOEC ÷ EEC) is >1000.

It is not possible to characterize risk to honey bees treated with Tribute™ Solo 32DF; however, from the data provided, it is expected that the EP will pose negligible risk to honey bees.

6.4.2.3 Other beneficial arthropods

The studies indicate that adverse effects on the parasitoid *Aphidius rhopalosiphi* and the ground-dwelling predator *Aleochara bilineata* are expected in the crop and in the field boundary. However, it is not possible to characterize risk to beneficial arthropods.

6.4.2.4 Wild birds

Wild birds, such as bobwhite quail and mallard ducks, could be exposed to iodosulfuron-methyl-sodium residues by consuming treated vegetation or contaminated prey, or from spray drift. The bobwhite diet may consist of approximately 30% small insects, 15% forage crops, and 55% grain and seeds. The EEC in the bobwhite diet after the application of iodosulfuron-methyl-sodium, based on the maximum application rate (2 g a.i./ha) is 0.35 mg a.i./kg dw diet. The mallard duck diet consists of approximately 30% large insects and 70% grain and seeds. The EEC in the mallard diet is 0.07 mg a.i./kg dw diet.

In the acute oral toxicity study with iodosulfuron-methyl-sodium, the BWI of bobwhite quail in the control treatment was 0.194 kg bw/individual, while the mean food consumption (FC) was 0.016 kg dw of diet/individual/d. The potential daily intake of iodosulfuron-methyl-sodium (DI = FC × EEC) was calculated as 0.0056 mg a.i. per individual/d. The reported LD_{50} and NOEL values were >1744 and 1744 mg a.i./kg bw, respectively. When expressed on a per individual basis, the $LD_{50\ (individual)}$ (= LD_{50} × BWI) was >338 mg a.i. per individual, and the $NOEL_{(individual)}$ (= NOEL × BWI) was 338 mg a.i. per individual. Based on the daily intake (DI), the $LD_{50(individual)}$ and the $NOEC_{\ (individual)}$, it would take a bobwhite quail at least 165 continuous years of consumption of a contaminated diet to attain the dose equivalent to that administered in the laboratory by gavage that had no observable effect on the laboratory population. Therefore, iodosulfuron-methyl-sodium poses a negligible risk to bobwhite quail.

The NOECs for the most sensitive end point, reproductive effects, in bobwhite quail and mallard duck are 980 and 905 mg/kg diet, respectively. As the EECs are lower than the NOEC, iodosulfuron-methyl-sodium will not pose a reproductive risk to bobwhite quail and mallard ducks when applied at the proposed maximum application rate. Likewise, the EECs are lower than the NOECs for the dietary studies for bobwhite quail

(NOEC = 4358 mg/kg diet) and mallard duck (NOEC = 4510 mg/kg diet), thus, iodosulfuron-methyl-sodium poses a negligible risk to bobwhite quail and mallard ducks. The MOS (NOEC ÷ EEC) are >1000 for both species of bird on an acute oral, dietary, and reproductive basis.

6.4.2.5 Wild mammals

Wild mammals, such as rats and mice, could be exposed to residues of iodosulfuron-methyl-sodium by consuming sprayed vegetation or contaminated prey. From Appendix I, Table 12, assuming no transformation and no interception of orchard blast spray, the EECs of iodosulfuron-methyl-sodium in the diets of rats and mice were 1.01 and 1.0 mg a.i./kg dw diet, respectively.

Based on the DI and the LD_{50} (individual), it would take a rat at least 42 continuous years of feeding to attain the dose equivalent to that administered in the laboratory by gavage that killed 50% of the laboratory population. Therefore, iodosulfuron-methyl-sodium poses a negligible risk to rats. The NOAELs for the dietary toxicity studies with rats (NOAEL = 1000 mg/kg diet) and mice (NOAEL = 700 mg/kg diet), as well as the NOAELs for the reproductive study with the rat (NOAEL = 500 mg/kg diet) were all greater than the respective EECs; thus, iodosulfuron-methyl-sodium poses negligible risk to rats and mice on a dietary or reproductive basis when applied at the proposed maximum application rate. The corresponding MOS (NOEL ÷ EEC) are 990 (rat dietary toxicity study), 700 (mice dietary toxicity study), and 495 (rat reproductive study).

The only studies submitted for Tribute™ Solo 32DF were for the rat. From Appendix I, Table 12, assuming no transformation and no interception of orchard blast spray, the EECs of Tribute™ Solo 32DF in the diets of rats was 50.4 mg EP/kg dw diet. Based on the DI and the $LD_{50\ (individual)}$, it would take a rat at least 403 continuous days of feeding to attain the dose equivalent to that administered in the laboratory by gavage that killed 50% of the laboratory population. Therefore, Tribute™ Solo 32DF poses a negligible risk to rats. The MOS (NOEC ÷ EEC) is 69.

6.4.2.6 Vascular plants

The EC_{25} for the most sensitive end point for vegetative vigour, dry weight in cucumber, was 16.1 g EP/ha, and the EC_{25} for the most sensitive end point for seedling emergence, dry weight in lettuce, was 14.1 g EP/ha. Iodosulfuron-methyl-sodium applied at the proposed maximum application rate will pose a moderate risk to terrestrial plants. The MOS values (NOEC ÷ EEC) are 0.14 for seedling emergence and 0.16 for vegetative vigour.

6.4.3 Aquatic organisms

The risk of iodosulfuron-methyl-sodium, and the EP Tribute™ Solo 32DF, to aquatic organisms is summarized in Appendix I, tables 18 and 19, respectively.

6.4.3.1 Freshwater invertebrates

The most sensitive acute and chronic NOECs for *Daphnia magna* were 28.1 mg/L (mortality) and 9.1 mg/L (weight and reproduction). The EEC in water for iodosulfuron-methyl-sodium was 0.67 mg/L; thus, the most sensitive NOECs were greater than the EEC. Therefore, iodosulfuron-methyl-sodium poses a negligible risk to *Daphnia magna* when applied at the proposed maximum application rate. The MOS (NOEC ÷ EEC) are both >1000.

The most sensitive acute and chronic NOECs for Tribute™ Solo 32DF to *Daphnia magna* were 100 mg EP/L (mortality) and 0.02 mg EP/L (length and reproduction). The EEC in water for Tribute™ Solo 32DF was 0.044 mg EP/L; thus, Tribute™ Solo 32DF will pose a moderate risk to *Daphnia magna* when applied at the proposed maximum application rate. The MOS (NOEC ÷ EEC) for mortality and for length and reproduction are >1000 and 0.61, respectively.

6.4.3.2 Freshwater fish

The most sensitive end point was the acute NOEC for rainbow trout, which was 88 mg/L (based on mortality) and, thus, greater than the EEC in water. Iodosulfuron-methyl-sodium poses a negligible risk to rainbow trout and bluegill sunfish when applied at the proposed maximum application rate. The MOS (NOEC ÷ EEC) are both >1000 for rainbow trout and bluegill sunfish.

The acute NOEC for Tribute™ Solo 32DF to rainbow trout and bluegill sunfish was the same at 1.0 mg EP/L (based on mortality) and, thus, greater than the EEC in water. Tribute™ Solo 32DF poses a negligible risk to rainbow trout and bluegill sunfish when applied at the proposed maximum application rate. The MOS (NOEC ÷ EEC) is 30.3 for both rainbow trout and bluegill sunfish.

6.4.3.3 Freshwater algae

The most sensitive end point was the NOEC (0.014 mg/L), based on cell density, for the freshwater *P. Subcapitata*, which is greater than the EEC in water. Iodosulfuron-methyl-sodium poses a negligible risk to freshwater algae when applied at the proposed maximum application rate. The MOS (NOEC ÷ EEC) is 20.9.

The only study conducted with Tribute™ Solo 32DF was for *P. Subcapitata* (NOEC < 0.4 mg EP/L, based on biomass). As a definitive NOEC could not be established, a calculated NOEC was determined by using 0.1 of the EC_{50} (0.74 mg EP/L). The calculated NOEC (0.074 mg EP/L) was used to determine the MOS. Tribute™ Solo 32DF poses a negligible risk to freshwater algae when applied at the proposed maximum application rate. The MOS (NOEC ÷ EEC) is 2.2.

6.4.3.4 Freshwater aquatic plants

The most sensitive end point was the NOEC (0.39 mg/L), based on frond density, for *Lemna gibba*. This is also the most sensitive freshwater aquatic end point. The MOS (NOEC ÷ EEC) is 0.58; thus, there is a high risk to freshwater aquatic plants at the proposed maximum application rate for iodosulfuron-methyl-sodium.

The NOEC for Tribute™ Solo 32DF to *Lemna gibba* was 1.0 mg/L, based on biomass. The MOS (NOEC ÷ EEC) is 0.03; thus, there is a high risk to freshwater aquatic plants at the proposed maximum application rate for Tribute™ Solo 32DF.

6.4.3.5 Marine organisms

Given the proposed use pattern (USC 7, 13, and 14 for use on corn), there is limited potential for marine/estuarine exposure; thus, a review of risk was not required.

6.5 Risk mitigation

Iodosulfuron-methyl-sodium is toxic to aquatic organisms and harmful to beneficial predatory or parasitic arthropods.

The calculation of buffer zones for iodosulfuron-methyl-sodium and Tribute™ Solo 32DF (2% iodosulfuron-methyl-sodium, 30% foramsulfuron, 30% isoxadifen-ethyl safener) has indicated that the aquatic buffer zone is driven by the toxicity of the technical a.i., foramsulfuron. Thus, the aquatic buffer zone for Tribute™ Solo 32DF is proposed for use. If changes in the formulation of the EP are made in the future, additional toxicity data may be required at that time.

The formulant isoxadifen-ethyl (AE F122006) is categorized as highly toxic to fish. Therefore, any formulated product containing isoxadifen-ethyl must contain the following statement under ENVIRONMENTAL HAZARDS: “Toxic to fish.”

The following labelling is required.

On container label and in the booklet:

ENVIRONMENTAL HAZARDS: Toxic to fish and other aquatic organisms. Very small quantities of spray solution may severely injure susceptible terrestrial plants. Observe buffer zones specified under Directions for Use.

This product may be harmful to beneficial predatory or parasitic arthropods. The best available application technique that minimizes off-target drift should be used to reduce effects on beneficial arthropods in the field boundary.

Do not apply in areas where there is potential for run-off. If rainfall is imminent, delay spraying. Do not apply, drain, or flush spray equipment on or near desirable trees or other plants, on areas where their roots may extend, or in locations where the chemical may be washed or moved into contact with their roots.

USE ONLY FOR RECOMMENDED PURPOSES AND AT RECOMMENDED RATES.

Under "Directions for Use" in the booklet:

Do not apply during periods of dead calm or when winds are gusty.

Over-spray or drift to sensitive habitats must be avoided. A buffer zone of 14 metres is required between the downwind point of direct application and the closest edge of sensitive aquatic habitats such as lakes, rivers, sloughs, ponds, coulees, prairie potholes, creeks, marshes, streams, reservoirs, and wetlands. Do not contaminate these habitats when cleaning and rinsing spray equipment or containers.

7.0 Efficacy

7.1 Effectiveness

7.1.1 Intended use

Tribute™ Solo 32DF is formulated as a water-dispersible granule with a guarantee of iodosulfuron at 2% and foramsulfuron at 30%, which must be applied with the surfactant Hasten.

Tribute™ Solo 32DF is proposed as a post-emergent herbicide in field corn (1–8 leaf stage of growth) for the control of specific grassy and broadleaf weeds. Tribute™ Solo 32DF must be applied with 1.75 L/ha Hasten spray additive plus 2.5 L/ha liquid nitrogen fertilizer (plus 28% urea ammonium nitrate [UAN]) in a minimum total spray volume of 140 L/ha with a maximum of 1 application per year using ground equipment only.

There are two proposed application rates for Tribute™ Solo 32DF.

- Tribute™ Solo 32DF applied at a rate of 50 g/ha (16 g a.i./ha) claims control of quackgrass (*Agropyron repens*) (3–6 leaves, up to early tillering).

- Tribute™ Solo 32DF applied at a rate of 100 g/ha (32 g a.i./ha) claims control of the following annual grasses, from the 1-leaf to the 6-leaf stage of growth (up to early tillering):

    - large crabgrass (*Digitaria saguinalis*),
    - fall panicum (*Panicum dichotomiflorum*),
    - green foxtail (*Setaria viridus*),
    - yellow foxtail (*Setaria glauca*), and
    - proso millet (*Panicum miliaceum*), as well as

    the following broadleaf weeds:

    - lamb's quarters (*Chenopodium album*) (2–8 leaf),
    - redroot pigweed (*Amaranthus retroflexus*) (1–7 leaf),
    - common ragweed (*Ambrosia artemisiifolia*) (2–6 leaf) and
    - velvetleaf (*Abutilon theophrasti*) (1–4 leaf).

A recropping interval of 10 days is proposed for field corn and sweet corn. A recropping interval of 4 months is proposed for winter wheat. A recropping interval of 10 months is proposed for soybeans, alfalfa, spring barley, dry common beans, spring canola, red clover, spring oats, sugar beets and timothy.

7.1.2 Mode of action

Iodosulfuron belongs to the general class of herbicides termed sulfonylureas (Group 2). Iodosulfuron inhibits the activity of ALS, which is the key enzyme in the biosynthesis of the branch-chain amino acids isoleucine, leucine, and valine. Although the actual sequence of phytotoxic processes is unclear, plant death results from events occurring in response to inhibition of the ALS enzyme.

