Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Proposed Regulatory Decision Document PRDD2005-05

AC 900001 (Picolinafen)

The active ingredient AC 900001 Technical Herbicide (picolinafen) and associated end-use product AC 900001 Water-Dispersible Granular Herbicide for the control of broadleaf weeds in spring wheat (including durum) and barley grown in the prairie provinces and the Peace River Region of British Columbia are proposed for full registration under the Pest Control Products Regulations.

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

(publié aussi en français)

2 November 2005

This document is published by the Alternative Strategies and Regulatory Affairs Division, Pest Management Regulatory Agency. For further information, please contact:

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ISBN: 0-662-42064-0 (0-662-42065-9)
Catalogue number: H113-9/2005-5E (H113-9/2005-5E-PDF)

Foreword

The PMRA has reviewed the submission for the conversion from temporary to full registration of AC 900001 Technical Herbicide (picolinafen) and the end-use product AC 900001 Water-Dispersible Granular Herbicide for the control of broadleaf weeds in spring wheat (including durum) and barley grown in the prairie provinces and the Peace River Region of British Columbia.

Health Canada's PMRA had previously issued a temporary registration (Regulatory Note REG2003-02) for this product with the requirement that BASF Canada Inc. carry out a poultry metabolism study and provide physicochemical data on transformation product CL 153815. These studies have now been completed.

The PMRA has carried out an assessment of available information in accordance with the Pest Control Products Regulations and has found it sufficient to allow a determination of the safety, merit and value of AC 900001 Technical Herbicide (picolinafen) and the end-use product, AC 900001 Water-Dispersible Granular Herbicide. The Agency has concluded that the use of AC 900001 Technical Herbicide (picolinafen) and the end-use product, AC 900001 Water-Dispersible Granular Herbicide in accordance with the label has merit and value consistent with the Pest Control Products Regulations and does not entail an unacceptable risk of harm. Therefore, based on the considerations outlined above, the use of AC 900001 Technical Herbicide (picolinafen) Technical and the end-use product, AC 900001 Water-Dispersible Granular Herbicide for the control of broadleaf weeds in spring wheat (including durum) and barley grown in the prairie provinces and the Peace River Region of British Columbia is proposed for full registration, pursuant to the Pest Control Products Regulations.

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

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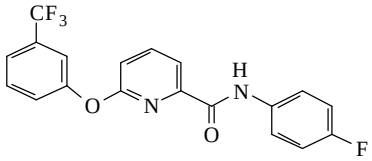
1.0 The Active Substance, its Properties and Uses

1.1 Identity of the Active Substance and Impurities

Active substance		Picolinafen
Function		Herbicide
Chemical name		
1.	International Union of Pure and Applied Chemistry	4'-Fluoro-6-[(α,α,α-trifluoro-m-tolyloxy)pyridine-2-carboxanilide **or** N-(p-Fluorophenyl)-6-[(α,α,α-trifluoro-m-tolyl)oxy]picolinamide
2.	Chemical Abstracts Service (CAS)	N-(4-Fluorophenyl)-6-[3-(trifluoromethyl)phenoxy]-2-pyridinecarboxamide
CAS number		137641-05-5
Molecular formula		$C_{19}H_{12}F_4N_2O_2$
Molecular weight		376.3
Structural formula		
Nominal purity of active		99.4% (limits: 96.4–100%)
Identity of relevant impurities of toxicological, environmental or other significance		The technical grade picolinafen does not contain any impurities or microcontaminants known to be Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Appendix II of DIR99-03.

1.2 Physical and Chemical Properties of Active Substances and End-use Product

Technical Product: AC 900001 Technical Herbicide (picolinafen)

Property	Result	Comment
Colour and physical state	Grey-yellow to sand colour powder solid	
Odour	Musty smell, similar to phenol	
Melting point or range	107.2–107.6°C	
Boiling point or range	Decomposed at > 230°C.	
Density	1.45	
Vapour pressure at 20°C	**Temp. (°C)** / **Vapour pressure (Pa)** 70 / 2.36×10^{-4} 80 / 8.49×10^{-4} 90 / 2.44×10^{-3} 20 / 1.6×10^{-7} (estimated)	Non-volatile under field conditions.
Henry's Law constant at 20°C	$K_H = 1.60 \times 10^{-3}$ Pa m^3/mole	Non-volatile from moist soil and water surfaces.
Ultraviolet (UV)–visible spectrum	**λ (nm)** / **ϵ (l•mol^{-1}•cm^{-1})** 202 / 39 500 230 (shoulder) / 14 600 290 / 13 000 No absorption at 350–400 nm was observed.	Potential for photolysis in the UV range.
Solubility in water at 20°C	**Solvent** / **g/L** pH 5 buffer / 3.8×10^{-5} pH 7 buffer / 4.7×10^{-5} pH 9 buffer / 3.8×10^{-5} Deionized water / 3.9×10^{-5}	Insoluble in water.

Property	Result	Comment
Solubility (g/100 mL) in organic solvents at 20°C	**Solvent** / **Solubility** acetone 5.7 dichloromethane 76.4 ethyl acetate 46.4 n-hexane 0.38 methanol 3.04	
n-Octanol–water partition coefficient (K_{ow})	**Solvent** / **log K_{ow}** Deionized water 5.37 pH 5 buffer 5.36 pH 7 buffer 5.43 pH 9 buffer 5.36	Potential for bioaccumulation but studies did not support this.
Dissociation constant (pK_a)	None between the pH values of 2–12.	Does not dissociate at environmentally relevant pH values.
Stability (temperature, metal)	Stable during storage at 45°C for > 3 months, at 37°C for > 1 year. The TGAI has no oxidizing properties.	

End-use Product: AC 900001 Water-Dispersible Granular Herbicide

Property	Result
Colour	Brown
Odour	Faint, musty smell
Physical state	Free flowing granules
Formulation type	Wettable granules
Guarantee	75% (limits: 73–77%)
Formulants	The product does not contain any USEPA List 1 formulants or formulants known to be TSMP Track 1 substances.
Container material and description	Soluble bags, 4 × 267 g
Bulk density	Pour bulk density: 628 kg/m^3 Tap bulk density: 693 kg/m^3
pH of 1% dispersion in water	9.6

Property	Result
Oxidizing or reducing action	No evidence of oxidizing properties.
Storage stability	Stable after 10 months in paper/AI/PE/block bottom bags and in HDPE bottles. Freezer storage stability studies indicated that residues of picolinafen were stable at –18°C for up to 12 months in cereal matrices.
Explodability	No evidence of explosive properties.

1.3 Details of Uses

AC 900001 Water-Dispersible Granular Herbicide is proposed as a foliar applied postemergence herbicide for the control of broadleaf weeds in spring wheat (*Triticum aestivum*), durum wheat (*Triticum durum*) and barley (*Hordeum vulgare*) in the prairie provinces and Peace River Region of British Columbia. AC 900001 Water-Dispersible Granular Herbicide is proposed as an alone treatment, or for use in a two-way tank mix with 2,4-D ester LV500, LV600 or LV700 (various registration numbers), or for use in a three-way tank mix with 2,4-D ester plus Assert 300 SC herbicide (active ingredient: imazamethabenz; Registration Number 21032). The product is to be applied by ground application and not more than once per season.

As an alone treatment, 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide claims the product controls redroot pigweed (*Amaranthus retroflexus*) and stinkweed (*Thlapsi arvense*) as well as suppresses volunteer canola (*Brassica napus* spp.), wild mustard (*Sinapis arvensis*), kochia (*Kochia scoparia*) and shepherd's purse (*Capsella bursa-pastoris*).

In a two-way tank mix of 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester, the label claims the product controls wild buckwheat (*Polygonum convolvulus*) and kochia (*Kochia scoparia*) as well as suppresses cleavers (*Galium spurium*) and chickweed (*Stellaria media*), plus the weeds listed for the AC 900001 alone treatment and the susceptible or easy-to-control weeds listed on the 2,4-D ester labels.

In a three-way tank mix, 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester plus 400 g a.i./ha Assert 300 SC, the label claims the product controls the broadleaf weeds listed for the two-way tank mix plus wild oats.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Substance as Manufactured

Product	Analyte	Method ID	Method Type	Linearity Range	Recovery (%)	RSD (%)	LOQ (%)	Method
AC 900001 Technical Herbicide	Picolinafen	CFS-DPA M27/1/N	HPLC/UV at 290 nm	0.05–0.25 mg/mL	N/A	0.77	Not required	Accepted
AC 900001 Technical Herbicide	Major impurities	CFS-DPA M28/3F	HPLC/UV at 220 nm	0.02–0.7 %	87–114	1.2–5.8	0.001–0.03	Accepted

2.2 Methods for Formulation Analysis

Product	Analyte	Method ID	Method Type	Linearity Range	Mean Recovery (%)	RSD (%)	Method
AC 900001 Water-Dispersible Granular Herbicide	Picolinafen	FAMS 086-01	HPLC/UV at 290 nm	4.8– 7.2 mg/50 mL	100.1% (n = 6)	0.23	Accepted

2.3 Analytical Methods for Residue Analysis

Two analytical methods were submitted for the determination of the residue of concern (ROC) in plant matrices: gas chromatography with nitrogen-phosphorus detector (GC/NPD) Method FAMS 079-01 and gas chromatography with mass spectrometry (GC/MS) Method M3313. Method FAMS 079-01 was used for data gathering while Method M3313 was used for data gathering and proposed for enforcement. The limits of quantitation (LOQs) for picolinafen were the same for both methods: 0.05 mg/kg. Good linearity (correlation coefficient, $r^2 > 0.995$) was observed in the range of 0.125–2000 ng/mL for picolinafen. The coefficients of variation (CVs) measured with respect to recoveries following spiking at the LOQ did not exceed 20%, indicative of the methods having good repeatability. Representative chromatograms of control samples showed no peaks above the chromatographic background. The spike sample chromatograms from both methods contained a well defined and symmetrical peak in the area of analytical interest with no carry-over to the following chromatograms. The independent laboratory validation (ILV) demonstrated good reliability and reproducibility of the GC/MS Method M3313 for the determination of residues of picolinafen in plant matrices.

For animal matrices, only one analytical method was submitted for data gathering and enforcement purposes: Method FAMS 109-01. The limits of detection (LODs) and the LOQs were reported to be 0.002 mg/kg and 0.02 mg/kg, respectively for each analyte, for muscle, fat and egg, and 0.001 mg/kg and 0.01 mg/kg, respectively for each analyte, for milk. Good linearity (correlation coefficient, $r^2 > 0.9992$), was observed in the range of 5–100 ng/mL for picolinafen. The CVs measured with respect to recoveries following spiking at the LOQ were within 20%, indicative of the method's good repeatability. Representative chromatograms of control samples showed no peaks above the chromatographic background. The spike sample chromatograms contained a well defined and symmetrical peak in the area of analytical interest with no carry-over to the subsequent chromatograms. The ILV demonstrated good reliability and reproducibility for the determination of residues of picolinafen and CL 153815 in milk, eggs and tissues.

2.3.1 Methods for Environmental Residue Analysis

Matrix	Method ID	Method	Spike Level	Overall Mean % Recovery (n)				LOQ	Method
				AC 900001	RSD (%)	CL 153815	RSD (%)		
Soil	M 3314	LC/MS	5 and 50 ppb	93.6 (8)	5.8	82.6 (8)	11.1	5 ppb	Accepted
Sediment		The applicant requested to use the soil method. The request was accepted based on the following: 1. No new transformation products formed in sediment. 2. Acetone-aqueous acetic acid solution is used as extraction solvent for soil.							Waiver accepted
Drinking water	P-14.106	GC/ECD	0.1 and 1.0 ppb	106 (10)	2	—	—	0.1 ppb	Accepted

3.0 Impact on Human and Animal Health

3.1 Integrated Toxicological Summary

A detailed review of the toxicological database available for the technical grade active ingredient AC 900001 Technical Herbicide and the end-use product AC 900001 Water-Dispersible Granular Herbicide has been completed. Data submitted were complete and comprehensive, and included the full battery of studies currently required for registration of a new technical grade active ingredient and end-use product based on use-site categories 13 and 14. The scientific and regulatory quality of the toxicology database is considered sufficient to adequately define the toxicity of this chemical for its intended purpose.

AC 900001 Technical Herbicide was incompletely absorbed, up to 60 and 84% of the administered oral dose for male and female rats, respectively, following low-dose administration (10 mg/kg bw). At the high dose (1000 mg/kg bw), absorption decreased to approximately 17–25% of the administered dose for both sexes. The decreased

absorption at the high dose was considered to be due to saturation of absorption processes. The majority was absorbed within 24 hours following single or multiple low dose administration and within 48 hours following single high-dose administration. No significant tissue accumulation was evident; less than 0.5% of the administered dose remained in the tissue/carcass at sacrifice (168 hours postdosing). The majority of radioactivity was eliminated within 24 (greater than 75% of administered dose) and 48 (greater than 80% of the administered dose) hours following low- and high-dose administration, respectively. Fecal/biliary excretion was the major route of excretion of metabolites of the pyridine-labelled AC 900001 Technical Herbicide, whereas urinary excretion was the major route of excretion of metabolites of the aniline-labelled AC 900001 Technical Herbicide. AC 900001 Technical Herbicide was extensively metabolized with hydrolytic cleavage of amide bond followed by a variety of biotransformation processes including N-acetylation, hydroxylation, methylation, dehalogenation and formation of mercapturic and sulfate conjugates. In the feces, the major residue was identified as the parent compound, AC 900001 Technical Herbicide. The major urinary metabolites were identified as CL 153815 and its glucuronic acid conjugate, the sulfate conjugate of 2-amino-5-fluorophenol and the sulfate conjugate of 4'-hydroxyacetanilide (CL 1009639). The major biliary metabolites were identified as CL 153815 and the glucuronide ester of CL 153815, p-fluoroaniline, 4'-fluoroacetanilide and 4'-hydroxyacetanilide. There were slight gender differences in absorption, metabolism and excretion.

Technical grade AC 900001 has low acute toxicity by the oral, dermal and inhalation routes of exposure. It is minimally irritating to the eyes and non-irritating to the skin; it is not considered to be a skin sensitizer. The end-use product, AC 900001 Water-Dispersible Granular Herbicide, has low acute toxicity by the oral, dermal and inhalation routes. It is minimally irritating to the eyes and mildly irritating to the skin; it is not considered to be a skin sensitizer. The formulants were on USEPA Lists 3, 4A or 4B, and/or the PMRA List of Formulants (REG2004-01), and were of no toxicological concern.

AC 900001 Technical Herbicide was tested in a battery of in vitro (bacterial and mammalian cell gene mutation assays 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 AC 900001 Technical Herbicide was not genotoxic under the conditions of the tests performed.

The subchronic and chronic toxicity of AC 900001 Technical Herbicide was investigated in the mouse, rat and dog. A 28-day repeat dose dermal toxicity study was also carried out in rats. Following subchronic and chronic dietary exposure, treatment-related hematological findings, increased spleen and/or liver weights and histopathological findings indicative of regenerative hemolytic anemia were noted for all species tested. Similar findings were also noted in the rat 2-generation reproduction study, in the rat and rabbit developmental studies and in the 28-day repeat dose dermal toxicity study. The rat

appears to be the most sensitive species with no observed adverse effect levels (NOAELs) of 10.5, 6.4 and 2.4 mg/kg bw/d following 28-day, 90-day and 2-year dietary administration, respectively.

Hematological findings were generally characterized by lower red blood cell count, hemoglobin and hematocrit with associated increases in mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration and reticulocyte counts. Other hematological findings associated with hemolytic anemia included significantly elevated methemoglobin levels and Heinz body formation as well as significantly reduced oxyhemoglobin levels. Elevated methemoglobin levels and Heinz body formation are indicative of oxidative hemolysis of red blood cells. Changes in methemoglobin and oxyhemoglobin levels as well as Heinz body formation were generally noted at the higher dose levels in mice (at 1000 ppm and above following 28-day and 90-day dietary administration) and rats (at 1000 ppm following 28-day dietary administration). Erythrocyte osmotic fragility was significantly lower for rats following 28-day dietary administration at a dose level of 1000 ppm; this was most likely associated with Heinz body attachment to the red blood cell membrane and with the increased population of circulating immature cells, as indicated by the increase in reticulocyte counts noted at this dose level. Increased red blood cell distribution width and diameter were noted in rats following 28-day dietary administration at 1000 ppm. This correlated with elevated reticulocyte counts.