Iodosulfuron behaves like both a contact and systemic herbicide when it is applied post-emergence to weed species. Uptake by the target plant is immediate upon application and phytotoxic effects within the plant are also immediate. The visible symptoms of herbicidal action are almost immediate arresting of growth, followed by leaf yellowing, inhibition of anthocyanin production, and, finally, progressive shoot necrosis. Depending on the weed species and environmental conditions, plant death will usually occur between 1 and 3 weeks after herbicide application.

7.1.3 Crops

Field corn is the only crop for which data was submitted and for which a label claim was made.

7.1.4 Effectiveness against pests

A total of 60 small-plot field trials over two years were conducted in Ontario, Quebec, Manitoba and northern U.S. border states, under conventional tillage practices. All trials were conducted as Randomized Complete Block Design with either 3 or 4 replicates. Treatments were conducted at the proposed label rates and a reduced application rate to confirm that the requested rates are the lowest to provide effective and consistent control on a weed-specific basis.

Efficacy was assessed as a visual rating of percentage of weed control and reported up to two times during the year of treatment on a weed-specific basis.

7.1.4.1 Quackgrass (*Agropyron repens*)

Control of quackgrass (3–6 leaf stage up to tillering) is proposed with a single application of 16 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for quackgrass (3–6 leaf stage up to tillering) were reported in 4 trials conducted over two years at locations in southern Ontario and northern U.S. border states under conventional tillage practices. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 89.3% (n = 3) at <35 DAT and 95.8% (n = 4) at >35 DAT.

Therefore, the data support a claim of quackgrass (3–6 leaf up to tillering) control in field corn with an application of 16 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN.

7.1.4.2 Large crabgrass (*Digitaria saguinalis*)

Control of large crabgrass (1–6 leaf stage up to tillering) is proposed with a single application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for large crabgrass (1–6 leaf stage up to tillering) were reported in 21 trials conducted over two years at locations in southern Ontario under conventional tillage practices. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (0.5-fold rate) were 77.1% (n = 12) at <35 DAT and 65.4% (n = 14) at >35 DAT. Mean control ratings at 28 g a.i./ha Tribute™ Solo 32DF (0.9-fold rate) were 78.0% (n = 6) at <35 DAT and 68.8% (n = 6) at >35 DAT. Mean control ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 89.1% (n = 21) at <35 DAT and 79.4% (n = 21) at >35 DAT.

Therefore, the data support a claim of large crabgrass (1–6 leaf stage up to tillering) suppression in field corn with an application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN.

7.1.4.3 Fall panicum (*Panicum dichotomiflorum*)

Control of fall panicum (1–6 leaf stage up to tillering) is proposed with a single application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for fall panicum (1–4 leaf stage up to tillering) were reported in 11 trials conducted over two years at locations in southern Ontario and northern U.S. border states under conventional tillage practices. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (0.5-fold rate) were 96.8% (n = 6) at <35 DAT and 93.3% (n = 6) at >35 DAT. Mean control ratings at 28 g a.i./ha Tribute™ Solo 32DF (0.9-fold rate) were 98.5% (n = 2) at <35 DAT and 93.0% (n = 2) at >35 DAT. Mean control ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 97.3% (n = 11) at <35 DAT and 93.6% (n = 11) at >35 DAT.

Therefore, the data support a claim of fall panicum (1–4 leaf stage up to tillering) control in field corn with an application of 16 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN.

7.1.4.4 Green foxtail (*Setaria viridus*)

Control of green foxtail (1–6 leaf stage up to tillering) is proposed with a single application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for green foxtail (2–5 leaf stage up to tillering) were reported in 21 trials conducted over two years at locations in southern Ontario, Quebec, and Manitoba under conventional tillage practices. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (0.5-fold rate) were 95.7% (*n* = 7) at <35 DAT and 96.0% (*n* = 7) at >35 DAT. Mean control ratings at 28 g a.i./ha Tribute™ Solo 32DF (0.9-fold rate) were 98.0% (*n* = 6) at <35 DAT and 95.7% (*n* = 6) at >35 DAT. Mean control ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 96.6% (*n* = 21) at <35 DAT and 95.8% (*n* = 21) at >35 DAT.

Therefore, the data support a claim of green foxtail (2–5 leaf stage up to tillering) control in field corn with an application of 16 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN.

7.1.4.5 Yellow foxtail (*Setaria glauca*)

Control of yellow foxtail (1–6 leaf stage up to tillering) is proposed with a single application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for yellow foxtail (2–5 leaf stage up to tillering) were reported in 13 trials conducted over two years at locations in southern Ontario and northern U.S. border states under conventional tillage practices. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (0.5-fold rate) were 72.5% (*n* = 4) at <35 DAT and 78.8% (*n* = 4) at >35 DAT. Mean control ratings at 28 g a.i./ha Tribute™ Solo 32DF (0.9-fold rate) were 76.5% (*n* = 2) at <35 DAT and 78.7% (*n* = 3) at >35 DAT. Mean control ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 88.3% (*n* = 8) at <35 DAT and 88.1% (*n* = 9) at >35 DAT.

The data support a claim of yellow foxtail (2–5 leaf stage up to tillering) control in field corn with an application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN.

7.1.4.6 Proso millet (*Panicum miliaceum*)

Control of proso millet (1–6 leaf stage up to tillering) is proposed with a single application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for proso millet (2–5 leaf stage up to tillering) were reported in 13 trials conducted over two years at locations in southern Ontario and northern U.S. border states under conventional tillage practices. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (0.5-fold rate) were 85.0% (*n* = 8) at <35 DAT and 94.5% (*n* = 8) at >35 DAT. Mean control ratings at 28 g a.i./ha Tribute™ Solo 32DF (0.9-fold rate) were 93.0% (*n* = 2) at <35 DAT and 96.0% (*n* = 2) at >35 DAT. Mean control ratings at

32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 93.8% (*n* = 13) at <35 DAT and 97.3% (*n* = 12) at >35 DAT.

Therefore, the data support a claim of proso millet (2–5 leaf stage up to tillering) control in field corn with an application of 16 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN.

7.1.4.7 Lamb's quarters (*Chenopodium album*)

Control of lamb's quarters (2–8 leaf stage) is proposed with a single application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for lamb's quarters (4–8 leaf stage) were reported in 49 trials conducted over 2 years at locations in southern Ontario, Quebec, Manitoba and northern U.S. border states under conventional tillage practices. Mean control ratings at 8 g a.i./ha Tribute™ Solo 32DF (0.25-fold rate) were 84.3% (*n* = 3) at <35 DAT and 91.0% (*n* = 3) at >35 DAT. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (0.5-fold rate) were 93.7% (*n* = 23) at <35 DAT and 92.9% (*n* = 23) at >35 DAT. Mean control ratings at 28 g a.i./ha Tribute™ Solo 32DF (0.9-fold rate) were 98.3% (*n* = 17) at <35 DAT and 98.1% (*n* = 15) at >35 DAT. Mean control ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 96.9% (*n* = 48) at <35 DAT and 96.7% (*n* = 47) at >35 DAT.

Therefore, the data support a claim of lamb's quarters (4–8 leaf stage) control in field corn with an application of 16 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN.

7.1.4.8 Redroot pigweed (*Amaranthus retroflexus*)

Control of redroot pigweed (1–7 leaf stage) is proposed with a single application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for redroot pigweed (1–7 leaf stage) were reported in 27 trials conducted over 2 years at locations in southern Ontario, Quebec, and northern U.S. border states under conventional tillage practices. Mean control ratings at 8 g a.i./ha Tribute™ Solo 32DF (0.25-fold rate) were 84.0% (*n* = 2) at <35 DAT and 94.5% (*n* = 2) at >35 DAT. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (0.5-fold rate) were 97.2% (*n* = 11) at <35 DAT and 98.4% (*n* = 10) at >35 DAT. Mean control ratings at 28 g a.i./ha Tribute™ Solo 32DF (0.9-fold rate) were 99.0% (*n* = 6) at <35 DAT and 99.0% (*n* = 6) at >35 DAT. Mean control ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 97.6% (*n* = 24) at <35 DAT and 98.5% (*n* = 21) at >35 DAT.

Therefore, the data support a claim of redroot pigweed (1–7 leaf stage) control in field corn with an application of 16 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN.

7.1.4.9 Common ragweed (*Ambrosia artemisiifolia*)

Control of common ragweed (2–6 leaf stage) is proposed with a single application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for common ragweed (2–6 leaf stage) were reported in 27 trials conducted over 2 years at locations in southern Ontario, Quebec, and northern U.S. border states under conventional tillage practices. Mean control ratings at 8 g a.i./ha Tribute™ Solo 32DF (0.25-fold rate) were 72.5% (*n* = 2) at <35 DAT and 76.5% (*n* = 2) at >35 DAT. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (0.5-fold rate) were 88.5% (*n* = 12) at <35 DAT and 89.5% (*n* = 13) at >35 DAT. Mean control ratings at 28 g a.i./ha Tribute™ Solo 32DF (0.9-fold rate) were 97.5% (*n* = 8) at <35 DAT and 95.9% (*n* = 8) at >35 DAT. Mean control ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 93.9% (*n* = 26) at <35 DAT and 95.2% (*n* = 26) at >35 DAT.

Therefore, the data indicate that consistent control of common ragweed (2–6 leaf stage) in field corn is achieved with an application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN. However, the data provided indicates that a rate lower than 32 g a.i./ha may provide acceptable control of common ragweed. Additional data may be requested in order to establish the lowest effective rate for the control of common ragweed.

7.1.4.10 Velvetleaf (*Abutilon theophrasti*)

Control of velvetleaf (1–4 leaf stage) is proposed with a single application of 32 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% or 32% UAN.

Control ratings for velvetleaf (1–4 leaf stage) were reported in 9 trials conducted over two years at locations in southern Ontario and northern U.S. border states under conventional tillage practices. Mean control ratings at 16 g a.i./ha Tribute™ Solo 32DF (0.5-fold rate) were 97.0% (*n* = 5) at <35 DAT and 96.7% (*n* = 6) at >35 DAT. Mean control ratings at 28 g a.i./ha Tribute™ Solo 32DF (0.9-fold rate) were 98.5% (*n* = 2) at <35 DAT and 95.5% (*n* = 2) at >35 DAT. Mean control ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) were 97.6% (*n* = 9) at <35 DAT and 97.5% (*n* = 8) at >35 DAT.

Therefore, the data support a claim of velvetleaf (1-4 leaf stage) control in field corn with an application of 16 g a.i./ha Tribute™ Solo 32DF + 1.0% v/v Hasten + 2.5 L/ha of 28% UAN.

7.1.5 Total spray volume

A single application of Tribute™ Solo 32DF is proposed for ground application in a minimum water volume of 140 L/ha.

A total of 51 trials were conducted in southern Ontario, Manitoba, Quebec, and northern U.S. border states where the water volumes ranged from 140 L/ha to 346 L/ha. As the majority of trials were conducted with water volumes of 150 L/ha or greater, the data support a label claim for a minimum spray volume of 150 L/ha.

7.2 Phytotoxicity to target plants or target plant products

Crop tolerance data were generated from 90 small-plot field trials that tested 32 varieties of field corn from the 1–8 leaf stage, or 5–6 visible collars (the leaf is counted once the next leaf is visible in the whorl) over two years at sites in Ontario, Quebec, Manitoba, and northern U.S. border states under conventional tillage practices. All trials were conducted as Randomized Complete Block Design with either three or four replicates.

Up to two visual assessments of crop injury were reported in each trial, with 87 trials reporting yield data.

Weed-free trials

A total of 28 dedicated crop tolerance trials with weed-free trials tested 28 varieties of field corn over two years at sites in Ontario, Quebec, Manitoba, and northern U.S. border states under conventional tillage practices. Each trial reported the visual crop tolerance of field corn following an application of the maximum requested rate of Tribute™ Solo 32DF at 32 g a.i./ha + Hasten adjuvant at 1% v/v + 28% UAN at 2.5 L/ha. Treatments were also conducted at twice the requested maximum rate to confirm the tolerance of field corn to a spray overlap situation.

Mean injury ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate) were 11.8% (n = 18) at <21 DAT and 5.2% (n = 18) at >21 DAT. Mean crop injury ratings at 64 g a.i./ha Tribute™ Solo 32DF (two-fold max. rate) were 13.6% (n = 13) at <21 DAT and 6.1% (n = 13) at >21 DAT.

Although injury was reported shortly after application, the crop recovered without a yield reduction following a treatment at the one-fold maximum rate (95.3% of weed-free check [n = 23]) and at the two-fold maximum rate (90.5% of weed-free check [n = 24]).

A number of trials were conducted on known SU-sensitive corn hybrids, which confirmed that Tribute™ Solo 32DF should not be applied to known SU hybrids. It is recommended that the label include a statement that the product must not be applied to known SU-sensitive corn hybrids.

Weedy Trials

A total of 62 trials tested 28 varieties of field corn over two years at sites in Ontario and northern U.S. border states. Mean injury ratings at 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate) were 4.8% (*n* = 84) at <21 DAT and 2.7% (*n* = 61) at >21 DAT. Mean crop injury ratings at 37.4 g a.i./ha Tribute™ Solo 32DF (1.2-fold max. rate) were 15.7% (*n* = 3) at <21 DAT and 5.3% (*n* = 3) at >21 DAT.

Although injury was reported shortly after application, the crop recovered without a yield reduction following a treatment at the one-fold maximum rate (230.8% of weedy check [*n* = 61]) and at the 1.2-fold maximum rate (193.5% of weedy check [*n* = 2]).