Histopathological findings were generally characterized by increased incidence/severity of hemosiderin deposition in the spleen and/or Kupffer cells of the liver as well as extramedullary hematopoiesis in the spleen and/or liver. Under normal physiological conditions, a certain amount of hemosiderin deposition is routinely observed in the spleen due to normal breakdown of effete red blood cells. However, for all species tested, increased incidence/severity were noted for both sexes at the higher dose levels. The increased incidence/severity of extramedullary hematopoiesis was most likely a compensatory response to the increased hemolysis of red blood cells noted for all species tested. Other histopathological findings associated with regenerative hemolytic anemia included increased erythropoietic activity in the bone marrow and liver at higher doses. This was noted in rats following 28-day dietary administration at 1000 ppm and was indicated by a change in the myeloid:erythroid ratio from 2:1 in the controls to 1:1 in rats at 1000 ppm. For males, this shift to a more immature, stronger population of red cells at 1000 ppm was considered to account for the slight but significant decrease in erythrocyte osmotic fragility. For females, this correlated with an increased incidence of erythropoiesis in the bone marrow (femur/joint and sternum).

Histopathological findings were often observed in the absence of hematological effects, particularly at lower doses. This was most likely due to compensatory mechanisms adequately compensating for increased hemolysis of red blood cells. At the higher doses, these compensatory mechanisms may not have been sufficient to compensate for the increased hemolysis of red blood cells and, therefore, anemia was manifest. The presence

of hemolytic anemia following exposure to AC 900001 Technical Herbicide was most likely due to the aniline group. Hemoglobin may be oxidized to methemoglobin in the presence of oxidant compounds such as aniline when given in sufficient levels in vivo. In addition, oxidant compounds such as aniline can also lead to Heinz body formation. The increase in methemoglobin and Heinz body formation can lead to an increased susceptibility of the red blood cell to hemolysis.

In rats, serum bilirubin levels were significantly elevated in both sexes following 28-day dietary administration at 1000 ppm. Elevated serum bilirubin levels were also noted in dogs following 90-day dietary administration at 2500 ppm. In the absence of any alterations in other liver function markers, this was considered to reflect increased red blood cell hemolysis and hemoglobin breakdown observed in these animals. Elevated serum bilirubin levels were not observed in mice. Gross pathological findings associated with the anaemic state were generally limited to discolouration of the spleen, liver, kidney, lungs, heart and/or small intestines in all species tested.

Although findings indicative of hemolytic anemia were noted in dogs following 90-day and 1-year dietary administration, the main target organ appeared to be the thyroid, as indicated by increased thyroid weight, diffuse hypertrophy of the thyroid follicular epithelial cells and scattered foci of thyroid follicular cell hyperplasia at 500 ppm (17.3 and 20.2 mg/kg bw/d and above for males and females, respectively) and above following 90-day dietary administration as well as at 1500 ppm (42.7 and 47.1 mg/kg bw/d for males and females, respectively) and above following 1-year dietary administration (the differences noted following 90-day and 1-year dietary administration were due to dose selection). Hormone levels (thyroxine, tri-iodothyronine and thyroid stimulating hormone) were not determined. Lower body weight and/or body-weight gain were also noted in dogs at 2500 ppm (equal to 87.5 and 92.1 mg/kg bw/d for males and females, respectively) following 90-day dietary administration and at 150 ppm (1.7 and 1.8 mg/kg bw/d and above for males and females, respectively) and above following 1-year dietary administration. The NOAEL following 90-day dietary administration was 50 ppm (equal to 1.7 and 1.8 mg/kg bw/d for males and females, respectively). The NOAEL following 1-year dietary administration was 50 ppm (equal to 1.4 and 1.6 mg/kg bw/d for males and females, respectively).

Following subchronic and chronic administration, mice also exhibited treatment-related findings in the liver, including centrilobular hepatocellular hypertrophy and hepatocellular vacuolation. These were noted following 28-day, 90-day and 78-week dietary administration. The NOAELs for mice were 23.4, 10.2 and 6.9 mg/kg bw/d following 28-day, 90-day and 78-week dietary administration, respectively.

In the 78-week dietary study, there was no evidence to indicate that AC 900001 Technical Herbicide was oncogenic in the mouse. In the rat 2-year dietary study, there was a non-statistically significant, increased incidence of benign neoplasms (benign pheochromocytomas) in the adrenal gland medullary region for males at 500 ppm

(highest dose tested). The incidence was within recent historical control data for benign medullary neoplasms. In addition, there was no decrease in the time to appearance of the induced tumour and no dose-response relationship in proliferative changes usually associated with benign/malignant neoplasms in the adrenal medulla. Published literature indicates that proliferative lesions of the adrenal medulla in male rats occur at relatively high incidences and can be spontaneous (age related) in nature. Based on these findings, the slight increased incidence of benign neoplasms in the adrenal gland medullary region noted for males at 500 ppm, was most likely spontaneous in nature and not treatment-related. The weight of evidence suggests that AC 900001 Technical Herbicide is not likely to be oncogenic in humans.

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. In addition, there was no evidence in the toxicology database to indicate a significant difference in gender sensitivity.

In a 4-week repeat-dose dermal toxicity study in the rat, treatment-related hematological findings, increased spleen weights and histopathological findings indicative of hemolytic anemia were noted for both sexes at 100 mg/kg bw/d and above. Hematological findings were first apparent at 1000 mg/kg bw/d by day 5 and appeared to be reversible following an 8-week recovery period. The NOAEL for systemic toxicity was 75 mg/kg bw/d.

In the rat 2-generation reproduction study, treatment in the P1/P2 parental animals did not influence reproduction function, reproductive parameters and litter parameters at any dose level up to and including 500 ppm (equal to 39 and 42 mg/kg bw/d in males and females, respectively), the highest dose tested. Hematological findings, increased spleen weights and histopathological findings indicative of regenerative hemolytic anemia were noted for P1/P2 males and females at 250 ppm (equal to 19 and 21 mg/kg bw/d for males and females, respectively) and above. Hematological findings, including lower red blood cell count, hemoglobin and hematocrit, were also noted for male and female F2 pups at 250 ppm and above on lactation day 21 (only time point evaluated). Although the hematological findings noted in the F2 offspring may be secondary to maternal toxicity, a direct treatment-related effect cannot be dismissed. Therefore, these findings were considered to be toxicologically relevant. The NOAEL for parental and offspring toxicity was 50 ppm (equal to 3.7 and 4.0 mg/kg bw/d in males and females, respectively). On the basis of the parental and offspring NOAELs in the rat 2-generation reproductive toxicity study (one litter/generation), there was no indication that neonates were quantitatively more sensitive than adults to the toxic effects of AC 900001 Technical Herbicide.

In the rat and rabbit developmental toxicity studies, hematological findings, increased spleen weights and histopathological findings indicative of regenerative hemolytic anemia were noted in the rats at 100 mg/kg bw/d and above, and in the rabbits at 20 mg/kg bw/d and above. The NOAEL for maternal toxicity was 50 mg/kg bw/d for rats and 5 mg/kg bw/d for rabbits. In the rat developmental toxicity study, the NOAEL for developmental

toxicity was 1000 mg/kg bw/d, the highest dose tested, based on the absence of any adverse treatment-related effects on the developmental parameters examined. In the rabbit developmental study, there was a possible slight decrease in embryonal-fetal viability, manifested as slight increases in abortion (1 on day 21; 1 on day 23), postimplantation loss, total number of resorptions (early and late) and mean resorption rate at 50 mg/kg bw/d. Although these effects on embryonal-fetal viability were not statistically significant from controls and were within historical control range for animals of this strain, a treatment-related effect could not be dismissed because the increased incidence was noted at the highest dose tested. The NOAEL for developmental toxicity was 20 mg/kg bw/d based on a possible slight decrease in embryonal-fetal viability at 50 mg/kg bw/d, the highest dose tested. On the basis of the maternal and developmental NOAELs in the rat and rabbit developmental toxicity studies, there was no quantitative evidence in either species to indicate an increased susceptibility of the fetus to in utero exposure to AC 900001 Technical Herbicide. There was no evidence of any irreversible structural changes related to treatment in either species; therefore, AC 900001 Technical Herbicide was not considered to be teratogenic in rats or rabbits. There was no evidence of any treatment-related developmental findings in either species.

The treatment-related findings noted in the thyroid (increased thyroid weight, diffuse hypertrophy of the thyroid follicular epithelial cells and scattered foci of thyroid follicular cell hyperplasia) in dogs following 90-day and 1-year dietary administration may be suggestive of a neurotoxicity potential. Similar lesions were not observed in the rat (including neonates) or the mouse following subchronic or chronic dietary exposure and there was no other evidence in any species tested to indicate a neurotoxicity potential. Thyroid hormone (thyroxine, tri-iodothyronine and thyroid stimulating hormone) levels were not determined. Thyroid hormones are crucial to normal growth and development in the central nervous system; in the absence of these hormones, brain development can be retarded. Therefore, in the absence of thyroid hormone data as well as any human data, these lesions cannot be disregarded and must be considered relevant to humans.

3.2 Determination of Acceptable Daily Intake

The most appropriate NOAEL of 1.4 mg/kg bw/d in the 1-year dietary study in dogs is recommended as the basis for the acceptable daily intake (ADI). Treatment-related findings at the lowest observed adverse effect level (LOAEL), the next highest dose level, included lower body weight and body-weight gain for males (approximately 20 and 48%, respectively). A safety factor of 100 to account for intraspecies and interspecies variations was considered to be adequate; no additional safety factors are required. The recommended ADI is 0.014 mg/kg bw/d.

$$\text{ADI} = \frac{\text{NOAEL}}{\text{SF}} = \frac{1.4 \text{ mg/kg bw/d}}{100} = 0.014 \text{ mg/kg/day of AC 900001 Technical Herbicide}$$

The margin of exposure (MOE) for other critical endpoints, calculated as NOAEL/ADI is as follows:

Developmental toxicity NOAEL = 20 mg/kg bw/d (rabbit). The MOE for developmental toxicity is 1428 compared to the ADI.

Two-generation reproduction study

Reproductive toxicity NOAEL = 39 mg/kg bw/d. The MOE is 2785 compared to the ADI

Offspring toxicity NOAEL = 3.7 mg/kg bw/d. The MOE is 264 compared to the ADI

Hematological and histopathological findings indicative of regenerative hemolytic anemia were noted in all species tested. The most sensitive species appears to be the rat. The most appropriate NOAEL for regenerative hemolytic anemia is 50 ppm (equal to 2.4 and 3.0 mg/kg bw/d for males and females, respectively) as determined in the 2-year rat dietary study. The MOE for regenerative hemolytic anemia is 171 compared to the ADI.

In the dog, treatment-related effects were noted in the thyroid in the 28-day, 90-day and 1-year dietary studies. Treatment-related findings included increased thyroid weight, enlarged thyroid, diffuse hypertrophy of the thyroid follicular epithelial cells and scattered foci of thyroid follicular cell hyperplasia. The most appropriate NOAEL for thyroid effects is 150 ppm (equal to 4.4 and 5.7 mg/kg bw/d for males and females, respectively). The MOE for thyroid effects is 314 compared to the ADI.

3.3 Acute Reference Dose

An acute reference dose (ARfD) was not established since AC 900001 Technical Herbicide (picolinafen) was considered unlikely to present an acute hazard. There were no significant treatment-related findings in the acute, short-term, two-generation reproduction or developmental toxicity studies to indicate a concern in acute dietary risk assessment.

3.4 Toxicological Endpoint Selection—Occupational and Bystander Risk Assessment

AC 900001 Technical Herbicide has low acute toxicity by the oral, dermal and inhalation routes of exposure. It is minimally irritating to the eyes and non-irritating to the skin; it is not considered to be a skin sensitizer. The end-use product, AC 900001 Water-Dispersible Granular Herbicide, has low acute toxicity by the oral, dermal and inhalation routes. It is minimally irritating to the eyes and mildly irritating to the skin; it is not considered to be a skin sensitizer.

AC 900001 Technical Herbicide was incompletely absorbed, up to 60 and 84% of the administered dose for males and females, respectively, following low-dose administration (10 mg/kg bw). At the high dose (1000 mg/kg bw), absorption decreased to approximately 17–25% of the administered dose for both sexes. No significant tissue accumulation was evident (less than 0.5% of the administered dose remained in the carcass at 168 hours postdosing). The majority of radioactivity was eliminated within 24 and 48 hours following low- and high-dose administration, respectively. AC 900001 Technical Herbicide was extensively metabolized. There were gender differences in absorption, metabolism and excretion.

Following subchronic and chronic dietary exposure, treatment-related hematological and histopathological findings indicative of regenerative hemolytic anemia were noted for all species tested. Similar findings were also noted in the rat two-generation reproduction study as well as in the rat and rabbit developmental studies. Hematological findings were generally characterized by lower red blood cell count, hemoglobin and hematocrit, with associated increases in mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration and reticulocyte counts. Histopathological findings were generally characterized by increased incidence/severity of hemosiderin deposition in the spleen and/or Kupffer cells of the liver as well as extramedullary hematopoiesis in the spleen and/or liver. The rat appears to be the most sensitive species with NOAELs of 10.5, 6.4 and 2.4 mg/kg bw/d following 28-day, 90-day and 2-year dietary administration, respectively.

Although findings indicative of hemolytic anemia were noted in dogs following 90-day and 1-year dietary administration, the main target organ appeared to be the thyroid, as indicated by increased thyroid weight, diffuse hypertrophy of the thyroid follicular epithelial cells and scattered foci of thyroid follicular cell hyperplasia. Thyroid hormones (thyroxine, tri-iodothyronine and thyroid stimulating hormone) are crucial to normal growth and development in the central nervous system and, in the absence of thyroid hormones, brain development can be retarded; however, hormone levels were not determined. Similar lesions were not observed in the rat (including neonates) or mouse following subchronic or chronic dietary exposure, and there was no other evidence in any species tested to indicate a neurotoxicity potential. In the absence of any thyroid hormone data as well as any human data, these lesions cannot be disregarded and must be considered relevant to humans. The most appropriate NOAEL for the treatment-related findings noted in the thyroid in dogs is 4.4 mg/kg bw/d, as indicated in the 1-year dietary study.

Following subchronic and chronic administration, treatment-related findings were also noted in the liver and included centrilobular hepatocellular hypertrophy and hepatocellular vacuolation. These findings were only noted in mice, with NOAEL’s of 23.4, 10.2 and 6.9 mg/kg bw/d following 28-day, 90-day and 78-week dietary administration, respectively.

In a rat 4-week repeat-dose dermal toxicity study, the NOAEL for systemic toxicity was 75 mg/kg bw/d based on hematological and histopathological findings indicative of hemolytic anemia at the LOAEL, 100 mg/kg bw/d (the next highest dose level). There were no treatment-related findings in the thyroid.

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. In addition, there was no evidence in the toxicology database to indicate a significant difference in gender sensitivity.

In the rat 2-generation (one litter/generation) reproduction study, hematological and histopathological findings indicative of regenerative anemia were noted in P1/P2 parental animals and in F2 pups at 19 mg/kg bw/d and above. The NOAEL for parental and offspring toxicity was 3.7 mg/kg bw/d. On the basis of the parental and offspring NOAELs, there was no indication that neonates were quantitatively more sensitive than adults to AC 900001 Technical Herbicide. Reproductive function, reproductive parameters or litter parameters were not influenced by treatment.

In the rat and rabbit developmental toxicity studies, hematological and histopathological findings indicative of regenerative hemolytic anemia were noted in rats at 100 mg/kg bw/d and above as well as in rabbits at 20 mg/kg bw/d and above. The NOAEL for maternal toxicity was 50 mg/kg bw/d for rats and 5 mg/kg bw/d for rabbits. In the rat, the NOAEL for developmental toxicity was 1000 mg/kg bw/d, the highest dose tested, based on the absence of any adverse treatment-related effects on the developmental parameters examined. In the rabbit, there was a possible slight decrease embryonal-fetal viability manifest as slight increases in abortion (1 on day 21; 1 on day 23), postimplantation loss, total number of resorptions (early and late) and mean resorption rate at 50 mg/kg bw/d; however, the differences from controls were not statistically significant and the values were within historical control range for animals of this strain. The NOAEL for developmental toxicity was 20 mg/kg bw/d, the highest dose tested. On the basis of the maternal and developmental NOAELs in the rat and rabbit developmental toxicity studies, there was no evidence in either species to indicate a quantitative increase susceptibility of the fetus to in utero exposure to AC 900001 Technical Herbicide. There was no evidence of any treatment-related irreversible structural changes in either species; therefore, AC 900001 Technical Herbicide was not considered to be teratogenic in rats or rabbits.

Occupational exposure will be predominately via the dermal route, and of short- to intermediate-term duration. Although a 4-week repeat dose dermal toxicity study is available, it is not considered adequate for occupational and bystander risk assessment since it does not adequately account for the treatment-related findings noted in the thyroid in dogs following 90-day and 1-year dietary administration. To account for these findings, it is recommended that the dog 90 day dietary study be used for the proposed exposure scenarios. The recommended NOAEL is 1.7 mg/kg bw/d. A safety factor of 100

to account for intraspecies and interspecies variations is considered to be adequate; no additional safety factors were used because there was an adequate MOE to the NOAEL of 4.4 mg/kg bw/d for thyroid effects in the 1-year dietary dog 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

The end-use product, AC 900001 Water-Dispersible Granular Herbicide, is a water-dispersible granular formulation packaged in water soluble packets that has a guarantee of 750 g picolinafen/kg. The product is proposed for use on spring wheat, including durum, and barley to control broadleaf weeds. Application would be postemergent using ground equipment only. The proposed application rate is 50 g a.i./ha with a maximum of one application per season. This end-use product may be tank mixed with 2,4-D ester and Assert 300 SC Wild Oat Herbicide.

The label specifies that handlers wear chemical-resistant gloves and dust- or splash-proof goggles or face shield during mixing/loading, clean-up and repair activities. No re-entry interval is specified. A preharvest interval of 60 days is proposed for AC 900001 Water-Dispersible Granular Herbicide. The label also proposed that treated fields may be grazed or cut for forage of hay 30 days after application.

Mixer/loader/applicator exposure is expected to be short-term in duration for farmers and short- to intermediate-term for custom applicators for the proposed uses of AC 900001 Water-Dispersible Granular Herbicide.

Mixer/Loader/Applicator Exposure
Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted. Using the Pesticide Handlers Exposure Database (PHED) Version 1.1, exposure estimates were calculated for farmers and custom applicators mixing/loading water-dispersible granular formulation in water soluble packets as well as for farmers and custom applicators applying liquid using groundboom. The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates. The PHED estimates meet criteria for data quality, specificity and quantity outlined under the North American Free Trade Agreement Technical Working Group on Pesticides.

To estimate exposure for each use scenario, appropriate subsets of A and B grade data were created from the mixer/loader and applicator database files of the PHED. All data were normalized for kilogram of active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e., summing the measure of central tendency for each body part which is most appropriate to the distribution of data for that body part. The exposure values are based on open

mixing/loading and workers wearing one layer of clothing and gloves during mixing/loading as well as workers wearing one layer of clothing and no gloves during application. There is no adequate PHED subset for mixing/loading a water-dispersible granular formulation in water soluble packaging. As such, a 90% protection factor was applied to the exposure value for mixing/loading a water-dispersible granule.

The exposure estimates and MOEs for mixing/loading/applying AC 900001 Water-Dispersible Granular Herbicide are presented in Table 3.5.1. The MOEs were calculated from the combined dermal and inhalation exposure from mixing, loading and applying picolinafen.

Table 3.5.1 Exposure Estimates and Resulting MOEs for Mixers/Loaders/Applicators

Crop	Exposure Scenario Mixers/Loaders/Applicators	Exposure (µg a.i./kg bw/d)[a]	MOE[b]
Spring wheat	Groundboom / farmer	5.1	333
	Groundboom / custom applicator	10.8	157

[a] Used maximum application rate and area treated per day for each crop; dermal absorption is considered equivalent to oral absorption; body weight is 70 kg.

[b] MOE = NOAEL/daily dose (short- and intermediate-term NOAEL = 1.7 mg/kg/d).

Based on a NOAEL of 1.7 mg/kg/day from a 90-day dietary dog study, the MOE for a farmer and a custom operator mixing/loading/applying AC 900001 Water-Dispersible Granular Herbicide by groundboom to wheat would be 333 and 157, respectively. Since the target MOE is 100, the MOEs for mixer/loader/applicator exposure are acceptable for the proposed uses of the end-use product.

3.5.2 Bystanders

Not applicable.

3.5.3 Workers

Re-entry activities are minimal for spring wheat and barley. Therefore, re-entry exposure for workers would be negligible.

3.5.4 Consumers

Not applicable.

4.0 Residues

4.1 Integrated Food Residue Chemistry Summary

Nature of the Residue in Plants

[^{14}C]-Picolinafen, uniformly labelled in the aniline ring ([aniline-^{14}C]-picolinafen) as well as at the 2 and 6 positions of the pyridine ring ([pyridine^{14}C]-picolinafen) and formulated as a 200 g/L emulsifiable concentrate formulation, was applied to wheat (variety: Turbo) at the end of the tillering stage (BBCH-Code 25-29) at a nominal rate of 100 g a.i./ha. Based on the very low radioactive residues detected in seed and husk, there was minimal translocation of the parent compound and its associated metabolites from the point of application to the seed. The parent compound, picolinafen, was the predominant residue in the 0- and 27-DAT (days after treatment) foliage and 86-DAT straw. The substituted picolinic acid metabolite (CL 183513), formed as a result of the cleavage of the amide bond of the parent molecule, was also detected in wheat matrices. The ROC may be defined as the parent compound, picolinafen. The metabolism of picolinafen in wheat is well understood.

Confined Accumulation in Rotational Crops

[^{14}C]-Picolinafen, uniformly labelled in the aniline ring ([aniline-^{14}C]-picolinafen) as well as at the 2 and 6 positions of the pyridine ring ([pyridine^{14}C]-picolinafen) and formulated as an emulsifiable concentrate, was applied to either wheat at the 4- to 6-leaf stage or to loam soil at a nominal rate of 100 g a.i./ha. Carrots, peas, sugar beets and sunflowers were planted 30 days while lettuce, soybean and carrots were planted 11 months following the foliar postemergence treatment to wheat. In a separate trial, lettuce, soybean and carrots were planted 30 days after direct application to soil. When harvested at maturity, there were no measurable residues in the raw agricultural commodities of the rotational crops; therefore, no attempt was made to identify or characterize the nature of the radioactive residues. Furthermore, the soil metabolism study demonstrated that picolinafen undergoes rapid transformation to CL 153815, classified as slightly to moderately persistent under aerobic conditions, and CL 7693, a minor transformation product that is strongly bound to soil and not expected to be readily available for uptake or transport. The MORs in the rotational crops from the confined crop rotation study did not trigger a need for field accumulation studies.

Nature of the Residue in Animals

[^{14}C]-Picolinafen, uniformly labelled in the aniline ring ([aniline-^{14}C]-picolinafen) as well as at the 2 and 6 positions of the pyridine ring ([pyridine^{14}C]-picolinafen), was administered orally (gelatin capsule), by balling gun, to eight lactating goats (La Mancha strain) at low doses (6.3 and 10.8 ppm) and high doses (47.2 and 65.1 ppm) daily for 7 consecutive days. Picolinafen was rapidly excreted, primarily as the unchanged parent compound, with minimal transfer to the tissues and milk. In the pyridine-label study, only the parent, picolinafen, was identified in fat samples, while the substituted picolinic acid metabolite, CL 153815, accounted for all of the identified residues in kidney, liver, and

milk. Similarly, in the aniline labelled study, only the parent compound was identified in fat samples. In liver, metabolite CL 44167, resulting from the acetylation of the p-fluoroaniline metabolite, accounted for the majority of the radioactive residue. However, in kidney and milk samples, the aniline-specific metabolite, CL 6497, resulting from the elimination of the fluorine substitutent of CL 44167, was the predominant metabolite.

[^{14}C]-Picolinafen, uniformly labelled in the aniline ring ([aniline-^{14}C]-picolinafen) and at the 2 and 6 positions of the pyridine ring ([pyridine^{14}C]-picolinafen) was administered orally (gelatin capsule), by balling gun, to 10 laying hens per group at a target dose level of 12.5 ppm daily for 13 consecutive days. A third group of hens was dosed with [aniline-^{14}C]-picolinafen at a lower level of 0.05 ppm. Greater than 97% of the administered dose was eliminated via the excreta. Less than 0.4% of the administered dose was found in edible tissues and eggs. In the pyridine-label study, the predominant residue detected in muscle, fat and eggs was the parent compound, picolinafen, followed by the pyridine-ring specific metabolites, picolinic acid (CL 153815) in muscle and eggs, and CL 952711 (methylated picolinic acid) in fat. CL 952711 was the major metabolite detected in liver. In the aniline label study, the predominant residue detected in fat and eggs was the parent compound. However, in eggs, the aniline-ring specific metabolite, CL 44167, also accounted for a significant portion of the radioactivity. Picolinafen was extensively metabolized in liver with CL 410142 (M700H01, hydroxy CL 44167) as the primary metabolite. Muscle was not analyzed due to its low total radioactive residue (TRR) level (<0.01 ppm).

An overall comparison of the metabolites identified in the goat, hen and rat demonstrated that the metabolism of picolinafen in all three species appears to proceed via the same major metabolic pathways.

The metabolic profiles in plants and animals suggest two major pathways: hydrolytic cleavage of the amide bond to yield the substituted picolinic acid, CL 153815, and p-fluoroaniline, CL 7693, followed by further degradation and conjugation. Based on these studies, the ROC in plant matrices, for risk assessment and enforcement purposes, may be defined as the parent compound, picolinafen. For risk assessment, the ROC in animal matrices, may be defined as the parent compound only, picolinafen. For enforcement purposes, the ROC may be defined as the parent compound and the substituted picolinic acid, CL 153815.

Methods for Residue Analysis of Plants and Plant Products

Two analytical methods, GC/NPD Method FAMS 079-01 and GC/MS Method M3313, were submitted for the determination of the ROC in plant matrices. Method FAMS 079-01 was used for data gathering while Method M3313 was proposed for enforcement and used for data gathering for the supervised residue trials. The method LOQ for picolinafen was the same for both methods: 0.05 mg/kg. The recoveries were within the guideline requirement of 70–120%, and the CVs measured with respect to recoveries following spiking at the LOQ did not exceed 20%, indicating that the methods have good

repeatability. The ILV support the reliability and reproducibility of the GC/MS Method M3313 for the determination of residues of picolinafen in plant matrices.

Methods for Residue Analysis of Food of Animal Origin
A high performance liquid chromatography with tandem mass spectrometry method (HPLC/MS/MS), FAMS 109-01, was submitted for data gathering and enforcement purposes. The LODs and the LOQs of the matrices described are 0.002 mg/kg and 0.02 mg/kg for muscle, fat and egg, respectively per analyte, as well as 0.001 mg/kg and 0.01 mg/kg for milk, respectively per analyte. The recoveries of the parent compound and the metabolite were within guideline requirement of 70–120%, and the CVs measured with respect to recoveries following spiking at the LOQ were within 20%. The ILV demonstrated good reliability and reproducibility for the determination of residues of picolinafen and CL 153815 in milk, eggs and tissues.

Storage Stability Data—Plant/Animals
Submitted freezer storage stability studies indicated that residues of picolinafen were stable at -18°C for up to 12 months in wheat whole green plant, straw and grain.

In the absence of measurable residues of picolinafen and CL 153815 in meat, meat by-products, milk and eggs following exposure of animals to feed treated according to the use pattern, a freezer storage stability study for animal matrices was not required.

Crop Field Trials
Supervised residue trials demonstrated that when wheat and barley, grown throughout the Canadian prairie provinces and North and South Dakota, USA (zones 5, 7, 7A and 14), are treated with the proposed end-use product, AC 900001 Water-Dispersible Granular Herbicide, at a seasonal application rate of 50 g a.i./ha and harvested at maturity, residues in grain did not exceed the method LOQ (0.05 mg/kg). Therefore, a maximum residue limit (MRL) of 0.05 ppm should be established to cover residues of picolinafen in/on wheat and barley grain. Residue decline studies in wheat and barley forage demonstrated that residues of picolinafen dissipated rapidly as a function of time post-treatment.

Processed Food/Feed
There were no measurable residues of picolinafen in wheat and barley grain when treated according to the use pattern. Furthermore, the wheat metabolism study demonstrated that when treated at twice the label rate, residues in seed were low (0.004 ppm). Therefore, the processing study used to determine residues in processed fractions (bran, germ, shorts and middlings) was not required.

Meat/Milk/Poultry/Eggs
When feed commodities (forage, hay, straw) are treated according to the use pattern, residues in feed commodities did not exceed 0.2 ppm, while residues in grain were below the method LOQ of 0.05 mg/kg. Furthermore, the livestock metabolism studies demonstrated a minimal transfer of residues of picolinafen and CL 153815 in tissues, eggs

and milk following exposure to highly exaggerated dietary doses (250–400-fold the maximum anticipated dietary burden). Based on this information, dairy cattle and poultry feeding studies were not required. Since anticipated residues of picolinafen and CL 153815 in livestock matrices are not expected to exceed the method LOQs of the proposed enforcement method, FAMS 109-01, MRLs for meat, meat by-products, eggs and milk will not be established.

Dietary Risk Assessment

The proposed use of picolinafen on wheat and barley in Canada does not pose an unacceptable chronic or acute dietary (both food and water) risk to any segment of the population, including infants, children, adults and seniors.

The temporary registration of picolinafen was granted pending the submission of a poultry metabolism study. As this poultry metabolism study had no impact on the risk assessment, the dietary risk assessment was not revised.

5.0 Fate and Behaviour in the Environment

The fate and behaviour of AC 900001 Technical Herbicide in the environment was investigated using [pyridine-2,6-^{14}C]- and [aniline-U-^{14}C]-labelled picolinafen (Figure 5.1 and Figure 5.2).

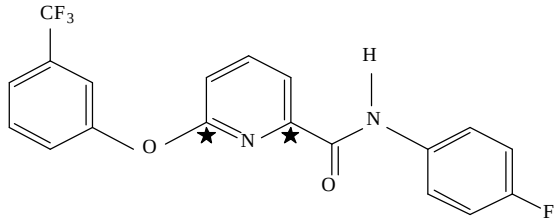


Figure 5.1 Pyridine-2,6-^{14}C-picolinafen

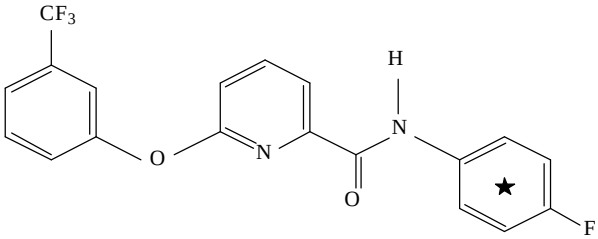


Figure 5.2 Aniline-U-^{14}C-picolinafen

5.1 Physical and Chemical Properties Relevant to the Environment

All chemical and physical properties required for the active ingredient were provided and are summarized in Table 1.2.1. AC 900001 Technical Herbicide is insoluble in water and non-volatile from moist soil and water surfaces under field conditions. AC 900001 Technical Herbicide does not dissociate at environmentally relevant pH values. The log K_{ow} of greater than 5 indicates that AC 900001 Technical Herbicide has a potential to bioaccumulate, but bioconcentration and metabolism studies did not support this (sections 3.1 and 5.6). The UV–visible absorption spectrum maximum at 290 nm indicates that there is potential for phototransformation.