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

7.3.1 Impact on succeeding crops

All trials were conducted as randomized complete design experiments with visual assessments of crop injury conducted up to three times during the growing season, and with either three or four replicates.

7.3.1.1 Field corn

A recropping interval of 10 days is proposed for field corn following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

A total of 4 trials conducted in southern Ontario over two reporting periods (1999–2000 and 2000–2001) tested the tolerance of field corn seeded 10 months following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) and 64 g a.i./ha (two-fold rate), with yield reported in two trials.

The mean injury rating at the one-fold rate was 0% (*n* = 4) (16–63 days after planting [DAP]) with a yield of 116% of a weed-free check (*n* = 2) and at the two-fold rate was 0% (*n* = 4) (16–63 DAP) with a yield of 123% of a weed-free check (*n* = 2).

The data support the recropping of field corn 10 months following an application of Tribute™ Solo 32DF at the proposed rate. However, data are insufficient data to draw a scientific conclusion as to the tolerance of field corn seeded as a salvage crop 10 days after an application of Tribute™ Solo 32DF as proposed on the label.

7.3.1.2 Sweet corn

A recropping interval of 10 days is proposed for sweet corn following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

Yield was reported in the one trial conducted in southern Ontario (1999–2000) that tested the tolerance of sweet corn seeded 10 months following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) and 64 g a.i./ha (two-fold rate).

The mean injury rating at the one-fold and two fold rates was 0% (n = 1) (30 DAP) with a yield of 96% of a weed-free check (n = 1).

The data are insufficient to draw a scientific conclusion as to the tolerance of sweet corn seeded as a salvage crop 10 days after an application of Tribute™ Solo 32DF as proposed on the label. The data are also insufficient to draw a scientific conclusion as to the tolerance of sweet corn seeded 10 months following an application of Tribute™ Solo 32DF.

7.3.1.3 Winter wheat

A recropping interval of 4 months is proposed following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

One trial was conducted in southern Ontario (1999–2000) that reported 0% crop injury (17 and 193 DAT) in the year following an application of one-fold rate and two-fold rate Tribute™ Solo 32DF. The mean yield was 98% (one-fold rate) and 98% (two-fold rate) of an untreated check.

The data are insufficient to draw a scientific conclusion as to the tolerance of winter wheat seeded in sites previously treated with Tribute™ Solo 32DF at the proposed replanting interval.

7.3.1.4 Soybeans

A recropping interval of 10 months is proposed for soybeans following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

Yield was reported in all 5 trials conducted in southern Ontario over two reporting periods (1999–2000 and 2000–2001). Each trial tested the phytotoxicity of soybeans to 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate) and 64 g a.i./ha (two-fold rate) in side-by-side treatment comparisons.

A mean injury rating of 0% was reported when soybeans were seeded in sites treated the previous year with one-fold and two-fold rates of Tribute™ Solo 32DF. The mean yield at the one-fold rate was 106.2% of a weed-free check (n = 6), and 98.6% of a weed-free check (n = 6) in sites previously treated with the two-fold rate of Tribute™ Solo 32DF.

The data support the recropping of soybeans at the proposed interval of 10 months following an application of Tribute™ Solo 32DF.

7.3.1.5 Alfalfa

A recropping interval of 10 months is proposed for alfalfa following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

A total of five trials were conducted in southern Ontario and northern U.S. border states over one reporting period (2000–2001). Alfalfa was seeded into sites treated with 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate), 56 g a.i./ha Tribute™ Solo 32DF (1.75-fold rate), and 64 g a.i./ha (two-fold rate) the previous year, with yield reported in two trials.

The mean injury rating at the one-fold rate was 0% (n = 2) (36–72 DAP), at the 1.75-fold rate was 5.7% (n = 3) (42–51 DAP) with one trial reporting 17% injury (42 DAP) without explanation, and at the two-fold rate was 0.7% (n = 2) (71–72 DAP).

The mean yield at the one-fold rate was 87% of a weed-free check (n = 2), and 88% of a weed-free check (n = 2) in sites previously treated with the two-fold rate of Tribute™ Solo 32DF.

The data are insufficient to draw a scientific conclusion as to the tolerance of alfalfa seeded in sites previously treated with Tribute™ Solo 32DF at the proposed replanting interval.

7.3.1.6 Spring barley

A recropping interval of 10 months is proposed for spring barley following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

Yield was reported in all four trials conducted in southern Ontario over two reporting periods (1999–2000 and 2000–2001). Barley was seeded in sites treated with 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate) and 64 g a.i./ha (two-fold max. rate) the previous year. Each trial tested the phytotoxicity of barley to the one-fold and two-fold rates of Tribute™ Solo 32DF in side-by-side treatment comparisons.

The mean injury rating at one-fold and two-fold rates of Tribute™ Solo 32DF was 0% (*n* = 4) (16–71 DAP). The mean yield at the one-fold rate was 110.0% of a weed-free check (*n* = 4) and at the two-fold rate was 112.0% of a weed-free check (*n* = 4).

The data support the recropping of spring barley at the proposed interval of 10 months following an application of Tribute™ Solo 32DF.

7.3.1.7 Dry common beans

A recropping interval of 10 months is proposed for dry common beans following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

The phytotoxicity levels tested over one reporting period [2000–2001] for kidney beans (four trials), navy beans (five trials), and cranberry beans (three trials) in the year following an application of the one-fold rate, 1.75-fold rate, and two-fold rate Tribute™ Solo 32DF.

The kidney bean trials reported 0% injury (*n* = 4) at the 1.75-fold rate with no yield data.

The navy bean trials reported 0% injury (*n* = 3) at the one-fold rate, with a yield of 90% of a weed-free check (*n* = 1). In the site treated at the 1.75-fold rate, the mean crop injury was 0% (*n* =2) with no yield reported. In the site treated at the two-fold rate, the mean crop injury was 2.9% (*n* = 3) with a yield of 100% of a weed-free check (*n* = 1).

The cranberry bean trials reported 5.2% injury (*n* = 3) at the one-fold rate, with a yield of 90% of a weed-free check (*n* = 1). In the site treated at the two-fold rate, the mean crop injury was 5.1% (*n* = 3) with a yield of 100% of a weed-free check (*n* = 1).

Due to the limited number of dry common bean varieties tested and the potential for varietal differences in the level of tolerance, only the varieties that have demonstrated acceptable crop tolerance will be acceptable to appear on the Tribute™ Solo 32DF label. This labelling approach is consistent with Regulatory Directive DIR93-14, *Classification of Beans on Labels and Research Requirements*. If subsequent crop tolerance information is provided that indicates there is no varietal difference among dry common beans in terms of tolerance to Tribute™ Solo 32DF, this limitation may be removed.

The data support the recropping of dry common beans (kidney, navy, cranberry) at the proposed interval of 10 months following an application of Tribute™ Solo 32DF.

7.3.1.8 Spring canola

A recropping interval of 10 months is proposed for spring canola following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

Six trials were conducted in southern Ontario and northern U.S. border states over two reporting periods (1999–2000 and 2000–2001). Canola was seeded in sites treated with 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate), 56 g a.i./ha Tribute™ Solo 32DF (1.75-fold max. rate), and 64 g a.i./ha (two-fold max. rate) the previous year, with yield reported in two trials.

The mean injury rating at the one-fold rate was 0% (n = 4) with a yield of 114% of a weed-free check (n = 2). In the site treated at the 1.75-fold rate, the mean crop injury was 5% (n = 2) with no yield reported. In the site treated at the two-fold rate, the mean crop injury was 0% (n = 4) with a yield of 134% of a weed-free check (n = 2).

The data support the recropping of spring canola at the proposed interval of 10 months following an application of Tribute™ Solo 32DF.

7.3.1.9 Red clover

A recropping interval of 10 months is proposed for red clover following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

Recropping data were not provided. Thus, the data are insufficient to draw a scientific conclusion as to the tolerance of red clover seeded in sites previously treated with Tribute™ Solo 32DF at the proposed replanting interval.

7.3.1.10 Spring oats

A recropping interval of 10 months is proposed for spring oats following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

Three trials were conducted in southern Ontario over one reporting period (2000–2001). Spring oats were seeded in sites treated with 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate) and 64 g a.i./ha (two-fold max. rate) the previous year, with yield reported in two trials.

The mean injury rating at the one-fold rate was 0% (n = 3) with a yield of 110% of a weed-free check (n = 2). In the site treated at the two-fold rate, the mean crop injury was 0.4% (n = 3), with a yield of 113% of a weed-free check (n = 2).

The data support the recropping of spring oats at the proposed interval of 10 months following an application of Tribute™ Solo 32DF.

7.3.1.11 Sugar beets

A recropping interval of 10 months is proposed for sugar beets following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

Six trials were conducted in southern Ontario and northern U.S. border states over two reporting periods (1999–2000 and 2000–2001). Sugar beets were seeded into sites treated with 32 g a.i./ha Tribute™ Solo 32DF (one-fold rate), 56 g a.i./ha Tribute™ Solo 32DF (1.75-fold rate) and 64 g a.i./ha (two-fold rate) the previous year, with yield reported in two trials.

The mean injury rating at the one-fold and two-fold rates was 0% (n = 2) (20–28 DAP), while at the 1.75-fold rate was 4.5% (n = 4) (14–26 DAP).

The mean yield at the one-fold and two-fold rate of Tribute™ Solo 32DF was 108% of a weed-free check (n = 2).

The data are insufficient to draw a scientific conclusion as to the tolerance of sugar beets seeded in sites previously treated with Tribute™ Solo 32DF at the proposed replanting interval.

7.3.1.12 Timothy

A recropping interval of 10 months is proposed for timothy following an application of 32 g a.i./ha Tribute™ Solo 32DF (one-fold max. rate).

Recropping data were not provided. Thus, the data are insufficient to draw a scientific conclusion as to the tolerance of timothy seeded in sites previously treated with Tribute™ Solo 32DF at the proposed replanting interval.

7.4 Sustainability

7.4.1 Survey of alternatives

7.4.1.1 Non-chemical control practices

Non-chemical means of weed control include cultivation and crop rotation. The post-emergence use of Tribute™ Solo 32DF in conventionally tilled field corn would not exclude the use of cultivation. Recropping data indicate that numerous crops may be planted the year following application of Tribute™ Solo 32DF.

7.4.1.2 Chemical control practices

Application of Tribute™ Solo 32DF would not exclude the sequential use of other herbicides with different modes of action for control of annual and perennial weeds not controlled by the product alone.

There are numerous post-emergence grass and broadleaf weed herbicides, with different modes of action, that may be used alone or in various tankmix combinations in field corn. Alternative active ingredients include, but are not limited to, diflufenzopyr/dicamba (Group 4), dimethenamid (Group 15), flumetsulam/clopyralid (Groups 2 & 4), metolachlor (Group 15), s-metolachlor (Group 15), nicosulfuron (Group 2), nicosulfuron/rimsulfuron (Group 2), rimsulfuron (Group 2), pendimethalin (Group 3), 2,4-D (Group 4), MCPA (Group 4), bromoxynil (Group 6), and bentazon (Group 6). These are presently commercially available.

7.4.2 Contribution to risk reduction

Tribute™ Solo 32DF will provide control of certain broadleaf and grassy weeds in field corn at a low rate of a.i. per hectare.

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

To address the issue of development of herbicide resistance, the Tribute™ Solo 32DF label will be amended to include the following resistance-management statement as outlined on the Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*:

> HERBICIDE RESISTANCE MANAGEMENT:
> For resistance management, Tribute™ Solo 32DF is a Group 2 herbicide. Any weed population may contain or develop plants naturally resistant to Tribute™ Solo 32DF and other Group 2 herbicides. The resistant biotypes may dominate the weed population if these herbicides are used repeatedly in the same field. Other resistance mechanisms that are not linked to site of action but are specific to individual chemicals, such as enhanced metabolism, may also exist. In order to delay herbicide resistance, the following appropriate resistance-management strategies should be used:
>
> 1. Where possible, rotate the use of Tribute™ Solo 32DF or other Group 2 herbicides with different herbicide groups that control the same weeds in a field.
>
> 2. Use tank mixtures with herbicides from a different group when such use is permitted.
>
> 3. Herbicide use should be based on an integrated pest management program that includes scouting and historical information related to herbicide use and crop rotation, and considers tillage (or other mechanical), cultural, biological, and other chemical control practices.

4. Monitor treated weed populations for resistance development.

5. Prevent movement of resistant weed seeds to other fields by cleaning harvesting and tillage equipment and planting clean seed.

6. Contact your local extension specialist or certified crop advisors for additional pesticide resistance-management and integrated weed-management recommendations for specific crops and weed biotypes.

7. For further information or to report suspected resistance, contact your local Bayer representative, or call Bayer CropScience Inc. toll-free at 1 888 283-6847.

7.5 Conclusions

Tribute™ Solo 32DF is a selective herbicide for use as a post-emergence application to field corn grown in Eastern Canada utilizing conventional tillage systems, for the control of specific broadleaf and grass weeds. Tribute™ Solo 32DF must be applied with Hasten spray additive at 1.0% v/v (volume to volume) (i.e., 1 L Hasten/100 L spray solution) and 2.5 L/ha of 28% liquid nitrogen fertilizer in a minimum total spray volume of 150 L/ha with a maximum of one application per year using ground equipment only.

There are two application rates:

- When applied at a rate of 50 g of product/hectare (ha) [16 g a.i./ha], Tribute™ Solo 32DF is effective for the control of quackgrass (*Agropyron repens*), fall panicum (*Panicum dichotomiflorum*), green foxtail (*Setaria viridus*), proso millet (*Panicum miliaceum*), lamb's quarters (*Chenopodium album*), redroot pigweed (*Amaranthus retroflexus*), and velvetleaf (*Abutilon theophrasti*).