The PMRA requested a summary of physical and chemical data for the major transformation product, CL 153815 (Appendix III, Table 1). The physical and chemical properties of CL 153815 are dependent on pH. It is a relatively strong acid and is an anion at environmentally relevant pH values (pH 5 to pH 9). It is very soluble in water at all pH values and the solubility increases as the alkalinity increases. Because solubility in water was mathematically estimated using log K_{ow} values, empirical data for solubility in water are required. Photolysis is not expected to be an important route of transformation of CL 153815, based on the UV–visible absorption spectrum maxima of less than 290 nm. CL 153815 is also expected to be non-volatile from moist soil and water surfaces; however, its potential to leach is much greater than the parent compound owing to its high solubilility in water and anionic state at environmentally relevant pH values.

5.2 Abiotic Transformation

Abiotic reactions are not important in the transformation of AC 900001 Technical Herbicide or its major transformation product (CL 153815) in the environment (Appendix III, Table 2).

5.3 Biotransformation

The biotransformation of AC 900001 Technical Herbicide occurs by cleavage of the amide bond to form the transformation products, CL 153815 (major product, 6-(3-trifluoromethylphenoxy)-2-pyridine carboxylic acid) and CL 7693 (minor product, 4-fluoroaniline). These are incorporated into the soil or sediment matrices where they are strongly bound. Carbon dioxide is the terminal transformation product. No organic volatile products are formed. The biotransformation pathway is proposed in Figure 5.3.1.

In aerobic laboratory studies, AC 900001 Technical Herbicide is non-persistent in soil under aerobic conditions (DT_{50} < 2–14 days), according to the classification of Goring et al. (1975). CL 153815 is the only major transformation product and is classified as slightly to moderately persistent under aerobic conditions (DT_{50} 30–77 days). The second cleavage product, CL 7693, is a minor transformation product that is strongly bound to

soil and not expected to be readily available for uptake or transport. Mineralization of AC 900001 Technical Herbicide was extensive.

Under anaerobic conditions in soil, very little mineralization of AC 900001 Technical Herbicide occurred. Although the conditions during the first 14 days of the study were aerobic, the results of the water-sediment studies indicate that AC 900001 Technical Herbicide will be non-persistent in anaerobic soil. The concentration of the transformation product CL 153815 increased in the anaerobic soil for 63 days (maximum 87% applied radioactivity). CL 153815 persisted until the end of the study (120 DAT). CL 153815 is classified as persistent in soil under anaerobic conditions.

AC 900001 Technical Herbicide was non-persistent in natural water systems under aerobic (water) and anaerobic (sediment) conditions (DT_{50} 1.1–1.4 days in water; DT_{50} 8.6–12.7 days in sediment), according to the classification of McEwen and Stephenson (1979). CL 153815 is classified as slightly persistent in the aerobic water phase (DT_{50} 10.9–24.4 days) and persistent in the anaerobic sediment phase (no dissipation) of natural water systems. Overall, CL 153815 is classified as moderately persistent in total water systems (DT_{50} 45.3–70.1 days).

In the anaerobic aquatic sediment-water systems, AC 900001 Technical Herbicide was slightly persistent in the water phase (DT_{50} 15.4 days) and non-persistent in the sediment phase (DT_{50} 6.4 days), according to the classification of McEwen and Stephenson (1979). Overall, AC 900001 Technical Herbicide is classified as slightly persistent in total anaerobic water systems (DT_{50} 18.7 days). CL 153815 is classified as persistent in anaerobic water systems (DT_{50} 197 days in water; DT_{50} 645 days in sediment).

A summary of biotransformation rates of AC 900001 Technical Herbicide and the major transformation product, CL 153815, is presented in Appendix III, Table 3. Overall, AC 900001 Technical Herbicide is non-persistent under aerobic and anaerobic conditions in soil and natural water systems. CL 153815 is moderately persistent under aerobic conditions in soil and natural water systems. CL 153815 is persistent in soil, sediment and water under anaerobic conditions.

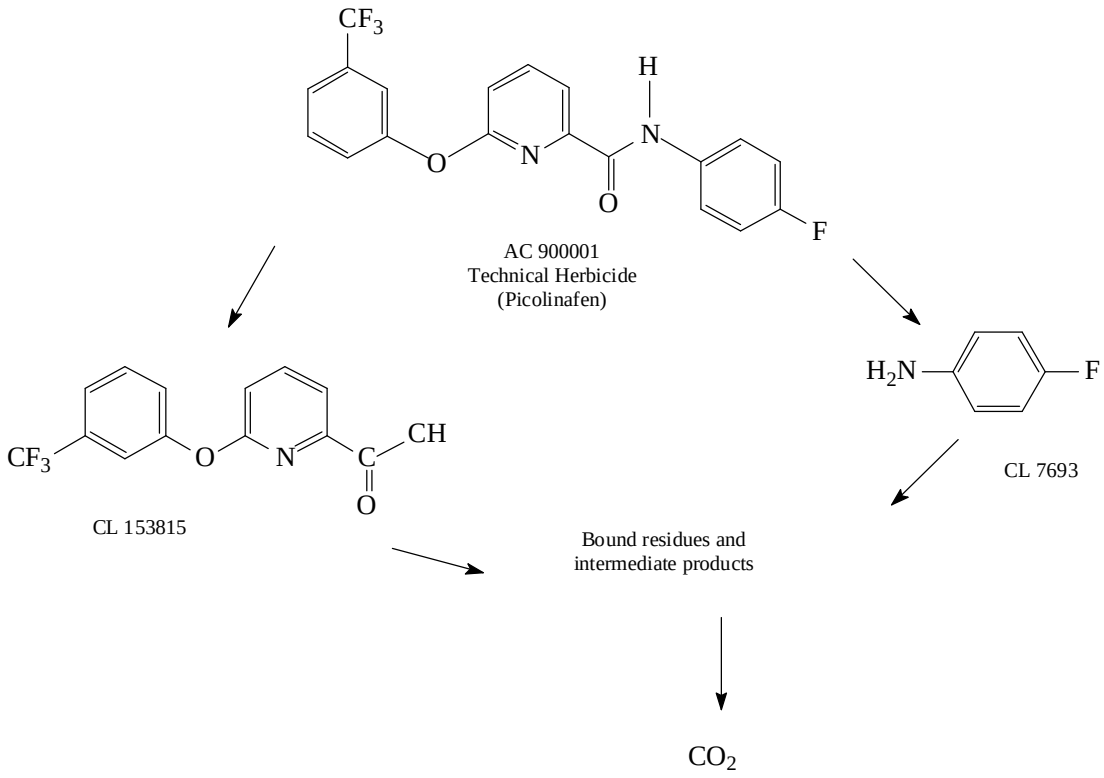


Figure 5.3.1 Proposed Biotransformation Pathway of AC 90000 Technical Herbicide in Soil

5.4 Mobility

The K_{oc} values (≥15 100) indicate that AC 900001 Technical Herbicide will bind strongly to the soil and is immobile in the soil, according to the classification of McCall et al. (1981). The mobility of CL 153815 is classified as low to medium based on the K_{oc} values ranging 160–783. However, physical and chemical properties and the persistence of CL 153815 indicate that it has potential to leach and contaminate groundwater (Appendix III, Table 4).

AC 900001 Technical Herbicide and CL 153815 are not expected to volatilize under field conditions owing to low Henry's Law constants (K_H 1.6×10^{-3} and 1.6×10^{-3} Pa m^3/mol at 20°C, respectively). These compounds did not occur in organic volatile traps of soil and aquatic system incubations.

5.5 Dissipation and Accumulation under Field Conditions

Terrestrial field dissipation studies at three locations in the Canadian prairie provinces indicate that AC 900001 Technical Herbicide is slightly to moderately persistent in typical soils in the Canadian prairie region (DT_{50} 15–62 days), according to the classification of Goring et al. (1975). AC 900001 Technical Herbicide was more persistent in the field than in the laboratory. The potential for carry-over of AC 900001 Technical Herbicide is

negligible; however, 53–64% of CL 153815 residues carried over to the next growing season under field conditions. Field data are summarized in Appendix III, Table 5.

CL 153815 and AC 900001 Technical Herbicide did not leach below the 15-cm soil depth under typical field conditions. While the lack of downward movement of AC 900001 Technical Herbicide is supported by the adsorption/desorption results (K_{oc} >15 000; immobile classification), the physical and chemical properties of CL 153815 (see Appendix III, Table 4) and the adsorption/desorption data (K_{oc} 160–783), indicate that there is potential for CL 153815 to leach should there be above-normal rainfall.

5.6 Bioconcentration

Bioconcentration factors of AC 900001 Technical Herbicide in the bluegill sunfish were 420–540 at 2 µg/L and 600–730 at 20 µg/L. The time for 50% depuration was very short (0.89–1.7 days at 2 µg/L and 1.2–1.4 days at 20 µg/L), with 95% depuration within 7.3 days. Because AC 900001 Technical Herbicide is not persistent in aquatic systems and the depuration rate of AC 900001 Technical Herbicide in fish is fast, bioconcentration is not of concern under the specific conditions of use.

AC 900001 Technical Herbicide was metabolized in the bluegill sunfish by hydroxylation of the *p*-fluoroaniline ring to yield two isomeric hydroxylated derivatives (CL 410856 and CL 411016), followed by sulfate conjugation of these two hydroxylated derivatives (CL 1000624 and CL 1000625), and by hydrolysis of the amide bond of AC 900001 Technical Herbicide to yield CL 153815 as the major metabolite. There was a very minor amount of CL 7693. In addition, hydrolysis of the amide bond of the hydroxylated and sulfate conjugated metabolites was also expected to occur, thereby giving rise to hydroxylated derivatives of CL 7693 and sulfate conjugates of the hydroxylated derivatives of CL 7693. These hydrolysis products could account for components of metabolite 1 (tentatively identified as a mixture of CL 7693 and its two hydroxylated derivatives) and/or the very minor polar and non-polar metabolites, respectively. Therefore, the data obtained from this study adequately define the uptake/depuration potential and the metabolic pathway of AC 900001 Technical Herbicide. The proposed metabolic pathway for AC 900001 Technical Herbicide is shown in Figure 5.6.1.

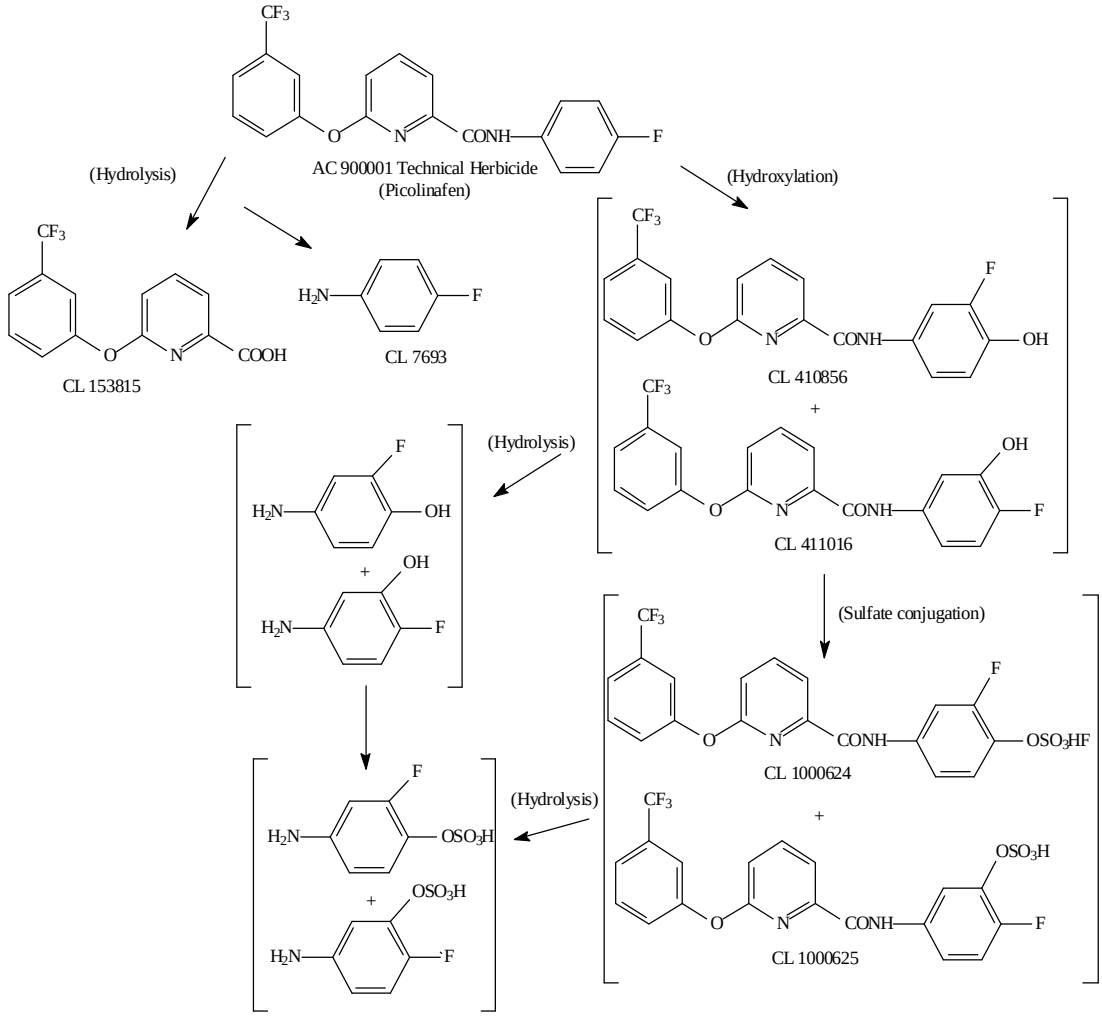


Figure 5.6.1 Proposed Metabolic Pathway of AC 90000 Technical Herbicide in Fish

5.7 Summary of Fate and Behaviour in the Terrestrial Environment

AC 900001 Water-Dispersible Granular Herbicide will be introduced to the terrestrial environment by application using ground equipment, once per year at a rate of 50 g a.i./ha, beginning as early as April 20 in the Peace River Region of British Columbia and ending approximately June 25 in the prairie region of Alberta, Saskatchewan and Manitoba.

The residues relevant to the environment are AC 900001 Technical Herbicide and its principal transformation product, CL 153815. No other compounds have been identified which account for greater than 10% of the applied parent compound.

The physical and chemical properties of AC 900001 Technical Herbicide and CL 153815 are summarized in Table 1.2.1 and in Appendix III, Table 1, respectively. AC 900001

Technical Herbicide is insoluble in water, whereas CL 153815 is very soluble in water. Both compounds are non-volatile from moist soil and water surfaces. AC 900001 Technical Herbicide and CL 153815 are expected to be stable to hydrolysis and photolysis.

The biotransformation of AC 900001 Technical Herbicide occurs by cleavage of the amide bond to form the major product, CL 153815 (6-(3-trifluoromethylphenoxy)-2-pyridine carboxylic acid) and the minor product, CL 7693 (minor product, 4-fluoroaniline). In soil, these transformation products become bound. Carbon dioxide is the terminal transformation product. The proposed biotransformation pathway appears in Figure 5.3.1.

In aerobic laboratory studies, AC 900001 Technical Herbicide is non-persistent in soil under aerobic conditions (DT_{50} < 2–14 days), according to the classification of Goring et al. (1975). CL 153815 is classified as moderately persistent under aerobic conditions (DT_{50} 30–77 days). The cleavage product, CL 7693, is strongly bound to soil. Mineralization of AC 900001 Technical Herbicide is significant.