- When applied at a rate of 100 g of product/ha (32 g a.i./ha), Tribute™ Solo 32DF is effective for the control of yellow foxtail (*Setaria glauca*) and the suppression of large crabgrass (*Digitaria saguinalis*).

Data indicated that a rate lower than 32 g a.i./ha may provide acceptable control of common ragweed (*Ambrosia artemisiifolia*). Additional data will be requested in order to establish the lowest effective rate for control of this weed. Field corn, soybeans, spring barley, spring canola, spring oats, and dry common beans (kidney, navy, cranberry) may be planted 10 months after application of Tribute™ Solo 32DF.

8.0 Toxic Substances Management Policy considerations

During the review of iodosulfuron-methyl-sodium and the EP Tribute™ Solo 32DF Herbicide, the PMRA has taken into account the federal Toxic Substances Management Policy[1] and has followed its Regulatory Directive DIR99-03[2]. It has been determined that this product does not meet TSMP Track 1 criteria because:

- Iodosulfuron-methyl-sodium does not meet the criteria for persistence. Its values for half-life in water (12.5–19 days), soil (4–22 days), and sediment (13.5–23.3 days in whole water/sediment system) are below the TSMP Track 1 cut-off criteria for water (≥182 days), soil (≥182 days), and sediment (≥365 days). Iodosulfuron-methyl-sodium is not expected to volatilize from water or moist soil surfaces.

- Iodosulfuron-methyl-sodium is not bioaccumulative. Studies have shown that the octanol–water partition coefficient (log K_{ow}) is −0.70, which is below the TSMP Track 1 cut-off criterion of ≥5.0.

- Iodosulfuron-methyl-sodium does not meet the criteria for toxicity (see sections 6.1 and 6.2).

- Metsulfuron-methyl, a transformation product of iodosulfuron-methyl-sodium, had a half-life of 99 days in an aerobic soil biotransformation study and a half-life of 55 days in aerobic water/sediment biotransformation study. Metsulfuron-methyl is also persistent in anaerobic aquatic water/sediment systems with a half-life of 291 days. However, metsulfuron-methyl does not meet the TSMP Track 1 criteria since the log K_{ow} of metsulfuron-methyl (log K_{ow} = −1.74) is below the TSMP Track 1 cut-off criterion of ≥5.0; thus, it is not bioaccumulative.

- The data for the transformation products, AE F161778 (half-life in soil of 35 days) and AE 0014966 (half-life in whole water/sediment system of 20.8 days), indicate that they do not meet the criteria for persistence as the reported half-lives are below the TSMP Track 1 cut-off criteria for water (≥182 days) and soil (≥182 days).

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1 The federal Toxic Substances Management Policy is available through Environment Canada's website at: www.ec.gc.ca/toxics

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

- Available data are insufficient to assess the major transformation products AE F059411, AE 000119 and AE 0034855.

- Iodosulfuron-methyl-sodium (technical grade) does not contain any by-product or microcontaminant that meets the TSMP Track 1 criteria. Impurities of toxicological concern are not expected to be present in the raw materials, nor are they expected to be generated during the manufacturing process.

- The formulated product does not contain any formulant known to contain a TSMP Track 1 substance.

9.0 Regulatory decision

9.1 Regulatory decision

Iodosulfuron-methyl-sodium and the EP Tribute™ Solo 32DF have been granted temporary registration for use on field corn, under Section 17 of the *Pest Control Products Regulations*, subject to the following requirements:

- Revised specifications for iodosulfuron-methyl-sodium technical if the full scale batch data are not in agreement with the data on the product specification forms for the active substance and all impurities present at >0.1% in the TGAI;

- Analytical data from five batches of iodosulfuron-methyl-sodium technical from full scale production, which was expected to be available in mid-2003;

- Revised Product Specification Form for Tribute™ Solo 32DF if the purities of the active ingredients in iodosulfuron-methyl-sodium technical and in foramsulfuron technical are changed based on the full scale production batch data;

- A rat 21–28 day repeat-dose dermal toxicity study to further characterize potential hazard and risk via the dermal route of exposure;

- A mouse oncogenicity study with an adequately high dose;

- A rabbit developmental toxicity study with an adequately high dose;

- An acute neurotoxicity study in rats to confirm clinical signs of neurotoxicity noted in the toxicology database;

- The octanol–water partition coefficient (log K_{ow}) for the transformation products AE F059411, AE 000119, and AE 0034855;

- An environmental analytical method to determine the residues of iodosulfuron-methyl-sodium and the major metabolites (if any) in the animal matrix;

- A minimum of five additional efficacy trials in order to establish the lowest effective rate (LER) for Tribute™ Solo 32DF to control common ragweed in field corn. (Each trial must include the currently accepted application one-fold rate of 32 g a.i./ha and reduced rates of 0.5-fold and 0.75-fold in order to provide a direct head-to-head treatment comparison. Visual assessments of weed control should be conducted throughout the season following application, with evaluations at 7–14, 21–35 and 42–56 days after treatment.)

List of abbreviations

µg	micrograms
µL	micro litre
AD	administered dose
ADI	acceptable daily intake
a.i.	active ingredient
ALAT	alanine aminotransferase
ALP	alkaline phosphatase
ALS	acetolactate synthase
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
ASAT	aspartate aminotransferase
AUC	area under the curve
bw	body weight
bwg	body-weight gain
BWI	body weight per individual
CAS	Chemical Abstracts Service
CD	cluster of differentiation (for naming cell surface molecules expressed on lymphocytes in immunology)
cm	centimetre(s)
Cmax	maximal plasma concentration(s)
CPK	creatine phosphokinase
d	day(s)
DAP	days after planting
DAT	days after treatment
DI	daily intake
DNA	deoxyribonucleic acid
dw	dry weight
EC_{50}	effects concentration 50%
EEC	expected environmental concentration
EP	end-use product
F	female(s)
FC	food consumption
F_0	parental animals
F_1	1^{st} generation offspring
F_2	2^{nd} generation offspring
fw	fresh weight
g	gram
GC	gas chromatography
GD	gestation day(s)
GSD	geometric standard deviation
h	hour
ha	hectare
HCT	hematocrit
HDPE	high-density polyethylene

HDT	highest dose tested
HGB	hemoglobin
HPLC	high-performance liquid chromatography
ILV	independent laboratory validation
K_d	adsorption quotient
kg	kilogram
K_{oc}	adsorption quotient normalized to organic carbon
K_{ow}	octanol–water partition coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LER	lowest effective rate
LOAEL	lowest observed adverse effect level
LOEC	lowest observed effect concentration
LOQ	limit of quantitation
M:E	myeloid to erythroid ratio
M	male(s)
MAS	maximum average score
mg	milligram
MIS	maximum irritation score
mL	millilitre
M/L/A	mixer/loader/applicator
mm Hg	millimetre of mercury
MMAD	mass median aerodynamic diameter
MOE	margin of exposure
MOS	margin of safety
MRL	maximum residue limit
MS	mass spectrometry
MTD	maximum tolerated dose
MTDB	maximum theoretical dietary burden
MWHC	maximum water holding capacity
n	number
NAFTA	North American Free Trade Agreement
ng	nanogram
nm	nanometre
NOAEL	no-observed adverse effect level
NOEC	no-observed effects concentration
O.C.	organic carbon
P_1	first parental generation
P_2	second parental generation
Pa	pascal
PCP	Pest Control Products
PHED	Pesticide Handlers Exposure Database
PHI	pre-harvest interval
pKa	dissociation constant

PMRA	Pest Management Regulatory Agency
ppm	parts per million
RAC	raw agricultural commodity
RBC	red blood cell
ROC	residue of concern
ROMD	repeat oral mid dose
RPLC	reverse-phase liquid chromatography
RSD	relative standard deviation
SF	safety factor
SOHD	single oral high dose
SOLD	single oral low dose
sp.	species
SU	sulfonylurea
TGAI	technical grade active ingredient
TRR	total radioactive residue
TS	test substance
TSMP	Toxic Substances Management Policy
TWG	Technical Working Group
USC	Use Site Category
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Administration
UAN	urea ammonium nitrate
UV	ultraviolet
v/v	volume-to-volume ratio
WG	wettable dispersible granule
WDG	water dispersible granule

Appendix I Summary tables

Table 1 Methods for analysis of the active substance as manufactured

Product	Analyte	Method type	Linearity range	Recovery (%)	RSD (%)	LOQ (%)	Method
Technical	iodosulfuron-methyl-sodium	RPLC-UV at 230 nm	20–120 mg/mL	N/A	0.37	Not required	Accepted
Technical	Major impurities	RPLC-UV at 230 nm	0.03–1.6%	94–104	1.2–5.8	0.1	Accepted

Table 2 Methods for formulation analysis

Product	Analyte	Method ID	Method type	Linearity range (mg/100 ml)	Mean recovery [% (*n*)]	RSD [% (*n*)]	Method
Tribute™ Solo 32DF	Iodosulfuron-methyl	AL054/99-0	RPLC/UV at 233 nm	1.58–10.54	99.9 (5)	0.36 (5)	Accepted
	Foramsulfuron			1.58–10.54	99.9 (5)	0.29 (5)	Accepted

Table 3 Methods for environmental residue analysis

Validation data for environmental residue methods											
Matrix	Method ID	Method	Spike level	Overall mean recovery [% (*n*)]						LOQ	Method [3]
				AE F115008	RSD (%)	AE F075736	RSD (%)	AE F059411	RSD (%)		
Soil	DCM F 06/97-0[1]	LC-UV	0.001–0.05 mg/kg	88 (15)	10	86 (20)	10	Not analysed		0.001 mg/kg	A
	RAM BY/01/99[2]	LC-MS	0.5–10 ppb	98 (3)	13	105 (3)	15.2			0.5 ppb	A
		GC/NPD						89 (3)	16.8		
Sediment	Method RAM BY/01/99 could be used for the following reasons: 1. Sediment/water metabolism studies demonstrate that the active substance and the metabolites remain in water and are not readily absorbed to sediment. 2. The principal degradation products in aerobic sediment/water systems is AE F075736 (metsulfuron-methyl). 3. The extraction solvent used in RAM BY/01/99 is an aqueous mixture. Therefore the extraction efficiency for sediment should be comparable to if not better than that for soil sample.										A
Drinking water	EM F01/98-0	LC-UV	0.1 & 1.0 µg/L	97.5 (10)	6	92 (10)	6.5	Not analysed		0.1 µg/L	A
Surface water			0.1 & 1.0 µg/L	95 (10)	7.5	Not analysed		Not analysed			A
Maize kernel	EM F02/99-0	LC-UV	0.1 & 1.0 mg/kg	93 (10)	6	Not analysed		Not analysed		0.01 mg/kg	A

Validation data for environmental residue methods											
Matrix	**Method ID**	**Method**	**Spike level**	**Overall mean recovery [% (*n*)]**						**LOQ**	**Method [3]**
				AE F115008	**RSD (%)**	**AE F075736**	**RSD (%)**	**AE F059411**	**RSD (%)**		
Animal matrix	The waiver requested based on the K_{ow} value being <3 at pH 4–10 was not acceptable.										R

[1] Method used in the "uniquely Canadian" studies

[2] Method used in North American soil

[3] A = acceptable, R = required but not submitted

Table 4 Toxicology

Metabolism (rats)—Iodosulfuron-methyl-sodium technical

Absorption: rapidly and extensively absorbed following oral administration: greater than 93% of AD absorbed following SOLD, greater than 70% of AD absorbed following SOHD and greater than 79% of AD absorbed following ROMD (100 mg/kg bw); Cmax achieved within 3.6–6.0 h following SOLD (10 mg/kg bw) and within 7.3–7.6 h following SOHD (500 mg/kg bw). A comparison of the AUC following oral and IV low dose indicates a calculated absorption rate or bioavailability of approx. 86 and 63% of AD for males and females, respectively.
Distribution: highest residue levels observed in plasma and whole blood; however, mean recovery of radioactivity in tissues/carcass at 72 h after dosing was less than 0.5% of AD for all dose groups, indicating little potential for accumulation.
Metabolism: majority of AD was excreted as unchanged parent compound, approximately 48.7–86.3% of AD in urine and approximately 1.1–11.1% of AD in feces. Major metabolites were identified as AE F145740 (approx. 0.9–4.5% of AD; 4-iodo-2-[3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)ureidosulfonyl] benzoic acid), AE F148741 (approx. 1.5–8.2% of AD; methyl 2-[3-(4-hydroxy-6-methyl-1,3,5-triazin-2-yl)ureidosulfonyl]-4-iodobenzoate) and AE F168532; (approx. 0.3-6.6% of AD; methyl 2-[3-(4-hydroxymethyl-6-methoxy-1,3,5-triazin-2-yl)ureidosulfonyl]-4-iodobenzoate). Each of these metabolites was present in both urine and feces; remaining metabolites each accounted for less than 0.6% of AD.
Excretion: major route of excretion was via urine with majority of AD being eliminated within 24 h; generally complete within 72 h. Biphasic elimination showing fast initial elimination followed by slower terminal phase. Following SOLD, there was no sex-related difference in the pattern of excretion with approx. 93.9–97.6% of AD being recovered in urine and approx. 4.3–7.3% being recovered in feces. Following SOHD, urinary excretion was reduced and there were slight sex-related differences: urinary excretion accounted for approx. 69.1–71.5% of AD in males and approx. 78.4–85.5% of AD in females; fecal excretion accounted for approx. 24.5–26.5% of AD in males and approx. 14.9–17.0% of AD in females. Radioactivity was not detected in exhaled air or organic volatiles.

Absorption, plasma kinetics, distribution, and elimination in dogs were comparable to those in rats. Overall, the studies show no significant difference in the metabolic profile between the rat and the dog.

Study	Species, strain and doses	NOAEL & LOAEL (mg/kg bw/day)	Target organ, significant effects, comments
Acute studies—iodosulfuron-methyl-sodium technical			
Oral—rat	Hoe: WISKf (SPF71) Wistar rats 5 animals/sex **Dose levels:** 1600, 2000, and 3150 mg/kg bw	**LD_{50}** males = 2947 mg/kg bw females = 2448 mg/kg bw combined = 2678 mg/kg bw	Mortality observed in 4 of 10 animals at 2000 mg/kg bw and 6 of 10 animals at 3150 mg/kg bw; deaths between days 1 and 4. Numerous treatment-related clinical observations; necropsy findings included feed mash and test compound found in the stomach, yellowish mucus in intestinal tract, and general autolysis. No change in bwg in either sex. **Low toxicity**
Dermal—rat	Hoe: WISKf (SPF71) Wistar rats 5 animals/sex **Dose level:** 2000 mg/kg bw	**LD_{50}** > 2000 mg/kg bw for both sexes	No mortality; no treatment-related clinical signs, necropsy findings or change in bw in either sex. Signs of skin irritation (erythema; dry, rough skin with fine and course scales) observed on days 2–3, but not present by days 5–7. **Low toxicity**
Inhalation (4-hour nose only)—rat	Hoe: WISKf (SPF71) Wistar rats 5 animals/sex **Dose levels**: Analytical: 2.81 mg/L air Nominal: 2–3 mg/L air MMAD: 2.62–3.04 µm GSD: 2.04–2.11 µm	LC_{50} greater than 2.81 mg/L air for both sexes	No mortality; no treatment-related change in bw in either sex. Impaired breathing, red encrusted noses, and narrowed palpebral fissures noted during exposure, resolved one day after exposure. **Low toxicity**
Eye irritation—rabbit	New Zealand albino rabbits 3 females **Dose level**: 0.1 g	MIS: 32.3/110 at 1 h MAS (for 24, 48, and 72 h): 16.7/110.	At 1 h, conjunctival redness (grade 1–2), conjunctival chemosis (grade 1–3) and conjunctival discharge (grade 1–2) in 3 of 3 animals. Continued to be observed in one animal at 72 h; completely resolved by 7 d. **Moderately irritating**
Dermal irritation—rabbit	New Zealand white rabbits 3 females **Dose level:** 0.5 g	MIS: 0.33/8 at 1 h MAS (for 24, 48, and 72 h): 0.11/8.	Initially, one animal exhibited slight erythema (grade 3); completely resolved by 48 h. None of the test animals exhibited edema. **Minimally irritating**

Study	Species, strain and doses	NOAEL & LOAEL (mg/kg bw/day)	Target organ, significant effects, comments
Dermal sensitization (guinea pig maximization method)	Pirbright-white guinea pigs 20 females in test group and 10 females in control group **Dose level:** 0.5 mL of 50% w/v mixture of TS in isotonic saline for both dermal induction and challenge treatments	No sign of dermal irritation was observed in any treated or control animal at 24 or 48 h following dermal challenge treatment.	**Not a dermal sensitizer**
Acute studies—Tribute™ Solo 32DF herbicide			
Oral	5 Hsd: Sprague-Dawley (CD) rats/sex/dose **Dose level:** 2000, 2600 (F), 3600 (M), 5000 mg/kg bw	LD_{50} = 3479 mg/kg bw in females	80% mortality at 5000 mg/kg bw by 48 h. Piloerection, hunched posture, abnormal gait, ungroomed appearance, and lethargy observed at all dose levels; resolved by day 9. **Low toxicity**
Dermal	5 Hsd: Sprague-Dawley (CD) rats/sex **Dose level:** 5000 mg/kg bw	LD_{50} > 5000 mg/kg bw	No mortality and no gross necropsy finding or change in bw; local irritation, resolved by day 8; edema resolved by day 4. **Low toxicity**
Inhalation (4-h nose only)	5 Sprague-Dawley (CD) rats/sex **Dose level:** 4.69 mg/L (analytical)	LC_{50} > 4.69 mg/L	1 male and 1 female died; wet fur, respiratory abnormalities, hunched posture; resolved by day 4. Necropsy findings include enlarged lungs with dark foci (1 animal), or red lungs with dark liver (2 animals); no change in bw. **Low toxicity**
Eye irritation	New Zealand white rabbits 3 males **Dose level:** 0.1 mL	MIS: 16.33/110 at 1 h MAS (24, 48, 72 h): 7.44/110	**Mildly irritating**
Skin irritation	New Zealand white rabbits 3 males **Dose level:** 0.5 mL	MIS: 3.33/8 at 1 h MAS (24, 48, 72 h): 0.56/8	**Moderately irritating**

Study	Species, strain and doses	NOAEL & LOAEL (mg/kg bw/day)	Target organ, significant effects, comments
Dermal sensitivity—Buehler method	Dunkin-Hartley guinea pigs (20 females in test group, 10 in control group) **Dose level:** 0.5 mL of 70% TS for induction and 25% TS in sterile water for challenge	Positive	**Potential skin sensitizer**
Short-term toxicity—iodosulfuron-methyl-sodium technical			
90-day dietary—mouse	[Crl:CD-1(ICR)BR] 10 mice/sex/dose **Dose levels:** 0, 700, 2100, or 7000 ppm (equal to 0/0, 119/139, 332/401, and 1311/1332 mg/kg bw/d in M/F)	**NOAEL:** **M:** 700 ppm (119 mg/kg bw/d) **F:** 2100 ppm (401 mg/kg bw/d) **LOAEL:** **M:** 2100 ppm (332 mg/kg bw/d) **F:** 7000 ppm (1332 mg/kg bw/d)	≥**2100 ppm**: increased liver wt (M); centrilobular hepatocellular enlargement (M); lipofuscin deposition possibly due to degradation of subcellular organelles in cytoplasm (M); centrilobular fat deposition (M) **7000 ppm:** lower bw/bwg (M); increased ALP (M); increased liver wt (F); cream areas/foci in liver (M/F); centrilobular hepatocellular enlargement (F); vacuolation of centrilobular hepatocytes due to fat deposition (M/F); focal necrosis (M/F) **Control wk 13 bw**: M: 41.4 g F: 30.5 g **Control wk 13 daily food consumption**: M: 6.2 g/animal; F: 4.8 g/animal
90-day dietary—rat	Sprague-Dawley [Crl:COBS CD (SD) BR] 10 rats/sex/dose **Dose levels:** 0, 200, 1000, 5000, or 10 000 ppm (equal to 0/0, 13.8/15.4, 67/74, 347/388, and 686/790 mg/kg bw/d for M/F)	**NOAEL:** 1000 ppm (67/74 mg/kg bw/d for M/F) **LOAEL:** 5000 ppm (347/388 mg/kg bw/d for M/F)	**5000 ppm:** lower bw/bwg (both sexes) **10 000 ppm:** lower bw/bwg (both sexes) **Control wk 13 bw:** M: 513 g F: 316 g **Control wk 13 daily food consumption:** M 27 g/animal F: 19 g/animal

Study	Species, strain and doses	NOAEL & LOAEL (mg/kg bw/day)	Target organ, significant effects, comments
90-day dietary—dog	Beagle 4 dogs/sex/dose **Dose levels:** 0, 200, 1200, or 7200 ppm (equal to 0/0, 8.1/8.4, 49/51, and 301/317 for M/F)	**NOAEL:** 200 ppm (8.1/8.4 mg/kg bw/d in M/F) **LOAEL:** 1200 ppm (49/51 mg/kg bw/d in M/F)	≥**1200 ppm:** decreased RBC, HGB, and HCT (M) and percentage late normoblasts (M/F); generalized hematopoietic hyperplasia bone marrow (F); decreased eosinophils (M/F); increase immature granulocytes bone marrow smear (F); increased ASAT, ALAT and CPK activity (M). **7200 ppm:** hunched posture, reduced activity, unsteady gait and prostration (M/F); conjunctivitis (M/F); decreased bw, bwg, and food efficiency (M/F); decreased RBC, HGB, and HCT (F), erythroblasts (M/F), proerythroblasts (F), and increased myeloid/erythroid ratio (M/F), generalized hematopoietic hyperplasia in bone marrow (M) and extramedullary hematopoiesis liver and spleen (M/F); decreased basophils (M), myeloblasts (F), and lymphocytes (F), and increased immature granulocytes in bone marrow smear (M); increased ALAT, ASAT and CPK activity (F); decreased total protein, albumin and A/G ratio (M); decreased creatinine (M/F); increased liver, spleen and/or and kidney wt (M/F); pigmentation Kupffer cells (M/F); slight centrilobular congestion (M); subscapular tubular necrosis with cyst formation (M), interstitial nephritis (F) and hyaline droplets (F) in kidney; atrophy lymphoid tissue in spleen (M) In the absence of any indication of peripheral blood loss via hemolysis or hemorrhaging, hematological and histopathological findings indicative of anemia, noted in males at 1200 ppm and in both sexes at 7200 ppm, may be due to interference of the test substance with cell maturation in hematopoietic tissue.
12-month dietary—dog	Beagle, purebred 6 dogs/sex/dose Dose **levels:** 0, 30, 200, or 1200 ppm (equal to 0/0, 1.03/1.08, 7.37/7.25, and 41.8/43.7 mg/kg bw/d for M/F)	**NOAEL:** **M**: 1200 ppm (41.8 mg/kg bw/d) **F**: 200 ppm (7.25 mg/kg bw/d) **LOAEL:** **M**: not determined **F**: 1200 ppm (43.7 mg/kg bw/d)	**1200 ppm:** increased incidence of peripheral swelling of spleen (F); generalized hematopoietic hyperplasia bone marrow (F); subscapular sinusoidal congestion and capsular fibrosis of the spleen (F)

Study	Species, strain and doses	NOAEL & LOAEL (mg/kg bw/day)	Target organ, significant effects, comments
Chronic toxicity and oncogenicity—iodosulfuron-methyl-sodium technical			
80-week dietary—mouse	Sprague-Dawley CD-1 50–60 mice/sex/dose **Dose levels:** 0, 35, 350 or 1750 ppm (equal to 0/0, 5.15/5.72, 54.2/57.6 and 279/277 mg/kg bw/d for M/F)	**NOAEL:** 350 ppm (54.2/57.6 mg/kg bw/d for M/F) **LOAEL:** 1750 ppm (279/277 mg/kg bw/d for M/F)	**1750 ppm:** increased liver wt (M/F). Centrilobular mononuclear infiltration (M/F), centrilobular hepatocyte enlargement (M/F), pigmentation of centrilobular hepatocytes (M) and centrilobular fat deposition (M) No evidence to indicate any carcinogenic potential of iodosulfuron at any dose level up to and including 1750 ppm, the HDT; however, dosing was not considered adequate since the animals were not tested at a high enough dose level to cause significant toxicity for evaluation of carcinogenicity in mice.
2-year dietary—rat	Sprague-Dawley Crl:CD 70 rats/sex/dose **Dose levels:** 0, 70, 700, or 7000 ppm (equal to 0/0, 2.96/3.91, 29.7/39.1, and 331/452 mg/kg bw/d for M/F)	**NOAEL:** 700 ppm (29.7/39.1 mg/kg bw/d for M/F) **LOAEL:** 7000 ppm (331/452 mg/kg bw/d for M/F)	**7000 ppm:** lower bw, bwg, and food efficiency (M/F); lower food consumption (M); increased incidence of wasted external appearance (M/F). No evidence to indicate any carcinogenic potential of iodosulfuron at any dose level up to and including 7000 ppm, the HDT. Dosing was considered adequate based on treatment-related decrease (greater than 10%) in bw/bwg in both sexes at 7000 ppm (HDT).

Study	Species, strain and doses	NOAEL & LOAEL (mg/kg bw/day)	Target organ, significant effects, comments
Reproduction and developmental toxicity—iodosulfuron-methyl-sodium technical			
Multi-generation—rat	Hoe:WISKf(SPF71) 25 rats/sex/dose **Dose levels:** 0, 50, 500 or 5000 ppm (equal to 0/0, 3.43/3.90, 34.2/39.7 and 346/390 mg/kg bw/d)	**Parental**: **NOAEL:** 5000 ppm (346/390 mg/kg bw/d in M/F) **LOAEL:** not determined **Offspring** **NOAEL:** 500 ppm (34.2/39.7 mg/kg bw/d for M/F) **LOAEL:** 5000 ppm (346/390 mg/kg bw/d for M/F) **Reproductive** **NOAEL:** 5000 ppm (346/390 mg/kg bw/d for M/F) **LOAEL:** not determined	**Parental:** There was no adverse treatment-related effect in either generation. **Offspring:** **5000 ppm:** decreased pup survival and decreased mean litter size in F_2 pups on lactation days 0 and 4 **Reproductive:** There was no adverse treatment-related effect in either generation. Neonates appear to be both qualitatively and quantitatively more sensitive than parental animals.
Developmental toxicity—rat	Wistar [Hoe:WISKf(SPF71)] 23 mated female rats/dose **Dose Level:** 0, 100, 315, or 1000 mg/kg bw/d.	**Maternal**: **NOAEL:** 315 mg/kg bw/d **LOAEL:** 1000 mg/kg bw/d **Developmental**: **NOAEL:** 315 mg/kg bw/d **LOAEL:** 1000 mg/kg bw/d	**Maternal:** **1000 mg/kg bw/d:** increased salivation during GD 8–17. **Developmental:** **1000 mg/kg bw/d:** increased incidence of weakly/non-ossification of sacral vertebral arch, individual skull bones, sternebrae, metacarpal 5 in forepaw and phalanx III of 1st to 5th toe of hindpaw; these findings generally within historical control range; however, when considered collectively they indicate delay in skeletal development at this dose level. Increased qualitative susceptibility of the fetus to in utero exposure. **Teratogenicity**: No evidence of any treatment-related irreversible structural change at any dose level up to and including 1000 mg/kg bw/d (limit dose); therefore, under the conditions of this study, iodosulfuron was not teratogenic.