Under anaerobic conditions in soil, AC 900001 Technical Herbicide is expected to be non-persistent. However, CL 153815 is expected to be persistent based on its accumulation under anaerobic conditions for the first 63 days with no decline for the remaining 57 days of the study.

Terrestrial field dissipation studies at three locations in the Canadian prairie provinces indicate that AC 900001 Technical Herbicide is slightly to moderately persistent in typical soils in the Canadian prairie region (DT_{50} 15–62 days), according to the classification of Goring et al. (1975). AC 900001 Technical Herbicide was more persistent in the field than in the laboratory. The potential for carry-over of AC 900001 Technical Herbicide is negligible; however, 53–64% of CL 153815 residues carried over to the next growing season under field conditions.

CL 153815 and AC 900001 Technical Herbicide did not leach below the 15-cm soil depth under typical field conditions. While the lack of downward movement of AC 900001 Technical Herbicide is supported by the adsorption/desorption results (K_{oc} > 15 000; immobile classification), the physical and chemical properties of CL 153815 (see Appendix III, Table 4) and the adsorption/desorption data (K_{oc} 160–783) indicate that there is potential for CL 153815 to leach should there be above-normal rainfall.

5.8 Summary of Fate and Behaviour in the Aquatic Environment

Contamination of aquatic environments could occur by spray drift during application or by runoff from treated soil.

The transformation of AC 900001 Technical Herbicide in aerobic sediment/water systems occurs by the same mechanism as in soil, with cleavage of the amide bond to form the major product, CL 153815 [6-(3-trifluoromethylphenoxy)-2-pyridine carboxylic acid], and the minor product, CL 7693 (4- fluoroaniline). These products partition to the sediment under laboratory conditions.

Both AC 900001 Technical Herbicide and its major transformation product (CL 153815) are stable to hydrolysis, and are considered to be stable to phototransformation in water under environmentally relevant conditions. Neither are expected to volatilize from water surfaces. AC 900001 Technical Herbicide is insoluble in water, whereas CL 153815 is very soluble.

A summary of biotransformation rates of AC 900001 Technical Herbicide and the major transformation product, CL 153815, in aquatic systems under laboratory conditions is presented in Appendix III, Table 3. Overall, AC 900001 Technical Herbicide is non-persistent in aerobic water systems (DT_{50} 6.2 days) and slightly persistent in anaerobic water systems (DT_{50} 18.7 days), according to the classification of McEwen and Stephenson (1979). CL 153815 is moderately persistent in aerobic water systems (DT_{50} 45.3–70.1 days), but will be persistent in anaerobic water systems (DT_{50} 197 days in water; DT_{50} 645 days in sediment).

5.9 Expected Environmental Concentrations

5.9.1 Soil

For assessing risk to earthworms, the expected environmental concentration (EEC) for AC 900001 Technical Herbicide was calculated to be 0.022 mg a.i./kg based on the following assumptions.

- The maximum proposed application rate of 50 g a.i./ha is applied to bare soil.
- The product is applied once per season (year).
- The product is evenly distributed in the 0- to15-cm depth of the soil.
- The bulk density of the soil is 1.5 g/cm^3.

The accumulated concentration of CL 153815 would plateau at 0.026 mg/kg soil after approximately 13 years, assuming initial maximum concentration of 0.0092 mg/kg soil (from Fairview field study at the label rate) and 64% carry-over (from Minto field study).

5.9.2 Aquatic Systems

Habitat

For initial screening of risk to aquatic organisms in surface waters, direct overspray is considered a conservative scenario in estimating the amount of active ingredient entering surface water. Assuming a water depth of 30 cm for agricultural ponds and an application rate of 50 g a.i./ha, the EEC in pond water as a result of direct overspray is calculated to be 0.0167 mg a.i./L. The limit of solubility of AC 900001 Technical Herbicide in water is 0.047 mg a.i./L.

Drinking Water

Level I drinking water concentrations of AC 900001 Technical Herbicide and its transformation product, CL 153815, in groundwater sources as a result of leaching were estimated over a 20-year period using the model LEACHM. The results indicated that AC 900001 Technical Herbicide is not expected to reach groundwater (0 µg/L). The maximum annual average concentration of CL 153815 in ground water was estimated to be 0.15 µg/L.

Level I drinking water concentrations in surface water sources (reservoirs and dugouts) as a result of runoff were estimated using the model PRZM/EXAMS. Two screening scenarios were used for modelling. Both scenarios used data for soils that are highly susceptible to run off.

- A dugout scenario (volume 2667 m^3 and 3.87-ha drainage area) using weather data typical of a region where dugouts are the primary source of drinking water.
- A reservoir scenario (volume 144 320 m^3 and 172.8-ha drainage area) using weather data typical of a region where reservoirs are the primary source of drinking water.

Due to the conservative nature of the scenarios used for modelling, the EEC values in drinking water as a result of leaching or runoff represent upper bound estimates of potential pesticide exposure. The AC 900001 Technical Herbicide concentrations were determined to be 1.61 and 0.08 µg a.i./L for acute and chronic exposures, respectively, while the corresponding CL 153815 concentrations were 1.15 and 0.61 µg/L. Water model input parameters for the screening assessment are summarized in Appendix III, Table 6.

5.9.3 Vegetation and Other Food Sources

Data that could be used to estimate the dissipation of AC 900001 Technical Herbicide on contaminated food sources for wildlife were not provided. Therefore, a scenario that assumes no transformation will occur on the surface of wildlife food sources was adopted. The estimated EEC values in vegetation are provided in Appendix III, Table 7, based on the nomogram in Hoerger and Kenaga (1972) and Kenaga (1973), which was modified by Fletcher et al. (1994). Based on these values, the estimated EEC in the diet of

non-target species immediately after application of AC 900001 Water-Dispersible Granular Herbicide for representative non-target species are as follows (Appendix III, Table 8):

- bobwhite quail—8.8 mg a.i./kg diet;
- mallard duck—1.7 mg a.i./kg diet;
- rat—25 mg a.i./kg diet;
- mouse—25 mg a.i./kg diet; and
- rabbit—38 mg a.i./kg diet.

6.0 Effects on Non-target Species

6.1 Effects on Terrestrial Organisms

The toxicity of AC 900001 Technical Herbicide and its transformation product, CL 153815, is summarized in Appendix III, Table 9. With the exception of plants, AC 900001 Technical Herbicide and CL 153815 are not inherently toxic to any non-target terrestrial organisms.

6.2 Effects on Aquatic Organisms

Technical grade AC 900001 is not acutely toxic to fish or freshwater invertebrates. Toxic effects to aquatic organisms will be limited by the solubility of the compound in water (0.047 mg a.i./L). Chronic effects in *Daphnia magna* (21-day no observed effect concentration [NOEC] of 0.007 mg a.i./L for survival, reproduction, and growth), fish (early life-stage NOEC of 0.0064 mg a.i./L for growth), algae (72-hour NOEC of 0.000068 mg a.i./L for biomass) and vascular plants (14-day NOEC of 0.006 mg a.i./L for frond number), however, were all observed at concentrations below the limit of solubility in water. The most sensitive organism was the green alga, *Selenastrum capricornutum.*

CL 153815 is classified as practically non-toxic to freshwater invertebrates (*Daphnia magna* LC_{50} > 98 mg/L). Algae are not very sensitive to CL 153815. The most sensitive endpoint was biomass for which the effective concentration to 50% (EC_{50}) and NOEC were 27 and 12 mg/L, respectively.

The toxicity of AC 900001 Technical Herbicide and its transformation product (CL 153815) are summarized in Appendix III, Table 10.

6.3 Effects on Biological Methods of Sewage Treatment

Data are not required.

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 endpoint divided by the EEC. Risks are then classified based on the scheme presented in Appendix III, Table 11.

6.4.1 Environmental Behaviour

AC 900001 Technical Herbicide is insoluble in water and non-volatile from moist soil and water surfaces. It is stable to hydrolysis and phototransformation. Biotransformation is the most important transformation process for AC 900001 Technical Herbicide and its major transformation product, CL 153815, in aquatic and terrestrial systems.

AC 900001 Technical Herbicide is classified as slightly to moderately persistent in soil under field conditions (DT_{50} 15–62 days) and non-persistent in aquatic systems (DT_{50} 6.2–18.7 days). CL 153815 is classified as slightly to moderately persistent in aerobic soil (DT_{50} 30–77 days), moderately persistent in aquatic systems (DT_{50} 45.3–70.1 days) and persistent under anaerobic conditions (DT_{50} 197 days in water; DT_{50} 645 days in sediment; no dissipation in soil). The potential for carry-over of AC 900001 Technical Herbicide in soil to the next growing season is negligible; however, 53–64% of CL 153815 carried over to the next growing season under field conditions.

CL 153815 and AC 900001 Technical Herbicide did not leach below the 15-cm soil depth under typical field conditions. While the lack of downward movement of AC 900001 Technical Herbicide is supported by the adsorption/desorption results (K_{oc} >15 000; immobile classification), the physical and chemical properties of CL 153815 (see Appendix III, Table 4) and the adsorption/desorption data (K_{oc} 160–783), indicate that there is potential for CL 153815 to leach should there be above-normal rainfall.

Bioconcentration factors of AC 900001 Technical Herbicide in fish ranged from 420 to 730. The time for 50% depuration was very short (0.89–1.7 days), with 95% depuration within 7.3 days. Because AC 900001 Technical Herbicide is not persistent in aquatic systems and the depuration rate of AC 900001 Technical Herbicide in fish is fast, bioconcentration of AC 900001 Technical Herbicide is not of concern under the specific conditions of use. Based on the rat metabolism study, AC 900001 Technical Herbicide and CL 153815 do not accumulate in mammals.

6.4.2 Terrestrial Organisms

Earthworms: For risk assessment, the lowest toxicity data from the studies available are used. The estimated initial EEC for one application is 0.022 and 0.026 mg/kg for AC 900001 Technical Herbicide and CL 153815, respectively. Taking the EEC data for

one application, the MOS for short-term toxicity (LC_{50}/EEC) for technical grade AC 900001 is > 45 454 (>1000/0.022). For CL 153815, the MOS for short-term toxicity is 18 326 (476.5/0.026). In addition, the short-term MOS for one application using the NOEC from the acute test amounts to 5045 (111/0.022) for AC 900001 Technical Herbicide and 4807 (125/0.026) for CL 153815. The MOS values for earthworms indicate that the risk of lethal and sublethal effects of AC 900001 Technical Herbicide and CL 153815 to earthworms is negligible (Appendix III, Table 12). Therefore, no restrictions on use of AC 900001 Water-Dispersible Granular Herbicide are required for the protection of earthworms.

Honeybees: Products that are applied as sprays can be evaluated initially by considering the likely exposure of bees and the toxicity of the product. According to the classification by Atkins et al. (1981), AC 900001 Technical Herbicide is classified as relatively non-toxic to honeybees (LD_{50} values were > 150 and > 200 µg a.i./bee for oral and contact exposures, respectively). No restrictions are required for the protection of honeybees for products that fall into this category.

Other arthropod species: The intended use of AC 900001 Water-Dispersible Granular Herbicide covers one application per season at a maximum rate of 50 g a.i./ha to control certain weed species. Non-target arthropods are likely to be exposed to formulated AC 900001 Technical Herbicide by direct spray as well as by contact with fresh or dry residues. As a screening scenario, the predicted initial environmental concentration to which non-target organisms are exposed is assumed to be equivalent to the maximum nominal field rate of 50 g a.i./ha. The field rates tested were twice and 0.012 times the maximum nominal field rate. The studies indicate that twice the maximum field application rate results in less than 30% lethal or sublethal effects in all four species (classified as “harmless” according to Hassan et al. 1994). Therefore, the risk of lethal and sublethal effects of AC 900001 Water-Dispersible Granular Herbicide to other arthropod species is low. No restrictions on the use of AC 900001 Water-Dispersible Granular Herbicide are required for the protection of other terrestrial arthropod species.

Birds: The possibility that birds will be exposed to AC 900001 Technical Herbicide(directly or indirectly) cannot be ruled out. Birds may be exposed to AC 900001 Technical Herbicide mainly by consuming contaminated feed. The risk assessment procedure is directed at risks to individuals as there are currently no commonly used criteria for judging the significance of effects for population-level processes. The MOS values for bobwhite quail mortality (LC_{50}/EEC) and effects on body weight (NOEC/EEC) are 604 (5314/8.8) and 30 (270/8.8), respectively. The MOS values for mallard duck mortality (LC_{50}/EEC) and effects on body weight and feed consumption (NOEC/EEC) are 3130 (5314/1.7) and 429 (729/1.7), respectively. Therefore, the risk of lethal and sublethal effects in birds is negligible (Appendix III, Table 12). No restrictions on the use of AC 900001 Water-Dispersible Granular Herbicide are required for the protection of birds.

Small wild mammals: The possibility that mammals will be exposed to AC 900001 Technical Herbicide (directly or indirectly) cannot be ruled out. Mammals may be exposed to AC 900001 Technical Herbicide mainly by the consumption of contaminated feed. As with birds, the risk assessment procedure is directed at risks to individuals. The lethal endpoint used was the 2-year dietary LC_{50} of >500 mg/kg bw for rats, while the sublethal endpoint used was the 78-week NOEC of 40 mg/kg diet for tissue effects (such as increased liver weight) in mice. The MOS values for mortality (LC_{50}/EEC) and sublethal effects (NOEC/EEC) are 20 (500/25) and 1.6 (40/25), respectively. Therefore, the risk of lethal and sublethal effects in small wild mammals is negligible (Appendix III, Table 12). No restrictions on the use of AC 900001 Water-Dispersible Granular Herbicide are required for the protection of small wild mammals.

Terrestrial plants: The lowest EC_{25} of 60 g formulation/ha (vegetative vigour of lettuce) was used to determine the risk of AC 900001 Water-Dispersible Granular Herbicide to non-target plants following a direct overspray at the maximum recommended application rate (67 g formulation/ha). The MOS (EC_{25}/EEC) after a single application was calculated to be 0.8. Therefore, plants are at moderate risk of growth reduction following a direct overspray (Appendix III, Table 12). No buffer zone is required for the protection of non-target plants. No restrictions on the use of AC 900001 Water-Dispersible Granular Herbicide are required for the protection of non-target terrestrial plants.

6.4.3 Aquatic Organisms

Although the proposed use does not include direct application to water, the possibility that aquatic organisms will be exposed to AC 900001 Technical Herbicide, directly or indirectly, cannot be ruled out. The first step is to identify the degree of risk expected by comparing the EEC in surface water as a result of direct overspray with acute toxicity (NOEC/EEC). This will give a MOS. The most sensitive organism tested was the green alga, *Selenastrum capricornutum* (NOEC of 0.000068 mg a.i./L). The results of the screening scenario (direct overspray) indicate that green algae are at very high risk of short-term toxicity (Appendix III, Table 13). Additional acute toxicity studies with a broader range of species indicate that two other species are also at risk: *Lemna gibba* and *Anabaena flos-aquae.*

6.5 Risk Mitigation

No restrictions on the use of AC 900001 Water-Dispersible Granular Herbicide are required for the protection of non-target terrestrial organisms.

Low to very high risk has been predicted for three species of aquatic plants. Therefore, the following restrictions are required on the label under the general heading "ENVIRONMENTAL HAZARDS":

> "Do not apply to terrains where there is potential for surface runoff to enter aquatic systems.
>
> Do not apply when rainfall is forecast for the next 48 hours."

As well as applying the restrictions outlined above, it is recommended that unsprayed buffer zones should be observed around all aquatic systems. The size of the buffer zone was determined to be 32 m using a model based on the expected drift from a boom sprayer (based on Nordby and Skuterud 1975). The input parameters were the lowest NOEC (0.000068 mg a.i./L for green algae) and the highest EEC (0.0167 mg a.i./L for all species). The following label statement is required under the general heading "ENVIRONMENTAL HAZARDS":

> "Overspray or drift to sensitive aquatic habitats should be avoided. A buffer zone of 32 m is required between the downwind point of direct application and the closest edge of sensitive aquatic habitats including sloughs, coulees, ponds, prairie potholes, lakes, rivers, streams, reservoirs and wetlands. Do not contaminate these habitats when cleaning and rinsing spray equipment or containers.
>
> Do not apply during periods of dead calm or when winds are gusty."