Study	Species, strain and doses	NOAEL & LOAEL (mg/kg bw/day)	Target organ, significant effects, comments
Developmental toxicity—rabbit	15 adult female Chbb: HM(SPF) Kleinrusse (Himalayan) rabbits/dose **Dose levels:** 0, 25, 100, or 400 mg/kg bw/d.	**Maternal:** **NOAEL:** 400 mg/kg bw/d **LOAEL:** not determined **Developmental:** **NOAEL:** 400 mg/kg bw/d **LOAEL:** not determined	**Maternal:** No adverse treatment-related finding **Developmental:** No adverse treatment-related finding. Susceptibility of fetus to in utero exposure was not determined due to inadequate dosing. **Teratogenicity:** No evidence of any treatment-related irreversible structural changes; however, in the absence of any toxicologically relevant treatment-related maternal or developmental findings at 400 mg/kg bw/d (HDT), the dose levels were deemed inadequate for evaluation of teratogenicity in rabbits.
Genotoxicity—iodosulfuron-methyl-sodium technical			
Study	**Species and strain or cell type**	**Concentrations or doses**	**Results**
Bacterial reverse gene mutation assay (in vitro)	*Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537; *E. Coli* WP2 *uvr*A	0, 4, 20, 100, 500, 2500, or 5000 µg/plate with/without S9 metabolic activation	**Negative**
Gene mutations in mammalian cells (in vitro)	Chinese hamster lung V79 fibroblasts (at the HGPRT locus)	0, 100, 300, 600, 1200, 1600, 2000, or 2649 µg/mL without S9 metabolic activation 0, 300, 600, 1200, or 2649 µg/mL with S9 metabolic activation	**Negative**
In vitro chromosomal aberration assay	Chinese hamster lung V79 fibroblasts	0, 500, 1500, or 2649 µg/mL with S9 metabolic activation 0, 100, 250, or 500 µg/mL without S9 metabolic activation	**Negative**
Micronucleus assay (in vivo)	5 NMRI mice/sex/dose/sampling time (12, 24, and 48 h)	0, 200, 1000, or 2000 mg/kg bw	**Negative**

Study	Species and strain or cell type	Concentrations or doses	Results
Unscheduled DNA synthesis (in vitro)	Primary rat hepatocytes (male Wistar rat)	**Initial Assay**: 0, 0.01, 0.03, 0.1, 0.3, 1.0, 3.0, 10, 30, 100, 300, 1000, or 3000 µg/mL **Confirmatory Assay**: 0, 0.01, 0.03, 0.1, 0.3, 1.0, 3.0, 10, 30, 100, 300, 1000, 3000, or 5000 µg/mL	**Negative**

Acute studies—metabolites of iodosulfuron-methyl-sodium technical

Study	Species, strain, and doses	NOAEL & LOAEL (mg/kg bw/day)	Target organ, significant effects, comments
Acute Oral—rat AE F114368	5 Sprague-Dawley rats/sex **Dose Level**: 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw for both sexes	No mortality; no treatment-related clinical sign, necropsy finding, or change in bw. **Low toxicity**
Acute Oral—rat AE F143133	5 Sprague-Dawley rats/sex **Dose Level**: 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw for both sexes	No mortality; no treatment-related necropsy finding or change in bw. Clinical signs included decreased spontaneous activity, squatting posture, stilted/uncoordinated gait, and irregular respiration; resolved by day 3. **Low toxicity**
Acute Oral—rat AE C627337	5 Sprague-Dawley rats/sex **Dose Level**: 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw for both sexes	No mortality; no treatment-related clinical signs, necropsy findings, or change in bw. **Low toxicity**
Acute Oral—rat AE C627339	5 Sprague-Dawley rats/sex **Dose Level**: 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw for both sexes	No mortality; no treatment-related necropsy findings or change in bw. Clinical signs included hypoactivity, irregular respiration, uncoordinated gait, and increased salivation; resolved by day 3. **Low toxicity**

Study	Species, strain, and doses	NOAEL & LOAEL (mg/kg bw/day)	Target organ, significant effects, comments
Acute Oral—rat 2-amino-4-methoxy-6-methyl-S-triazine	5 Sprague-Dawley rats/sex/dose Dose **levels:** 2000, 2500, 2750, or 3000 mg/kg bw	**LD_{50} (95% C.I.)**: **M:** 3247.2 mg/kg bw (1156.5–9117.7) **F:** 2533.9 mg/kg bw (1885.5–3399.9) **Combined**: 2767.6 mg/kg bw (2031.1–3771.1)	Mortality observed in 4/10, 3/10, 4/10, and 7/10 animals at 2000, 2500, 2750, and 3000 mg/kg bw/d, respectively; all deaths occurring between days 1 and 5. Clinical signs observed at all dose levels; persisted in some animals throughout the study. Most animals lost weight during 1st week of study but regained loss by day 14. No gross lesion in animals sacrificed at scheduled termination. Animals dying during study exhibited necropsy findings in lungs, spleen, liver, stomach, intestines, and kidneys. **Low toxicity**
Acute dermal—rat AE F114844	Sprague-Dawley 5 rats/sex **Dose Level:** 2000 mg/kg bw	**LD_{50}** > 2000 mg/kg bw	No mortality; no treatment-related clinical signs, necropsy findings, or change in bw. **Low toxicity**
Mutagenicity studies—metabolites of iodosulfuron-methyl-sodium technical			
Study	**Species and strain or cell type**	**Concentrations or doses**	**Results**
Bacterial reverse gene mutation assay (in vitro) AE F059411	*Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537; *E. Coli* WP2 *uvr*A	0, 50, 160, 500, 1600, or 5000 µg/plate with/without S9 metabolic activation	**Negative**
Bacterial reverse gene mutation assay (in vitro) AE C627337	*Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537; *E. Coli* WP2 *uvr*A	0, 50, 160, 500, 1600, or 5000 µg/plate with/without S9 metabolic activation	**Negative**
Bacterial reverse gene mutation assay (in vitro) AE F114368	*Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537; *E. Coli* WP2 *uvr*A	0, 50, 160, 500, 1600, or 5000 µg/plate with/without S9 metabolic activation	**Negative**

Study	Species and strain or cell type	Concentrations or doses	Results
Bacterial reverse gene mutation assay (in vitro) AE F114844	*Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537; *E. Coli* WP2 *uvr*A	**Initial assay:** 0, 50, 160, 500, 1600, or 5000 µg/plate with/without S9 metabolic activation **Confirmatory assay:** *S. Typhimurium* strains at 0, 1.6, 5, 16, 50, 160, or 500 µg/plate with S9 metabolic activation and 0, 5, 16, 50, 160, 500, or 1600 µg/plate without S9 metabolic activation; *E coli* at 0, 50, 160, 500, 1600, or 5000 µg/plate with/without S9 metabolic activation	**Negative**
Bacterial reverse gene mutation assay (in vitro) AE F114133	*Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537; *E. Coli* WP2 *uvr*A	0, 50, 160, 500, 1600, or 5000 µg/plate with/without S9 metabolic activation	**Negative**
Bacterial reverse gene mutation assay (in vitro) AE F114368	*Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537; *E. Coli* WP2 *uvr*A	0, 50, 160, 500, 1600, or 5000 µg/plate with/without S9 metabolic activation	**Negative**

Table 5 Integrated food residue chemistry summary table

DIRECTIONS FOR USE OF IODOSULFURON-METHYL-SODIUM			
Crop	**Formulation/Type**	**Method/Timing**	**Rates**
Field corn	Tribute™ Solo 32DF	1–8 leaf stage or 5–6 visible collars (the leaf is counted once the next leaf is visible in the whorl).	One application of 1 g or 2 g iodosulfuron-methyl-sodium/ha + 1.0% v/v Hasten + 2.5L/ha of 28% UAN

Analytical methodology		
Parameters	**Plant matrices**	
Method ID	BY/02/99	
Type	Data-gathering and enforcement purposes (LC-MS only)	
Analytes	Iodosulfuron-methyl-sodium (AE F115008); metsulfuron-methyl (AE F075736)	
Instrumentation	HPLC-UV (corn grain), HPLC-MS (corn grain and forage)	
LOQ	0.025 ppm (corn grain); 0.05 ppm (corn forage and fodder)	
Standards	External bracketing standards	
ILV	For method No. BY/02/99 (LC-MS only)	
Extraction	Residues of AE F115008 and AE F075736 are extracted by blending the sample with acetonitrile, followed by sonication for 5 minutes. The extract is then filtered, reduced in volume and partitioned with hexane to remove oils. The extract is evaporated to dryness under reduced pressure and dissolved in dichloromethane. The extract is further cleaned up through a series of solid phase extraction columns in the following order: silica gel, Bond Elut™ ENV, and polyamide 6S. The extract is evaporated to dryness and reconstituted either in 70:30 deionized water:acetonitrile for analysis by HPLC-MS/MS, or in 50:50 deionized water:acetonitrile for analysis by HPLC-UV.	
Multiresidue method	The multiresidue methods are not suitable for the analysis of iodosulfuron-methyl-sodium (AE F115008) or the metabolite metsulfuron-methyl (AE F075736).	

Nature of the residue in plants		
Crop	Wheat (Yecora or Ralle variety)	
Radiolabel	2-^{14}C-triazinyl	phenyl-UL-^{14}C
Test site	Plant containers in an outdoor vegetation area.	Plant steel chambers in a climatic chamber.
Treatment	Foliar by spray	
Rate	One application at 20 g a.i./ha (10-fold) including the safener mefenpyr-diethyl in 1:3 ratio.	

EP	Wettable powder (WP)	
PHI	87 days	77 days
Major metabolites (>10% of the TRRs)	Forage: iodosulfuron-methyl-sodium Hay: iodosulfuron-methyl-sodium, AE F145741, AE 0031838 Straw: iodosulfuron-methyl-sodium, metsulfuron-methyl Grain: AE 0031838	Forage, hay, straw: iodosulfuron-methyl-sodium
	Although metabolites other than the parent were identified as >10% of the TRRs, the absolute TRR values were low.	
ROC	Iodosulfuron-methyl-sodium	
Confined rotational crop study—soybean, wheat, sugar beet (U.S. study)		
Formulation used for trial	A 70WDG, water-dispersible granule, containing the safener isoxadifen-ethyl and radiolabelled [2-triazinyl-^{14}C]iodosulfuron-methyl-sodium	
Application rate and timing	Soybeans and sugar beets were planted 7 and 14 days after soil was treated at 5.4 g a.i./ha (three-fold); wheat was planted 65 days after soil was treated at 8.1 g a.i./ha (four-fold).	
Succeeding crops		
Soybean forage, seeds; wheat forage, grain and straw; sugar beet tops and roots	At 7 and 14 days plantback, TRRs were 0.003 ppm. No further analysis. At 65 days plantback, TRRs were <0.001–0.007 ppm. No further analysis. At 60 days plantback, TRRs were 0.001 ppm. No further analysis. Therefore, proposed rotational crop restrictions are adequate.	
ROC	Iodosulfuron-methyl-sodium	
Confined rotational crop study—wheat, spinach, carrot (German study)		
Formulation used for trial	A WP20, wettable powder, containing radiolabelled [2-triazinyl-^{14}C]iodosulfuron-methyl-sodium	
Application rate and timing	[2-triazinyl-^{14}C]iodosulfuron-methyl-sodium was applied to bare soil at 20 g a.i./ha (10-fold) and spinach, carrots and wheat were sown after 29 days, 120 days, and 365 days.	
Succeeding crops		
Wheat grain, chaff, and straw	TRRs were < 0.01 ppm at all plantback intervals, with the exception of straw. Only straw was further analysed. Triazine-containing metabolites were identified at 7 to 14% of the TRRs.	
Spinach	TRRs were < 0.01 ppm at all plantback intervals.	
Carrot roots and foliage	TRRs were <0.01 ppm at all plantback intervals for carrot roots; TRRs were >0.01 ppm in carrot tops at 120 and 365 plantback intervals. Since the application rate is exaggerated (10-fold) and only livestock feed commodities have TRRs greater than 0.01 ppm, the proposed rotational crop restrictions are adequate.	
ROC	Iodosulfuron-methyl-sodium	

Nature of the residue in livestock			
Species	**Radiolabel**	**Dose level**	**Sacrifice**
Dairy cow (British Friesian)	[phenyl-^{14}C]iodosulfuron-methyl-sodium	Dosed orally for 7 consecutive days, 14.23 ppm (0.29 mg/kg bw/day)	Interval from last dose to sacrifice, 22 hours
71% of the administered dose was excreted in urine and 21% in feces; with approximately 8% remaining in tissues, organs, and milk.			
Laying hen (*Gallus gallus domesticus*)	[phenyl-^{14}C]iodosulfuron-methyl-sodium	Dosed orally for 14 consecutive days, 10 ppm (1.47 mg/kg BW/day)	Interval from last dose to sacrifice, 22 hours
92% of the administered dose was excreted in urine and feces, with approximately 8% remaining in tissues, organs, and eggs.			

	Cow	**Hen**
Major metabolites (>10% TRRs)	omental fat, kidney: iodosulfuron-methyl-sodium renal fat: none identified liver: iodosulfuron-methyl-sodium, AE F114368 milk: AE C627337	egg yolk, liver, skin: iodosulfuron-methyl-sodium egg white: iodosulfuron-methyl-sodium, AE 145741
ROC	Iodosulfuron-methyl-sodium	

Storage stability
Iodosulfuron-methyl-sodium is stable in wheat grain (24 months), forage (26 months), and straw (26 months). These data support the available corn field trial and processing studies.
Crop field trials—corn WDG treatment
In the U.S., 21 field corn trials were conducted in Zones 1 (two trials), 2 (one trial), 5 (sixteen trials), and 6 (two trials). Field corn trials were not conducted in Zone 5B in Canada. However, in all zones examined, residues in field corn were less than the LOQ when treated at approximately four-fold to five-fold the maximum recommended use rate. Consequently, it is unlikely that additional Canadian trials would provide any new information. Residues of iodosulfuron-methyl-sodium and the metabolite metsulfuron-methyl were less than the reported LOQs of 0.025 ppm in corn grain and 0.05 ppm in corn forage and stover, when applied at total application rate of 7.2–9.3 g a.i./ha (three-fold to five-fold).

Proposed MRLs	
Field corn	0.025 ppm
Field accumulation in rotational crops—mustard greens, turnip, wheat	
Data were not submitted with the iodosulfuron-methyl-sodium petition for a field accumulation study in rotational crops, since residues in crops from the confined study were all less than the LOQ (DIR98-02, *Residue Chemistry Guidelines*, Section 14).	
Processed food and feed	
The data indicate that residues of iodosulfuron-methyl-sodium and the metabolite metsulfuron-methyl were below the respective method LOQs (less than 0.025 ppm) in or on samples of the RAC, field corn grain, harvested 100 days following two applications (broadcast spray and drop nozzle), with a three-day retreatment interval, of iodosulfuron-methyl-sodium and isoxadifen-ethyl at 23 g a.i./ha followed by 9.9 g a.i./ha for a total rate of 32.9 g a.i./ha. No concentration factor needed.	
Livestock feeding	
Based on data from the ruminant and poultry metabolism studies, in which a cow and hen were dosed at the exaggerated rates of 0.08 ppm and 0.02 ppm, respectively, there is no reasonable expectation that finite residues of iodosulfuron-methyl-sodium will occur in livestock commodities (DIR98-02, *Residue Chemistry Guidelines*, Section 2). Therefore, livestock feeding studies and MRLs for livestock commodities are not required at this time.	

Table 6 Overview of plant/animal metabolism studies and risk assessment

Plant studies	
Crops (*n*=1)	Wheat
ROC for monitoring and enforcement	Iodosulfuron-methyl-sodium
ROC for risk assessment	Iodosulfuron-methyl-sodium
Metabolic profile in diverse crops	Only one crop was examined.
Animal studies	
Animals (*n*=2)	Dairy cow, hen
ROC for monitoring and enforcement	Iodosulfuron-methyl-sodium
ROC for risk assessment	Iodosulfuron-methyl-sodium
Metabolic profile in livestock	Similar
Fat-soluble Residue	No

Dietary Risk from Food and Water			
Chronic Non-Cancer Dietary Risk **ADI = 0.024 mg/kg bw/day** **EEC (chronic and acute)** **= 0.172 µg a.i./L (90th percentile)**	**Population**	**Estimated Risk (% of ADI)**	
		Food (MRLs)	**Food + EEC**
	All infants <1 yr old	0.2	0.2
	Children 1 to 2 yrs	0.3	0.3
	Children 3 to 5 yrs	0.3	0.3
	Children 6 to 12 yrs	0.3	0.3
	Youth 13 to 19 yrs	0.2	0.2
	Adults 20 to 49 yrs	0.1	0.1
	Adults 50+ yrs	0.1	0.1
	Females 13 to 49 yrs	0.1	0.1
	Total population	0.1	0.2

Table 7 Physical and chemical properties of the active ingredient relevant to the environment

Property	Test substance	Value	Comments
Water solubility (at 20°C)	Iodosulfuron-methyl-sodium (96.6%)	pH / g/L 7.6 (unbuffered) 60.0 4 0.02 5 0.17 7 25.0 9 65.0	Soluble to very soluble Potential to leach
Vapour pressure	Iodosulfuron-methyl-sodium (96.6%)	2.6×10^{-9} Pa (1.95×10^{-11} mm Hg) at 20 °C 6.7×10^{-9} Pa (5.02×10^{-11} mm Hg) at 25 °C	Not likely to volatilize from water and moist soil surfaces
Henry's Law constant (1/H)	Calculated	Temp. (°C) / (1/H) 20 1.082×10^{14} 25 4.193×10^{13}	
log K_{ow}	Iodosulfuron-methyl-sodium (96.6%)	pH / Log K_{ow} 4 1.96 5 1.07 6 0.07 7 −0.70 9 −1.22	Low potential to bioaccumulate
pK_a (at 20°C)	Iodosulfuron-methyl-sodium (96.6%)	3.22 ± 0.06	Potential for mobility in soil

Property	Test substance	Value	Comments
UV-visible absorption	Iodosulfuron-methyl-sodium (97.3%)	solvent λmax (nm) ε [L/(mol×cm)] MeOH 203 2.990×10^4 MeOH + 238 3.184×10^4 NaOH 239 3.170×10^4 (90/10, v/v) No observed absorption at λ 300–800 nm.	Not likely to undergo phototransformation in the environment

Table 8 Fate and behaviour in the terrestrial environment

Property	Test substance	Value	Comments
Abiotic transformation			
Hydrolysis	Iodosulfuron-methyl-sodium	**Half-lives** 2.5 d at pH 4 18.4 d at pH 5 197 d at pH 6 > 365 d at pH 7 167 d at pH 9 (Arrhenius equation was used to estimate half-lives for 25°C)	This is an important route of transformation in the environment in acid conditions, and transformation is slow in neutral to basic conditions. AE F149760, AE F114368, and AE F145741 were major transformation products (30–50°C)
Phototransformation on soil	Iodosulfuron-methyl-sodium	**Half-life** Dark: stable Irradiated: 9.1 d	Phototransformation on soil may be a transformation route AE 0002166 was a major transformation product
Phototransformation in air	Iodosulfuron-methyl-sodium	Not required—not volatile	

Property	Test substance	Value	Comments
Biotransformation			
Biotransformation in aerobic soil (Half-lives for transformation products were estimated using the multi-compartment model, TopFit 2.)	Iodosulfuron-methyl-sodium	**Half-lives** 0.8–3.3 d (30–50% MWHC) 10–21.8 d (25% MWHC) 15.4 d (10°C)	Non-persistent (30–50% MWHC) Slightly persistent (25% MWHC or 10°C) AE F075736, AE F059411, and AE F161778, and three unidentified compounds (M2, U1, and U2) were major transformation products.
	AE F075736	Half-lives = 20–78 d (30-50% MWHC) Half-lives = 65–99 d (25% MWHC)	Slightly to moderately persistent
	AE F161778	Half-lives = 9.4–21 d (30-50% MWHC) Half-lives = 27–35 d (25% MWHC)	Non-persistent to slightly persistent
	AE F059411	Half-lives = 119–269 d (all test conditions)	Moderately persistent to persistent
Biotransformation in anaerobic soil	Iodosulfuron-methyl-sodium	Not required	
Mobility			
Adsorption/desorption in soil	Iodosulfuron-methyl-sodium	Adsorption K_{oc}: 15.5–22.6 mL/g	Very high mobility
	AE F075736	Adsorption K_{oc}: 2.9–15.1 mL/g	Very high mobility
	AE F059411	Adsorption K_{oc}: 21.3–74.4 mL/g	High to very high mobility
Soil leaching	Iodosulfuron-methyl-sodium	Not required	
Volatilization	Iodosulfuron-methyl-sodium	Not required—not volatile	

Property	Test substance	Value	Comments
Field studies			
Field dissipation—Ontario	AE F115008 00 WG20 A1 (20% iodosulfuron-methyl-sodium)	Half-life = 4 d	Non-persistent Parent compound and transformation products were detected in the top 0–15 cm soil layer. AE F075736 and AE F059411 were major transformation products.

d = days; MWHC = maximum water-holding capacity

Table 9 Fate and behaviour in the aquatic environment

Property	Test material	Value	Comments
Abiotic transformation			
Hydrolysis	Iodosulfuron-methyl-sodium	**Half-life** 2.5 d (pH 4) 18.4 d (pH 5) 197 d (pH 6) > 365 d (pH 7) 167 d (pH 9) (Arrhenius equation was used to estimate half-lives for 25°C.)	This is an important route of transformation in the environment in acidic conditions, and transformation is slow in neutral to basic conditions. AE F149760, AE F114368, and AE F145741 were major transformation products (30-50°C).
Phototransformation in water	Iodosulfuron-methyl-sodium	**Half-life** Dark: stable Irradiated: 9–10.2 d	Phototransformation in water may be a transformation route. AE 0002166 was a major transformation product.

Property	Test material	Value	Comments
Biotransformation			
Biotransformation in aerobic water system (Half-lives for transformation products were estimated using the multi-compartment model, TopFit 2.)	Iodosulfuron-methyl-sodium	**Half-life** Whole system: 13.5–23.3 d Water: 12.5–19 d	Non-persistent to slightly persistent AE F075736, AE F059411, AE 0000119, AE 0014966, and AE 0034855 were major transformation products.
	AE F075736	Whole system half-lives: 34.4–55.2 d	Slightly to moderately persistent
	AE F161778	Whole system half-lives: 2.9–21.3 d	Non-persistent to slightly persistent
	AE 0014966	Whole system half-lives: 5.8–20.8 d	Non-persistent to slightly persistent
	AE F059411	Whole system half-lives: 87.6 d	Moderately persistent
Biotransformation in anaerobic water systems (Half-lives for transformation products were estimated using the multi-compartment model, TopFit 2.)	Iodosulfuron-methyl-sodium	Whole system half-lives: 14.3–28.1 d	Non-persistent to slightly persistent AE F075736 was a major transformation product.
	AE F075736	Whole system half-lives: 291 d	Persistent

Table 10 Maximum EEC in vegetation and insects after a direct over-spray of iodosulfuron-methyl-sodium

Matrix	EEC (mg a.i./kg fw)[a]	fw/dw ratios	EEC (mg a.i./kg dw)
Short range grass	0.43	3.3[b]	1.41
Leaves and leafy crops	0.22	11[b]	2.46
Long grass	0.20	4.4[b]	0.86
Forage crops	0.24	5.4[b]	1.30
Small insects	0.10	3.8[c]	0.39
Pods with seeds	0.02	3.9[c]	0.08
Large insects	0.02	3.8[c]	0.07
Grain and seeds	0.02	3.8[c]	0.07
Fruit	0.03	7.6[c]	0.20

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973) and modified according to Fletcher et al. (1994)
[b] Fresh/dry weight ratios from Harris (1975)
[c] Fresh/dry weight ratios from Spector (1956)

Table 11 Maximum EEC in vegetation and insects following direct over-spray of Tribute™ Solo 32 DF

Matrix	EEC (mg EP/kg fw)[a]	fw/dw ratios	EEC (mg EP/kg dw)
Short range grass	21.4	3.3[b]	70.6
Leaves and leafy crops	11.2	11[b]	123
Long grass	9.8	4.4[b]	43.1
Forage crops	12	5.4[b]	64.8
Small insects	5.2	3.8[c]	19.8
Pods with seeds	1.07	3.9[c]	4.17
Large insects	0.89	3.8[c]	3.38
Grain and seeds	0.89	3.8[c]	3.38
Fruit	1.34	7.6[c]	10.2

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973) and modified according to Fletcher et al. (1994)
[b] Fresh/dry weight ratios from Harris (1975)
[c] Fresh/dry weight ratios from Spector (1956)

Table 12 Maximum EEC in diets of birds and mammals

Organism	Matrix	Iodosulfuron-methyl-sodium (mg a.i./kg dw diet)	Tribute™ Solo 32 DF (mg EP/kg dw diet)
Bobwhite quail	30% small insects 15% forage crops 55% grain	0.35	17.5
Mallard duck	30% large insects 70% grain	0.07	3.38
Rat	70% short grass 20% grain/seeds 10% large insects	1.01	50.4
Mouse	25% short grass 50% grain/seeds 25% leaves and leafy crops	1	50.1
Rabbit	25% short grass 25% leaves and leafy crops 25% long grass 25% forage crops	1.51	75.4

Table 13 Effects on terrestrial organisms

Organism	Exposure	Test substance	End point value	Degree of toxicity[ab]
Invertebrates				
Earthworm	Acute	Iodosulfuron-methyl-sodium (87.4%)	LC_{50} > 1000 mg/kg soil NOEC = 1000 mg/kg soil LOEC > 1000 mg/kg soil	—
		AE F075736 (92.2%)	LC_{50} > 1000 mg/kg soil NOEC = 320 mg/kg soil (W) LOEC = 560 mg/kg soil	—
		AE F059411 (99.6%)	LC_{50} > 1000 mg/kg soil NOEC = 1000 mg/kg soil LOEC > 1000 mg/kg soil	—
		Tribute™ Solo 32DF	LC_{50} > 1000 mg EP/kg soil NOEC = 320 mg EP/kg soil (W)	—