Two-way and three-way tank mixes with 2,4-D ester and Assert 300 SC are recommended on the label of AC 900001 Water-Dispersible Granular Herbicide for the control of a greater range of weed species. The following label statement is required under the general heading "TANKMIXING INSTRUCTIONS" to mitigate risk to non-target species from application of the recommended tank mixes:

> "Consult the label of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture."

7.0 Efficacy

7.1 Effectiveness

7.1.1 Mode of Action

AC 900001 Technical Herbicide, a Group 12 herbicide, inhibits the activity of phytoene desaturase, an enzyme responsible for the conversion of phytoene to phytofluene in the carotenoid biosynthetic pathway of plants. Inhibition of this enzyme leads to a reduction in carotenoid pigments and, ultimately, destruction of leaf chlorophyll in the foliage of

sensitive species. Symptomology in the field occurs as bleaching or whitening (often with mauve discolouration) of leaf tissue, followed by necrosis and death.

7.2 Effectiveness Against Pests

A total of 122 trials over 4 years across the Canadian prairie provinces were conducted as modified Randomized Complete Block Design with 4 replicates. Each trial included a reduced application rate to confirm that the requested rate is the lowest to provide effective and consistent weed control.

7.2.1 AC 900001 Water-Dispersible Granular Herbicide (alone treatment)

Redroot pigweed (*Amaranthus retroflexus*): Control ratings for redroot pigweed were reported in 34 trials conducted over 3 years across the Canadian prairie provinces. Mean control ratings at half the rate were 67.2% (n = 8) at < 41 DAT and 77.2% (n = 13) at > 41 DAT. Mean control ratings at the label rate were 86.7% (n = 21) at < 41 DAT and 91.3% (n = 34) at > 41 DAT. The data support a claim of redroot pigweed (1- to 4-leaf stage) control in spring wheat, durum wheat and barley at 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide.

Stinkweed (*Thlapsi arvense*): Control ratings for stinkweed were reported in 13 trials conducted over 3 years across the Canadian prairie provinces. Mean control ratings at half the label rate were 36.6% (n = 4) at < 41 DAT and 68.3% (n = 7) at > 41 DAT. Mean control ratings at the label rate were 68.9% (n = 7) at < 41 DAT and 83.2% (n = 13) at > 41 DAT. The data support a claim of stinkweed (1- to 6-leaf stage) suppression in spring wheat, durum wheat and barley at 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide.

Wild mustard (*Sinapis arvensis*): Control ratings for wild mustard were reported in 56 trials conducted over 3 years across the Canadian prairie provinces. Mean control ratings at half the label rate were 52.7% (n = 15) at < 41 DAT and 59.4% (n = 23) at > 41 DAT. Mean control ratings at the label rate were 66.1% (n = 30) at < 41 DAT and 76.9% (n = 43) at > 41 DAT. The data support a claim of wild mustard (1- to 8-leaf stage) suppression in spring wheat, durum wheat and barley at 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide.

7.2.2 AC 900001 Water-Dispersible Granular Herbicide + 2,4-D Ester Tank Mix

The weed claim for the two-way tank mix of 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester includes the weed list from the AC 900001 Water-Dispersible Granular Herbicide alone treatment, the weeds listed as susceptible or easy to control on the 2,4-D ester label as well as kochia, chickweed and wild buckwheat.

Confirmatory data made available support the weed claims from the components of the two-way tank mix.

Kochia (*Kochia scoparia*): Control ratings for kochia were reported in 23 trials conducted over 2 years across the Canadian prairie provinces. Mean control ratings at half the label rate were 77.4% (n = 8) at < 41 DAT and 77.5% (*n* = 8) at > 41 DAT. Mean control ratings at the label rate were 92.6% (*n* = 14) at < 41 DAT and 90.0% (*n* = 23) at > 41 DAT. The data support a claim of kochia (2- to 9-leaf stage) control in spring wheat, durum wheat and barley when applied at 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester.

Chickweed (*Stellaria media*): Control ratings for chickweed were reported in 15 trials conducted over 3 years across the Canadian prairie provinces. Mean control ratings at half the label rate were 68.8% (*n* = 5) at < 41 DAT and 61.3% (*n* = 5) at > 41 DAT. Mean control ratings at the label rate were 82.2% (*n* = 15) at < 41 DAT and 60.1% (*n* = 14) at > 41 DAT. The data support a claim of chickweed (1- to 8-leaf stage) suppression in spring wheat, durum wheat and barley when applied at 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester.

Wild buckwheat (*Polygonum convolvulus*): Control ratings for wild buckwheat were reported in 33 trials conducted over 3 years across the Canadian prairie provinces. Mean control ratings at half the label rate were 72.3% (*n* = 7) at < 41 DAT and 65.8% (*n* = 10) at > 41 DAT. Mean control ratings at the label rate were 82.5% (*n* = 22) at < 41 DAT and 79.3% (*n* = 33) at > 41 DAT. The data support a claim of wild buckwheat (1- to 4-leaf stage) suppression in spring wheat, durum wheat and barley when applied at 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester.

7.2.3 AC 900001 Water-Dispersible Granular Herbicide + 2,4-D Ester + Assert 300 SC Tank Mix

The weed claim for the three-way tank mix of 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester plus 400 g a.i./ha Assert 300 SC includes the weed list from the two-way tank mix plus wild oats. The tank mix of 2,4-D ester plus Assert 300 SC is presently registered for use on spring wheat, durum wheat and barley in the Canadian prairie provinces and Peace River Region of British Columbia.

Confirmatory data made available support the weed claims accepted for the two-way tank mix. The addition of Assert 300 SC did not reduce the level of broadleaf weed control.

Wild oat (*Avena fatua*): Control ratings for wild oat were reported in 53 trials conducted over 3 years across the Canadian prairie provinces. Mean control ratings at half the label rate were 76.9% (*n* = 5) at < 41 DAT and 83.9% (*n* = 9) at > 41 DAT. Mean control ratings at the label rate were 87.4% (*n* = 18) at < 41 DAT and 92.6% (*n* = 32) at > 41 DAT. The data support a claim of wild oat (1- to 3-leaf stage) control in spring wheat, durum wheat

and barley when applied at 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester plus 400 g a.i./ha Assert 300 SC.

To be consistent with the use directions on the Assert 300 SC label when applied at 400 g a.i./ha, the three-way tank mix is restricted to wild oat control in brown and dark brown soil zones.

7.3 Phytotoxicity to Target Plants (including different cultivars) or to Target Plant Products (OECD 7.4)

Replicated small-plot field trials were conducted between 1997 to 1999 across the prairie provinces of Canada on spring wheat, durum wheat and barley. Tolerance was assessed up to three times during the growing season as a visual estimate of crop injury: early season ratings (7–18 DAT), mid-season ratings (18–45 DAT) and late season ratings (46–106 DAT). Yields were reported as a percent of the untreated weedy check for each crop tested.

7.3.1 Spring Wheat (*Triticum aestivum*)

A total of 28 trials over 3 years (1997–1999) reported the tolerance of spring wheat. Of these trials, 15 reported crop yield. Trials were conducted on 12 spring wheat varieties: AC Barrie, AC Splendor, AC Taber, CDC Teal, Conway, Domain, Imi-SWP, Invader, Laura, Majestic, Michael, and Roblin. Treatments were applied at the 3-leaf to 3-tiller stage, with the majority applied at the 3- to 5-leaf stage of growth.

7.3.1.1 AC 900001 Water-Dispersible Granular Herbicide (alone treatment)

A total of 27 trials over 3 years across the Canadian prairie provinces reported the tolerance of spring wheat. Yield was reported in 14 trials over 2 years.

Early season crop injury ratings were 4% (n = 25) at the label rate and 4% (n = 14) at twice the label rate. Mid-season crop injury ratings were 0% (n = 26) at the label rate and 0% (n = 13) at twice the label rate. Late season crop injury ratings were 0% (n = 20) at the label rate and 0% (n = 11) at twice the label rate.

When yield was compared to the untreated weedy check, the reported label rate was 199% (n = 14) and the doubled rate was 116% (n = 8).

Although slight injury was reported shortly after application, the crop recovered without a yield reduction. The data support the addition of the alone treatment for use in spring wheat when applied between the 3- to 5-leaf stage of growth.

7.3.1.2 AC 900001 Water-Dispersible Granular Herbicide + 2,4-D Ester Tank Mix

A total of 20 trials over 3 years across the Canadian prairie provinces reported the tolerance of spring wheat. Yield was reported in 11 trials over 2 years.

Early season crop injury ratings were 9% (n = 19) at the label rate and 13% (n = 7) at twice the label rate. Mid-season crop injury ratings were 3% (n = 19) at the label rate and 8% (n = 6) at twice the label rate. Late season crop injury ratings were 2% (n = 15) at the label rate and 5% (n = 6) at twice the label rate.

When yield was compared to the untreated weedy check, the reported label rate was 129% (n = 11) and 109% (n = 4) at twice the label rate.

Although injury was reported shortly after application, the crop recovered without a yield reduction. The data support the addition of the two-way tank mix for use in spring wheat when applied between the 3- to 5-leaf stage of growth.

7.3.1.3 AC 900001 Water-Dispersible Granular Herbicide + 2,4-D Ester + Assert 300 SC Tank Mix

A total of 15 trials over 3 years across the Canadian prairie provinces reported the tolerance of spring wheat. Yield was reported in 8 trials over 3 years.

Early season crop injury ratings was 10% (n = 14) at the lable rate and was 12% (n = 8) at twice the label rate. Mid-season crop injury ratings were 4% (n = 14) at the label rate and 6% (n = 8) at twice the label rate. Late season crop injury ratings were 2% (n = 12) at the label rate and 4% (n = 6) at twice the label rate.

When yield was compared to the untreated weedy check, the reported label rate was 137% (n = 8) and 142% (n = 5) at twice the label rate.

Crop injury at the label rate and at twice the label rates were more than doubled of that reported for the AC 900001 Water-Dispersible Granular Herbicide alone treatment although yield was not affected. The data support the addition of the three-way tank mix for use in spring wheat when applied between the 3- to 5-leaf stage of growth.

7.3.2 Durum Wheat (*Triticum durum*)

A total of 18 trials over 3 years (1997–1999) reported the tolerance of durum wheat. Of these trials, 16 reported crop yield. Trials were conducted on 3 durum wheat varieties: AC Morse, Kyle and Sceptre. Treatments were applied at the 3-leaf to 1-tiller stage, with the majority applied at the 3- to 4-leaf stage.

7.3.2.1 AC 900001 Water-Dispersible Granular Herbicide (alone treatment)

A total of 18 trials over 3 years across the Canadian prairie provinces reported the tolerance of durum wheat. Yield was reported in 16 trials over 3 years.

Early season crop injury ratings were 4% (n = 17) at the label rate and 8% (n = 9) at twice the label rate. Mid-season crop injury ratings were 2% (n = 16) at the label rate and 2% (n = 9) at twice the label rate. Late season crop injury ratings were 1% (n = 10) at the label rate and 1% (n = 5) at twice the label rate.

When yield was compared to the untreated weedy check, the reported the label rate was 105% (n = 16) and 101% (n = 8) at twice the label rate.

There was a two-fold increase in the initial crop injury ratings following a doubled application rate of AC 900001 Water-Dispersible Granular Herbicide but recovered without yield reduction. The data support the addition of the alone treatment for use in durum wheat when applied between the 3- to 4-leaf stage of growth.

7.3.2.2 AC 900001 Water-Dispersible Granular Herbicide + 2,4-D Ester Tank Mix

A total of 17 trials over 2 years across the Canadian prairie provinces reported the tolerance of durum wheat. Yield was reported in 15 trials over 2 years.

Early season crop injury ratings were 13% (n = 16) at the label rate and 18% (n = 6) at twice the label rate. Mid-season crop injury ratings were 4% (n = 16) at the label rate and 5% (n = 5) at twice the label rate. Late season crop injury ratings were 2% (n = 9) at the label rate and 2% (n = 2) at twice the label rate.

When yield was compared to the untreated weedy check, the reported the label rate was 106% (n = 15) and 99% (n = 5) at twice the label rate.

There was a two-fold increase in crop injury ratings for the two-way tank mix compared to the alone treatment in durum wheat. Durum wheat also showed sensitivity to an overspray scenario with yield reductions when compared to the tank mix rate.

The data support the addition of the two-way tank mix for use in durum wheat when applied between the 3- to 4-leaf stage of growth.

7.3.2.3 AC 900001 Water-Dispersible Granular Herbicide + 2,4-D Ester + Assert 300 SC Tank Mix

A total of 13 trials over 2 years across the Canadian prairie provinces reported the tolerance of durum wheat. Yield was reported in 11 trials over 2 years.

Early season crop injury ratings were 15% (n = 12) and 17% (n = 7) at twice the label rate. Mid-season crop injury ratings at the lable rate was 8% (n = 13) at the label rate and 8% (n = 8) at twic the label rate. Late season crop injury ratings at the label rate was 2% (n = 6) at the label rate and 3% (n = 5) at twice the label rate.

When yield was compared to the untreated weedy check, the reported label rate was 111% (n = 11) and was 103% (n = 7) at twice the label rate.

Crop injury at the label rate and at twice the label rate were more than doubled of that reported for the AC 900001 Water-Dispersible Granular Herbicide alone treatment although yield was not affected. Durum wheat also showed sensitivity to an overspray scenario with yield reductions when compared to the tank mix rate.

The data support the addition of the three-way tank mix for use in durum wheat when applied between the 3- to 4-leaf stage of growth.

7.3.3 Spring Barley (*Hordeum vulgare*)

A total of 19 trials over 2 years (1998–1999) reported the tolerance of barley. Of these trials, 16 reported crop yield. Trials were conducted on seven spring barley varieties: AC Lacombe 6-row, Brier, Foster, Harrington, Manley, Richard, and Stein 2-row. Treatments were applied at the 3- to 4-leaf stage of growth.

7.3.3.1 AC 900001 Water-Dispersible Granular Herbicide (alone treatment)

A total of 19 trials over 2 years across the Canadian prairie provinces reported the tolerance of barley. Yield was reported in 16 trials over 2 years.

Early season crop injury ratings were 6% (n = 15) at the label rate and 9% (n = 10) at twice the label rate. Mid-season crop injury ratings were 2% (n = 17) at the label rate and 3% (n = 11) at twice the label rate. Late season crop injury ratings were 1% (n = 17) at the label rate and 3% (n = 10) at twice the label rate.

When yield was compared to the untreated weedy check, the reported label rate was 117% (n = 16) and was 116% (n = 10) at twice the label rate.

Although slight injury was reported shortly after application, the crop recovered without a yield reduction. The data support the addition of the alone treatment for use in spring barley between the 3- to 4-leaf stage of growth.

7.3.3.2 AC 900001 Water-Dispersible Granular Herbicide + 2,4-D Ester Tank Mix

A total of 15 trials over 2 years across the Canadian prairie provinces reported the tolerance of barley. Yield was reported in 12 trials over 2 years.

Early season crop injury ratings were 14% (n = 12) at the label rate and 14% (n = 4) at twice the label rate. Mid-season crop injury ratings were 7% (n = 12) at the label rate and 8% (n = 4) at twice the label rate. Late season crop injury ratings were 5% (n = 13) at the label rate and 4% (n = 5) at twice the label rate.

When yield was compared to the untreated weedy check, the reported label rate was 125% (n = 12) and 103% (n = 4) at twice the label rate.

Crop injury was reported shortly after application of the label rate and the double rate treatments but recovered without a yield reduction. The data support the addition of the two-way tank mix for use in spring barley between the 3- to 4-leaf stage of growth.