Organism	Exposure	Test substance	End point value	Degree of toxicity[ab]
Bee	Oral	Iodosulfuron-methyl-sodium (87.4%)	LC_{50} > 81.4 mg/bee NOEC = 22.7 mg/bee (M) LOEC = 81.4 mg/bee	Practically non-toxic
		Tribute™ Solo 32DF	LC_{50} > 22.9 mg EP/bee NOEC = 22.9 mg EP/bee	Practically non-toxic
	Contact	Iodosulfuron-methyl-sodium (87.4%)	LC_{50} > 150 mg/bee NOEC = 100 mg/bee (M) LOEC = 125 mg/bee	Practically non-toxic
		Tribute™ Solo 32DF	LC_{50} > 159 mg EP/bee NOEC = 159 mg EP/bee	Practically non-toxic
Predatory mite *(T. pyri)*	Contact	Tribute™ Solo 32DF	5–12% (M) 85–89% (R) 7–26% (E)	Harmless
Ground-dwelling predator (*P. cupreus*)	Contact	Tribute™ Solo 32DF	86% (N) 4% (E)	Harmless
Ground-dwelling predator (*Pardosa* spp.)	Contact	Tribute™ Solo 32DF	0–10% (M) 88–101% (N) 4–21% (E)	Harmless
Ground-dwelling predator (*A. bilineata*)	Contact	Tribute™ Solo 32DF	27–34% (M) 86–93% (P) 32–42% (E)	Slightly harmful
Foliage-dwelling predator (*C. carnea*)	Contact	Tribute™ Solo 32DF	2–13% (M) 85–94% (R) 7.5–22% (E)	Harmless
Parasitic wasp (*A. rhopalosiphi*)	Contact	Tribute™ Solo 32DF	39–100% (M) 0–4% (P) 98–100% (E)	Moderately harmful to harmful
Birds				
Bobwhite quail	Acute	Iodosulfuron-methyl-sodium (87.2%)	LD_{50} > 1744 mg/kg bw NOEC = 1744 mg/kg bw (M) LOEC > 1744 mg/kg bw	At most, slightly toxic
	Dietary	Iodosulfuron-methyl-sodium (87.2%)	LD_{50} > 4358 mg/kg diet NOEC = 4358 mg/kg diet (M) LOEC > 4358 mg/kg diet	At most, slightly toxic
	Reproduction	Iodosulfuron-methyl-sodium (87.2%)	NOEC = 980 mg/kg diet (M, R) LOEC > 980 mg/kg diet	—

Organism	Exposure	Test substance	End point value	Degree of toxicity[ab]
Japanese quail	Reproduction	Iodosulfuron-methyl-sodium (87.4%)	NOEC = 984 mg/kg diet (M, R) LOEC > 984 mg/kg diet	—
Mallard duck	Dietary	Iodosulfuron-methyl-sodium (88.7%)	LD_{50} > 4510 mg/kg diet NOEC = 4510 mg/kg diet (M) LOEC > 4510 mg/kg diet	At most, slightly toxic
	Reproduction	Iodosulfuron-methyl-sodium (87.0%)	NOEC = 905 mg/kg diet (M, R) LOEC > 905 mg/kg diet	—
Mammals				
Rat	Acute	Iodosulfuron-methyl-sodium	$LD_{50} \geq$ 2678 mg/kg bw	Low toxicity
		Tribute™ Solo 32DF	LD_{50} = 3479 mg EP/kg bw	Low toxicity
	Dietary	Iodosulfuron-methyl-sodium	NOAEL: 67 mg/kg bw/d (male) 74 mg/kg bw/d (female)	—
	Dermal	Iodosulfuron-methyl-sodium	LD_{50} > 2000 mg/kg bw	Low toxicity
		Tribute™ Solo 32DF	LD_{50} > 5000 mg EP/kg bw	Low toxicity
	Inhalation	Iodosulfuron-methyl-sodium	LC_{50} > 2.81 mg/L	Low toxicity
		Tribute™ Solo 32DF	LC_{50} > 4.69 mg EP/L	Low toxicity
	Oncogenicity	Iodosulfuron-methyl-sodium	NOAEL: 29.7 mg/kg bw/d (male) 39.1 mg/kg bw/d (female)	—
	2-Generation Reproduction	Iodosulfuron-methyl-sodium	NOAEL: 346 mg/kg bw/d (male) 390 mg/kg bw/d (female)	—
	Development	Iodosulfuron-methyl-sodium	NOAEL: 315 mg/kg bw/d	—
Mouse	Dietary	Iodosulfuron-methyl-sodium	NOAEL: 119 mg/kg bw/d (male) 401 mg/kg bw/d (female)	—
	Oncogenicity	Iodosulfuron-methyl-sodium	NOAEL: 54.2 mg/kg bw/d (male) 57.6 mg/kg bw/d (female)	—
Rabbit	Development	Iodosulfuron-methyl-sodium	NOAEL: 400 mg/kg bw/d	—

Organism	Exposure	Test substance	End point value	Degree of toxicity[ab]
Dog	Dietary	Iodosulfuron-methyl-sodium	NOAEL: 8.1 mg/kg bw/d (male) 8.4 mg/kg bw/d (female)	—
		Iodosulfuron-methyl-sodium	NOAEL: 41.8 mg/kg bw/d (male) 7.25 mg/kg bw/d (female)	—
Vascular plants				
Vascular plant	Seedling emergence	Tribute™ Solo 32DF	EC_{25} = 14.1 g/ha	—
	Vegetative vigour	Tribute™ Solo 32DF	EC_{25} = 16.1 g/ha	—

[a] Atkins et al. (1981) for bees and the USEPA classification for others, where applicable.

[b] Classification by Hassen et al. (1994) for laboratory tests conducted with inert substrates.
Beneficial capacity: <30% harmless; 30–79% slightly harmful; 80–99% moderately harmful; >99% harmful.
Based on EPA classifications, for avian acute: <10 mg/kg (very highly toxic), 11–50 mg/kg (highly toxic), 51–500 mg/kg (moderately toxic), 501–2000 mg/kg (slightly toxic), >2000 mg/kg (practically non–toxic); and for avian dietary: <50 ppm (very highly toxic), 51–500 ppm (highly toxic), 501–1000 ppm (moderately toxic), 1001–5000 ppm (slightly toxic), and >5000 ppm (practically non toxic).

E = reduction in beneficial capacity; M = mortality; N = feeding rate; P = parasitism; R = reproduction; W = weight

Table 14 Effects on aquatic organisms

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Freshwater species				
Daphnia magna	Acute	Iodosulfuron-methyl-sodium (87.4%)	LC_{50} > 86.9 mg/L NOEC = 28.1 mg/L (M) LOEC = 49.9 mg/L	At most, slightly toxic
		Tribute™ Solo 32DF	LC_{50} > 100 mg EP/L NOEC = 100 mg EP/L	Practically non-toxic
	Chronic	Iodosulfuron-methyl-sodium (87.4%)	LC_{50} > 49.8 mg/L NOEC = 9.1 mg/L (W, R) LOEC = 15.9 mg/L	—
		Tribute™ Solo 32DF	LC_{50} = 0.064 mg EP/L NOEC = 0.02 mg EP/L (R, L)	—
Rainbow trout	Acute	Iodosulfuron-methyl-sodium (87.4%)	LC_{50} > 88 mg/L NOEC = 88 mg/L (M) LOEC > 88 mg/L	At most, slightly toxic
		Tribute™ Solo 32DF	LC_{50} = 2.6 mg EP/L NOEC = 1 mg EP/L (M)	Moderately toxic

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Bluegill sunfish	Acute	Iodosulfuron-methyl-sodium (87.4%)	LC_{50} > 92 mg/L NOEC = 92 mg/L (M) LOEC > 92 mg/L	At most, slightly toxic
		Tribute™ Solo 32DF	LC_{50} = 2.8 mg EP/L NOEC = 1.0 mg EP/L (M)	Moderately toxic
Freshwater alga	*P. subcapitata*	Iodosulfuron-methyl-sodium (87.4%)	EC_{50} = 0.041 mg/L NOEC = 0.014 mg/L (D)	—
		AE F075736 (92.2%)	EC_{50} = 0.12 mg/L NOEC = 0.018 mg/L (B)	—
		AE F059411 (99.6%)	EC_{50} > 101 mg/L NOEC = 101 mg/L (M)	—
		Tribute™ Solo 32DF	EC_{50} = 0.74 mg EP/L NOEC = < 0.4 mg EP/L (B)	—
	A. flos-aquae	Iodosulfuron-methyl-sodium (86.9%)	EC_{50} = 1.4 mg/L NOEC = 0.63 mg/L (D)	—
	N. pelliculosa	Iodosulfuron-methyl-sodium (87.4%)	EC_{50} > 81.5 mg/L NOEC = 81.5 mg/L (M)	—
Vascular plant	*Lemna gibba*	Iodosulfuron-methyl-sodium (87.4%)	EC_{50} = 0.83 mg/L NOEC = 0.39 mg/L (D) LOEC = 0.63 mg/L	—
		AE F059411 (99.6%)	EC_{50} = 101 mg/L NOEC = 57 mg/L (B) LOEC = 101 mg/L	—
		Tribute™ Solo 32DF	EC_{50} = 2.5 mg EP/L NOEC = 1.0 mg EP/L (B) LOEC = 2.0 mg EP/L	—

[a] USEPA classification, where applicable

M = mortality; W = weight; R = reproduction; L = length; D = cell or frond density; B = biomass

Table 15 PMRA Risk Classification Scheme

Margin of safety (MOS)	Degree of risk
≥10	Negligible
1 to <10	Low
0.1 to <1	Moderate
0.01 to <0.1	High
0.001 to <0.01	Very High
<0.001	Extremely High

Table 16 Risk of iodosulfuron-methyl-sodium (TGAI) to terrestrial organisms

Organism	Exposure	End point value	EEC	MOS	Risk
Invertebrates					
Earthworm	Acute	NOEC = 1000 mg/kg soil	0.89 mg/kg soil	>1000	Negligible
Bee	Oral	LD_{50} > 91.2 kg/ha	2 g/ha	>1000	Negligible
Birds					
Bobwhite quail	Acute	NOEC = 1744 mg/kg bw	0.35 mg/kg diet	>1000	Negligible
	Dietary	NOEC = 4358 mg/kg diet	0.35 mg/kg diet	>1000	Negligible
	Reproduction	NOEC = 980 mg/kg diet	0.35 mg/kg diet	>1000	Negligible
Mallard duck	Dietary	NOEC = 4510 mg/kg diet	0.07 mg/kg diet	>1000	Negligible
	Reproduction	NOEC = 905 mg/kg diet	0.07 mg/kg diet	>1000	Negligible
Mammals					
Rat	Acute	LD_{50} ≥ 2678 mg/kg bw	1.01 mg/kg diet	>1000	Negligible
	Dietary	NOAEL = 1000 mg/kg bw/d	1.01 mg/kg diet	990	Negligible
	Reproduction	NOAEL = 500 mg/kg bw/d	1.01 mg/kg diet	495	Negligible
Mouse	Dietary	NOAEL = 700 mg/kg bw/d	1.01 mg/kg diet	700	Negligible

Table 17 Risk of Tribute™ Solo 32DF to terrestrial organisms

Organism	Exposure	End point value	EEC	MOS	Risk
Invertebrates					
Earthworm	Acute	NOEC = 320 mg/kg soil	0.044 mg/kg soil	>1000	Negligible
Mammals					
Rat	Acute	LD_{50} = 3479 mg/kg bw	50.4 mg/kg dw diet	69	Negligible
Vascular plants					
Vascular plant	Seedling emergence	EC_{25} = 14.1 g/ha	100 g/ha	0.14	Moderate
	Vegetative vigour	EC_{25} = 16.1 g/ha	100 g/ha	0.16	Moderate

Table 18 Risk of iodosulfuron-methyl-sodium (TGAI) to aquatic organisms (Freshwater species)

Organism	Exposure	End point value	EEC	MOS	Risk
Daphnia magna	Acute	NOEC = 28.1 mg/L	0.67 mg/L	>1000	Negligible
	Chronic	NOEC = 9.1 mg/L	0.67 mg/L	>1000	Negligible
Rainbow trout	Acute	NOEC = 88 mg/L	0.67 mg/L	>1000	Negligible
Bluegill sunfish	Acute	NOEC = 92 mg/L	0.67 mg/L	>1000	Negligible
Freshwater alga	Acute	NOEC = 0.014 mg/L	0.67 mg/L	20.9	Negligible
Vascular plant	Dissolved	NOEC = 0.39 mg/L	0.67 mg/L	0.58	High

Table 19 Risk of Tribute™ Solo 32DF to aquatic organisms (Freshwater species)

Organism	Exposure	End point value	EEC	MOS	Risk
Daphnia magna	Acute	NOEC = 100 mg/L	0.033 mg/L	>1000	Negligible
	Chronic	NOEC = 0.02 mg/L	0.033 mg/L	0.61	Moderate
Rainbow trout	Acute	NOEC = 1.0 mg/L	0.033 mg/L	30.3	Negligible
Bluegill sunfish	Acute	NOEC = 1.0 mg/L	0.033 mg/L	30.3	Negligible
Freshwater alga	Acute	NOEC = 0.074 mg/L	0.033 mg/L	2.2	Negligible
Vascular plant	Dissolved	NOEC = 1.0 mg/L	0.033 mg/L	0.03	High

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