7.3.3.3 AC 900001 Water-Dispersible Granular Herbicide + 2,4-D Ester + Assert 300 SC Tank Mix

A total of 12 trials over 2 years across the Canadian prairie provinces reported the tolerance of barley. Yield was reported in 9 trials over 2 years.

Early season crop injury ratings were 15% (n = 9) at the label rate and 21% (n = 8) at twice the label rate. Mid-season crop injury ratings were 10% (n = 10) at the label rate and 12% (n = 8) at twice the label rate. Late season crop injury ratings were 6% (n = 9) at the label rate and 8% (n = 7) at twice the label rate.

When yield was compared to the untreated weedy check, the reported label rate was 129% (n = 9) and 126% (n = 7) at twice the label rate.

Crop injury at the label rate and at twice the label rate were more than doubled of that reported for the AC 900001 Water-Dispersible Granular Herbicide alone treatment although yield was not affected. The data support the addition of the three-way tank mix for use in spring barley between the 3- to 4-leaf stage of growth.

7.4 Impact on Succeeding Crops (OECD 7.5.1)

The mode of action of picolinafen does not lend itself to residual herbicide carry-over into the year following application. As a Group 12 herbicide, the product is absorbed through the foliage of plants and works by disrupting and destroying the photosynthetic process of sensitive species. It does not have soil activity and, therefore, is not anticipated to have residual effects in the year following application.

The environmental degradation profile of AC 900001 Technical Herbicide and that of its major transformation product, CL 153815, do not lend themselves to residual herbicide carry-over into the year following application of AC 900001 Water-Dispersible Granular Herbicide in Canadian Prairie soils.

There is no requirement for a recropping statement on the label for an alone treatment of AC 900001 Water-Dispersible Granular Herbicide. However, when used in combination with Assert 300 SC, the user is advised to follow all recommendations, precautions and restrictions that appear on the label.

7.5 Sustainability

7.5.1 Survey of Alternatives

There are currently no other Group 12 herbicides registered for use in western Canada to control broadleaved weeds in cereal crops.

However, there are numerous postemergent broadleaf weed herbicides, with different modes of action, that may be used alone or in various tankmix combinations on cereal crops to control broadleaf weeds in western Canada. Other groups of broadleaf herbicides that may be used alone or in various tank mix combinations are as follows:

Group	Examples of herbicide(s)
2	metsulfuron-methyl, chlorsulfuron, triasulfuron, tribenuron-methyl, thifensulfuron-methyl and sulfosulfuron
4	2,4-D, MCPA, picloram, dicamba, clopyralid and mecoprop
5	metribuzin
6	bromoxynil and bentazon
7	linuron

7.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

Application of AC 900001 Water-Dispersible Granular Herbicide would not exclude the sequential use of other herbicides with different modes of action for control of annual and perennial species not controlled by AC 900001 Water-Dispersible Granular Herbicide alone or a tank mix containing this product.

There are no recropping restrictions in the year following an alone treatment of AC 900001 Water-Dispersible Granular Herbicide, or a tank mix treatment of AC 900001 Water-Dispersible Granular Herbicide and 2,4-D ester. However, the user is advised to follow all recommendations, precautions and restrictions that appear on the Assert 300 SC label when AC 900001 Water-Dispersible Granular Herbicide is tank mixed with 2,4-D ester plus Assert 300 SC.

7.5.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

The introduction of a novel mode of action product for broadleaf weed control would assist in maintaining and perhaps extending the current weed control products on the market.

To address the issue of development of herbicide resistance, the AC 900001 Water-Dispersible Granular Herbicide label includes the resistance-management statement as outlined in Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*, as follows.

> HERBICIDE RESISTANCE MANAGEMENT:
> For resistance management, AC 900001 is a Group 12 herbicide. Any weed population may contain or develop plants naturally resistant to AC 900001 and other Group 12 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 specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance-management strategies should be followed.

To delay herbicide resistance:

- Where possible, rotate the use of AC 900001 or other Group 12 herbicides with different herbicide groups that control the same weeds in a field.
- Use tank mixtures with herbicides from a different group when such use is permitted.
- Herbicide use should be based on an IPM program that includes scouting, historical information related to herbicide use and crop rotation, and considers tillage (or other mechanical), cultural, biological and other chemical control practices.
- Monitor treated weed populations for resistance development.
- Prevent movement of resistant weed seeds to other fields by cleaning harvesting and tillage equipment and planting clean seed.
- Contact your local extension specialist or certified crop advisors for any additional pesticide resistance-management and/or integrated weed-management recommendations for specific crops and weed biotypes.

- For further information or to report suspected resistance, contact AgSolutions at 1 800 454-2673 or www.agsolutions.ca.

7.6 Conclusions

The data made available indicate that spring wheat, durum wheat and barley grown in the prairie provinces and the Peace River Region of Canada are expected to be acceptably tolerant to a postemergent application of AC 900001 Water-Dispersible Granular Herbicide when applied according to label directions. Control of redroot pigweed and suppression of stinkweed and wild mustard can be expected following application of 50 g a.i./ha.

The weed claim for the two-way tank mix of 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester includes the weed list from the AC 900001 Water-Dispersible Granular Herbicide alone treatment, the weeds listed as susceptible or easy to control on the 2,4-D ester label as well as the control of kochia and the suppression of chickweed and wild buckwheat.

The weed claim for the three-way tank mix of 50 g a.i./ha AC 900001 Water-Dispersible Granular Herbicide plus 280 g a.e./ha 2,4-D ester plus 400 g a.i./ha Assert 300 SC includes the weed list from the two-way tank mix plus the control of wild oats.

There is no requirement for a recropping statement on the label for an alone treatment of AC 900001 Water-Dispersible Granular Herbicide. However, the user is advised to follow all recommendations, precautions and restrictions that appear on the Assert 300 SC label when AC 900001 Water-Dispersible Granular Herbicide is tank mixed with 2,4-D ester plus Assert 300 SC.

8.0 Toxic Substances Management Policy

During the review of AC 900001 Water-Dispersible Granular Herbicide, 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 is not a TSMP Track 1 substance.

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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 Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, 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.pmra-arla.gc.ca

- AC 900001 Technical Herbicide does not meet the criteria for persistence. AC 900001 Technical Herbicide values for half-life in water (1.1–1.4 days), soil (15–62 days) and sediment (6.4–12.7 days) are below the TSMP Track 1 cut-off criteria for water (≥ 182 days), soil (≥ 182 days) and sediment (≥ 365 days). The criterion for half-life in air is not relevant since AC 900001 Technical Herbicide is non-volatile and is not expected to be present in the vapour phase under environmental conditions.

- The transformation product, CL 153815, meets the criterion for persistence in sediment. The CL 153815 half-life in sediment (645 days) exceeds the TSMP Track 1 cut-off criterion (≥ 365 days).

- AC 900001 Technical Herbicide and its transformation product, CL 153815, are not bioaccumulative. Although the log K_{ow} of AC 900001 Technical Herbicide is > 5, laboratory data have shown that the bioconcentration factor in fish is < 1000, which is below the TSMP Track 1 cut-off criterion of bioconcentration factor ≥ 5000. In addition, AC 900001 Technical Herbicide is metabolized by fish and rapidly depurated with a half-life of < 2 days. Based on the rat metabolism study, AC 900001 Technical Herbicide and CL 153815 do not accumulate in mammals. In addition, the estimated log K_{ow} values of CL 153815 are 2.95 at pH 5, 1.15 at pH 7 and 0.66 at pH 9, which are below the TSMP Track 1 cut-off criterion of log $K_{ow} \geq 5$.

- The toxicity of AC 900001 Technical Herbicide and its transformation product, CL 153815, are summarized in sections 3.6, 4.7 and 6.4. AC 900001 Water-Dispersible Granular Herbicide is predicted to pose a risk to aquatic plants following a direct overspray. However, its conditions of use can be adequately mitigated to minimize exposure of aquatic habitats.

- AC 900001 (technical grade) does not contain any by-products or microcontaminants that meet 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 formulants that are known to contain TSMP Track 1 substances.

Therefore, the use of AC 900001 Water-Dispersible Granular Herbicide is not expected to result in the entry of TSMP Track 1 substances into the environment.

9.0 Regulatory Decision

The PMRA has carried out an assessment of available information in accordance with the Pest Control Products Regulations and has found it sufficient to allow a determination of

the safety, merit and value of AC 900001 Technical Herbicide (picolinafen) and the end-use product, AC 900001 Water-Dispersible Granular Herbicide. The Agency has concluded that the use of AC 900001 Technical Herbicide (picolinafen) and the end-use product, AC 900001 Water-Dispersible Granular Herbicide in accordance with the label has merit and value consistent with the Pest Control Products Regulations and does not entail an unacceptable risk of harm. Therefore, based on the considerations outlined above, the use of AC 900001 Technical Herbicide (picolinafen) and the end-use product AC 900001 Water-Dispersible Granular Herbicide for the control of broadleaf weeds in spring wheat (including durum) and barley grown in the prairie provinces and the Peace River Region of British Columbia is proposed for full registration, pursuant to the Pest Control Products Regulations.

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

List of Abbreviations

a.e.	acid equivalent
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
AI	aluminum
ARfD	acute reference dose
bw	body weight
bwg	body-weight gain
°C	degree Celsius or centigrade
CD	cesarian derived
cm	centimetre
CMC	carboxymethyl cellulose
CV	coefficient of variation
d	day(s)
DAT	days after treatment
DT_{50}	disappearance time for 50% of highest amount
DT_{90}	disappearance time for 90% of highest amount
dw	dry weight
EC_{50}	effective concentration, 50% population
ECD	electron capture detector
EEC	expected environmental concentration
EXAMS	Exposure Analysis Modeling System
F	female(s)
F2	2nd generation offspring
fw	fresh weight
GC/NPD	gas chromatography with nitrogen-phosphorus detector
GC/MS	gas chromatography with mass spectrometry
GPC	gel permeation chromatography
GSD	geometric standard deviation
h	hour(s)
ha	hectare
HAFT	highest average field trial
HCT	hematocrit
HD	high dose
HDPE	high-density polyethelene
HDT	highest dose tested
HGB	hemoglobin
HPLC/MS/MS	high performance liquid chromatography with tandem mass spectrometry
ILV	independent laboratory validation
K_d	adsorption coefficient
Kh	Henry's Law constant
K_{oc}	organic carbon adsorption coefficient
K_{ow}	*n*-octanol–water partition coefficient

LC	liquid chromatography
LC_{50}	lethal concentration 50%
LD	low dose
LD_{50}	lethal dose 50%
LEACHM	Leaching Estimation and Chemistry Model
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LOEC	lowest observed effect concentration
LOQ	limit of quantitation
M	male(s)
MIS	maximum irritation score
MAS	maximum average score (at 24, 48 and 72 hours)
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume
mL	millilitre
MMAD	mass median aerodynamic diameter
MOE	margin of exposure
MOLD	multiple oral low dose
MOR	magnitude of the residue
MOS	margin of safety
MRL	maximum residue limit
MS	mass spectrometry
ND	not detected
NPD	nitrogen phosphorus detection
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
P1	1^{st} generation parental animals
P2	2^{nd} generation parental animals
PBI	plantback interval
PC	positive control
PE	polyethylene
PHI	preharvest interval
pK_a	dissociation constant for the acid form
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
ppm	parts per million
PRZM	Pesticide Root Zone Model
r^2	correlation coefficient
RBC	red blood cell
ROC	residue of concern
RSD	relative standard deviation
SDEV	standard deviation
SF	safety factor
SOHD	single oral high dose

SOLD	single oral low dose
SPE	solid phase extraction
$t_{1/2}$	half life
$t_{9/10}$	time to reduce initial concentration by 90%
TRR	total radioactive residue
TS	test substance
TSMP	Toxic Substances Management Policy
USA	United States of America
USEPA	United States Environmental Protection Agency
UV	ultraviolet
WBC	white blood cell
w/v	weight/volume ratio
w/w	weight/weight ratio
µg	micrograms
µL	microlitre

Appendix I Summary Tables

Table 1 Toxicology

METABOLISM—AC 900001 Technical Herbicide (picolinafen)

Absorption: AC 900001 Technical Herbicide was incompletely absorbed; at the LD (10 mg/kg bw) absorption (expressed as % AD) was approx. 51/67% for males/females (M/F), respectively, for ^{14}C-pyridine label and approx. 60/84% for M/F, respectively, for ^{14}C-aniline label; at the HD (1000 mg/kg bw), absorption decreased to approx. 25/23% for M/F, respectively, for ^{14}C-pyridine label and to approximately 17% for both sexes for ^{14}C-aniline label; majority absorbed within 24 h following SOLD and MOLD, respectively and within 48 h following SOHD; decreased absorption at HD considered to be due to saturation of absorption processes.

Distribution:, highest residues found in fat, liver, kidneys, and lungs for pyridine label and in blood, spleen, liver, kidneys, lungs, and heart for aniline label; mean recovery of radioactivity in tissue/carcass at sacrifice (168 h postdosing) was low, less than 0.5% of AD for all groups irrespective of label, indicating little potential for accumulation.

Metabolism: extensively metabolized with hydrolytic cleavage of amide bond followed by a variety of biotransformation processes including N-acetylation, hydroxylation, methylation, dehalogenation and formation of mercapturic and sulfate conjugates; Feces: major residue was AC 900001 Technical Herbicide (95–99 %); Urine: pyridine-label major metabolites were CL 153815 (84.1/58.2% M/F) and its glucuronic acid conjugate (7.3/29.2% M/F); aniline-label major metabolites were sulfate conjugate of 2-amino-5-fluorophenol (52.9 %) and sulfate conjugate of 4'-hydroxyacetanilide (CL 1009639,26.1 %); Bile: pyridine-label major metabolites were CL 153815 (86.4/89.5% M/F) and the glucuronide ester of CL 153815 (9.4/5.8% M/F); aniline label major metabolites were p-fluoroaniline, 4'-fluoroacetanilide and 4'-hydroxyacetanilide (64.6 %).

Excretion: major route of excretion following SOLD was via feces for pyridine-label and via urine for aniline-label; a greater proportion of AD was eliminated in urine following MOLD in comparison to SOLD; major route of excretion following SOHD for the pyridine label was via the feces and for the aniline-label urine and fecal excretion were comparable for males whereas fecal excretion was 2-fold greater than urinary excretion for females; rate of excretion following SOHD was slightly slower for females but not males for pyridine-label and slower for both sexes for aniline label when compared to SOLD; > 75 and 90% of AD were eliminated within 24 h following SOLD and MOLD, respectively, irrespective of label; > 88% of AD eliminated within 48 h following SOHD for pyridine label; > 90% of AD eliminated within 48 and 72 h for females at males, respectively, following SOHD administration for aniline label; biliary excretion accounted for approx. 34/25% (M/F) and 8/12% (M/F) of AD within 48 h following SOLD for pyridine and aniline label, respectively and for approx. 17/12% (M/F) and 2% (both sexes) of AD within 48 h following SOHD for pyridine and aniline label, respectively.

There were gender differences in absorption, metabolism and excretion.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
ACUTE STUDIES—AC 900001 Technical Herbicide (picolinafen)			
Oral	5 Sprague-Dawley rats/sex **Dose level** 5000 mg/kg bw	LD_{50} greater than 5000 mg/kg bw for both sexes	No treatment-related mortality, clinical signs, necropsy findings or changes in bw in either sex. One female died on d 6, death attributed to dosing accident. **LOW TOXICITY**

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
Dermal	5 Sprague-Dawley rats/sex **Dose level** 4000 mg/kg bw	LD_{50} greater than 4000 mg/kg bw for both sexes	No mortality; no treatment-related clinical signs or necropsy findings in either sex; 5/5 males and 4/5 females exhibited a bw gain, the remaining female exhibited a bw loss (4 g). **LOW TOXICITY**
Inhalation—limit test (4-hour nose-only)	5 Sprague-Dawley rats/sex **Dose level** Analytical: 5.9 mg/L air Nominal: 13.0 mg/L air (MMAD 5.8 µm, GSD 1.6)	LC_{50} greater than 5.9 mg/L air for both sexes	No mortality; no treatment-related necropsy findings or changes in bw in either sex. Laboured breathing noted during exposure. Secretory responses (clear nasal discharge, salivation and chromodacryorrhea) and respiratory responses (laboured breathing and moist rales) noted immediately following exposure, resolved by d 3. **LOW TOXICITY**
Eye irritation	6 male New Zealand White rabbits **Dose level** 0.1 mL (equal to 0.032 g)	MIS: 2.67/110 at 1 h MAS (for 24, 48 and 72 h): 0.22/110	Minimal conjunctival redness (grade 1) noted in 6 animals at 1 h persisted in 1 animal at 24 h, minimal conjunctival discharge (grade 1) in 2 animals at 1 h and in 1 animal at 24 h, completely resolved by 48 h. **MINIMALLY IRRITATING**
Skin irritation	6 male New Zealand White rabbits **Dose level** 0.5 g moistened with 0.5 mL water	MAS (for 24, 48 and 72 h): 0.0/8	No signs of dermal irritation observed at any time during the study period. **NON-IRRITATING**
Skin sensitization (Guinea pig maximization test)	Crl:(HA)BR strain guinea pigs Treated: 20 males Naive control: 20 males **Dose levels** Intradermal induction: 5% w/v suspension TS in 0.5% CMC in distilled water Topical induction: 25% w/w mixture TS in petrolatum Challenge treatment: 25% w/w mixture TS in petrolatum	No dermal reactions observed at 24 or 48 h after challenge treatment.	**NOT A DERMAL SENSITIZER**

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
ACUTE STUDIES—AC 900001 Water-Dispersible Granular Herbicide			
Oral—mouse	CD-1 mice 5 animals/sex **Dose level** 5000 mg/kg bw	LD_{50} greater than 5000 mg/kg bw for both sexes	No mortality; no treatment-related clinical observations or necropsy findings in either sex. All animals gained weight during study, with the exception of 2 females (1 lost 0.3 g and 1 exhibited no overall change in bw). **LOW TOXICITY**
Oral—rat	Sprague-Dawley rats 5 animals/sex **Dose level** 5000 mg/kg bw	LD_{50} greater than 5000 mg/kg bw for both sexes	No mortality; no treatment-related clinical observations, necropsy findings or changes in bw in either sex. **LOW TOXICITY**
Dermal	Sprague-Dawley rats 5 animals/sex **Dose level** 4000 mg/kg bw	LD_{50} greater than 4000 mg/kg bw for both sexes	No mortality; no treatment-related clinical signs, necropsy findings or changes in bw in either sex. **LOW TOXICITY**
Inhalation (4-hour nose-only)	Sprague-Dawley rats 5 animals/sex **Dose level** Analytical: 3.83 mg/L air Nominal: 7.6 mg/L air (MMAD 2.8 µm, GSD 1.9)	LC_{50} greater than 3.83 mg/L air for both sexes	No mortality; no treatment-related necropsy findings or changes in bw in either sex. Laboured breathing and secretory responses (lacrimation, chromodacryorrhea, dried red/black red material facial area) noted immediately following exposure, completely resolved by day 11. **LOW TOXICITY**
Eye irritation	New Zealand White rabbits 3 males **Dose level** 0.1 mL aliquot (equal to 0.054 g)	MIS: 4.67/110 at 1 h MAS (for 24, 48 and 72 h): 0.0/110	At 1 h slight conjunctival redness (grade1) observed 3/3 animals, slight conjunctival chemosis (grade 1) in 1/3 animals and slight to moderate conjunctival discharge (grade 1–2) 2/3 animals, completely resolved by 24 h. **MINIMALLY IRRITATING**
Skin irritation	New Zealand White rabbits 3 males **Dose level** 0.5 g	MIS: 1.67/8 at 1 h MAS (for 24, 48 and 72 h): 0/8	At 1 h, 3/3 animals exhibited very slight erythema (grade 1), 2/3 animals exhibited very slight edema (grade 1), completely resolved by 24 h. **MILDLY IRRITATING**

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
Skin sensitization (Buehler method)	Dunkin Hartley Haz:(DH)FBR albino guinea pigs 10 animals/sex in test group and 5 animals/sex in control group **Dose level** 0.3 cc aliquot of TS moistened with 0.3 mL sterile water for both induction and challenge treatments	At 24 h following challenge treatment, 1 treated male exhibited very faint erythema (grade 0.5), completely resolved by 48 h. No signs of dermal irritation in any of the other treated animal or in any of the control animals at 24 or 48 h following challenge treatment.	**NOT A DERMAL SENSITIZER**
SHORT TERM—AC 900001 Technical Herbicide (picolinafen)			
28-day dietary—mouse	5 CD-1 [Crl:CD-1(ICR)BR] mice/sex/dose **Dose levels** 0, 100, 1000, 2000, 3500 or 7000 ppm (equal to 0, 23.4, 227, 438, 839 and 1721 mg/kg bw/d for males and 0, 28.0, 235, 598, 1140 and 2019 mg/kg bw/d for females)	NOAEL: 100 ppm (equal to 23.4/28.0 mg/kg bw/d in M/F) LOAEL: 1000 ppm (equal to 227/235 mg/kg bw/d in M/F)	≥1000 ppm: discolouration (pale) spleen (F); centrilobular hepatocellular hypertrophy (M); extramedullary hematopoiesis/ hemosiderin deposition spleen (M/F). ≥2000 ppm: increased spleen and liver weight (M/F); discolouration spleen/liver/kidney/lungs/heart and/or small intestines (M/F); centrilobular hepatocellular hypertrophy (F); hemosiderin deposition in Kupffer cells of liver (M/F). ≥3500 ppm: increased reticulocyte count, MCHC and MCHC (M/F); Heinz body formation (F). 7000 ppm: decreased bw/bwg (M); increased MCV (M/F); Heinz body formation (M); slight decrease RBC count (F). Findings considered to be indicative of regenerative hemolytic anemia for M/F at 3500 ppm and above; possibly suggestive of regenerative hemolytic anemia M/F at 1000 and 2000 ppm.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
28-day dietary—rat	10 Crl:CD(SD)BR rats/sex/dose **Dose levels** 0, 25, 50, 100 or 1000 ppm (equal to 0, 2.7, 5.4, 10.5 and 107 mg/kg bw/d for males and 0, 3.0, 5.9, 11.7 and 119 mg/kg bw/d for females)	NOAEL: 100 ppm (equal to 10.5/11.7 mg/kg bw/d in M/F) LOAEL: 1000 ppm (equal to 107/119 mg/kg bw/d in M/F)	1000 ppm: decreased RBC counts, HGB, HCT, MCHC, oxyhemoglobin and osmotic fragility and increased MCV, RBC distribution width and diameter, reticulocyte counts, MCH, methemoglobin, Heinz body formation and erythropoietic activity in bone marrow in one or both sexes; increased WBC and lymphocyte counts (F); increased serum bilirubin (M/F); increased spleen and liver weight (M/F); enlargement and discolouration of spleen; extramedullary hematopoiesis in spleen (M/F); active erythropoietic foci in liver (M/F); hemosiderin deposition spleen, Kupffer cells and kidney (M/F); lymphocyte depletion marginal zones white pulp, congestion and focal capsular inflammation and/or fibrotic proliferation spleen (M/F); centrilobular hepatocellular hypertrophy (M). Findings for M/F at 1000 ppm considered indicative of regenerative hemolytic anemia.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
90-day dietary—mouse	10 CD-1 strain [Crl:CD-1(ICR)BR] mice/sex/dose **Dose levels** 0, 50, 500, 1000 or 2000 ppm (equal to 0. 10.2, 103, 202 and 388 mg/kg bw/d for males and 0, 12.7, 148, 280 and 577 mg/kg bw/d for females)	NOAEL: 50 ppm (equal to 10.2/12.7 mg/kg bw/d in M/F) LOAEL: 500 ppm (equal to 103/148 mg/kg bw/d in M/F)	≥500 ppm: increased liver (M) and spleen (F) weight; centrilobular hepatocellular hypertrophy (M); hemosiderin deposition (M/F) and extramedullary hematopoiesis (F) in spleen. ≥1000 ppm: decreased RBC counts, HCT and HGB and increased reticulocyte counts and Heinz body formation in one or both sexes; increased liver (F) and spleen (M) weight; enlarged spleen (M/F); centrilobular hepatocellular hypertrophy and hepatocellular vacuolation (F); extramedullary hematopoiesis spleen (M). 2000 ppm: decreased food consumption (M); increased MCV (F); discoloured spleen (F); hemosiderin deposition Kupffer cells in liver (M/F). Findings for M/F at ≥1000 ppm considered indicative of regenerative hemolytic anemia and possibly indicative for M/F at 500 ppm. No apparent increase hematopoietic activity in bone marrow, liver or other tissue. **Control week 13 bw** M: 40.5 g F: 31.3 g **Control week 13 daily food consumption** M: 7.9 g/animal F: 7.4 g/animal

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
90-day dietary—rat	10 Crl:CD(SD)BR rats/sex/dose **Dose levels** 0, 80, 400 or 800 ppm (equal to 0, 6.4, 32 and 65 mg/kg bw/d in males and 0, 6.8, 35 and 69 mg/kg bw/d in females)	NOAEL: 80 ppm (equal to 6.4/6.8 mg/kg bw/d in M/F) LOAEL: 400 ppm (equal to 32/35 mg/kg bw/d in M/F)	≥400 ppm: decreased RBC/HCT/HGB (M/F); increased reticulocytes (M) and MCV (M/F); increased spleen and liver weight (M/F); increase incidence/severity hemosiderin deposition spleen and Kupffer cells of liver (M/F). 800 ppm: decreased bw, bwg and food consumption (F). Findings in M/F at ≥400 ppm considered indicative of hemolytic anemia; no apparent increase hematopoietic activity in spleen, bone marrow, liver or other tissue. **Control week 13 bw** M: 546.8 g F: 336.2 g **Control week 13 daily food consumption** M 30.2 g/animal F: 23.2 g/animal
90-day dietary—dog	4 Beagle dogs/sex/dose **Dose levels** 0, 50, 500 or 2500 ppm (equal to 0,1.7, 17.3 and 87.5 mg/kg bw/d for males and 0, 1.8, 20.8 and 92.1 mg/kg bw/d for females)	NOAEL: 50 ppm (equal to 1.7/1.8 mg/kg bw/d for M/F) LOAEL: 500 ppm (equal to 17.3/20.2 mg/kg bw/d for M/F)	≥500 ppm: lower RBC, HGB and HCT(F); increased thyroid/parathyroid weight (M/F); diffuse hypertrophy/focal hyperplasia of thyroid follicular cells (M/F). 2500 ppm: lower bwg (M); lower RBC, HGB and HCT (M); increased serum bilirubin (F); enlarged thyroid (M/F). Hematological findings for F at 500 ppm and M/F at 2500 ppm considered indicative of hemolytic anemia. Thyroid hormone levels not determined.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
12-month dietary—dog	4 Beagle dogs/sex/dose **Dose levels** 0, 50, 150 or 1500 ppm (equal to 0, 1.4, 4.4 and 42.7 mg/kg bw/d for males and 0, 1.6, 5.2 and 47.1 mg/kg bw/d for females)	NOAEL: 50 ppm (equal to 1.4/1.6 mg/kg bw/d for M/F) LOAEL: 150 ppm (equal to 4.4/5.7 mg/kg bw/d for M/F)	≥150 ppm: lower bw and bwg (M). 1500 ppm: decreased RBC, HCT and HGB at 3/6 months and increased reticulocyte counts at 3/6/9 months (F); increased thyroid/parathyroid weight (M/F); enlarged thyroid (M/F); diffuse hypertrophy of thyroid follicular epithelial cells (M/F); scattered foci of thyroid follicular cell hyperplasia (M). Hematological findings for F at 1500 ppm considered indicative of hemolytic anemia; at 12 months, no hematology findings and no correlating histopathological findings. Thyroid hormone levels not determined.
4-week dermal—rat	10 CD (Sprague-Dawley derived) [Crl: CD IGS BR] rats/sex/dose **Dose levels** 0, 25, 50, 75, 100, 200 or 1000 mg/kg bw/d (6 h/d, 7 d/week for 26 d)	**Systemic toxicity** NOAEL: 75 mg/kg bw/d for both sexes LOAEL: 100 mg/kg bw/d for both sexes **Local dermal irritation** NOAEL: greater than 1000 mg/kg bw/d for both sexes LOAEL: not determined	≥100 mg/kg bw/d: lower RBC count, HGB and HCT (M/F); increased spleen weight (M/F); increased severity hemosiderin deposition and extramedullary deposition in spleen (M/F). ≥200 m/kg bw/d: lower bwg (M). 1000 mg/kg bw/d: lower bw and bwg (M/F). Findings in M/F at ≥ 100 mg/kg bw/d considered indicative of regenerative hemolytic anemia. **Local dermal irritation**: No treatment-related signs of local dermal irritation.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
CHRONIC TOXICITY/ONCOGENICITY—AC 900001 Technical Herbicide (picolinafen)			
78-week dietary—mouse	65 CD-1 (Crl:CD-1(ICR)BR strain) mice/sex/dose **Dose levels** 0, 40, 400 or 800 ppm (equal to 0, 6.9, 68.6 and 137.1 mg/kg bw/d for males and 0, 8.2, 81.0 and 165.8 mg/kg bw/d for females)	**Chronic toxicity** NOAEL: 40 ppm (equal to 6.9/8.2 mg/kg bw/d for M/F) LOAEL: 400 ppm (equal to 68.6/81.0 mg/kg bw/d for M/F)	≥400 ppm: increased reticulocyte counts at 3 months (M/F); increased liver weight (M/F); centrilobular hepatocellular hypertrophy (M); hemosiderin deposition (F) and extramedullary hematopoiesis (M) in spleen. 800 ppm: centrilobular hepatocellular hypertrophy (F); hemosiderin deposition in Kupffer cells (F); hemosiderin deposition (M) and extramedullary hematopoiesis (F) spleen. Hematological/histopathological findings may be indicative of slight regenerative hemolytic anemia, no significant relevant correlating changes in RBC parameters or indices were noted for either sex at 400 or 800 ppm at 3, 6, 12 or 18 months. No evidence to indicate any carcinogenic potential of AC 900001 at any dose level up to and including 800 ppm, the HDT.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
2-year dietary—rat	55 Sprague-Dawley rats/sex/dose **Dose levels** 0, 50, 250 or 500 ppm (equal to 0, 2.4, 12.1 and 24.5 mg/kg bw/d for males and 0, 3.0, 15.0 and 31.0 mg/kg bw/d for females)	**Chronic toxicity** NOAEL: 50 ppm (equal to 2.4 and 3.0 mg/kg bw/d for M/F) LOAEL: 250 ppm (equal to 12.1/15.0 mg/kg bw/d for M/F)	≥250 ppm: lower RBC, HGB and HCT 3/6 months (M/F); increased spleen weight 12 months (M); increased severity hemosiderin deposition spleen 12/24 months (M/F). 500 ppm: lower RBC and HGB 12 months (M); increased spleen weight 24 months (M/F); enlarged spleen 24 months (F). Findings in M/F at ≥250 ppm considered indicative of hemolytic anemia; no apparent increase hematopoietic activity in spleen, bone marrow, liver or other tissue. Slight, non-significant, increased incidence benign neoplasms (benign pheochromocytomas) adrenal gland medullary region males at 500 ppm, considered spontaneous in nature; no evidence to indicate any carcinogenic potential of AC 900001 at any dose level up to and including 500 ppm, the HDT.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
REPRODUCTION / DEVELOPMENTAL TOXICITY—AC 900001 Technical Herbicide (picolinafen)			
Multigeneration — rat (1 litter/ generation)	30 CD (Sprague-Dawley derived) rats/sex/group **Dose levels** 0, 50, 250 or 500 ppm (equal to 0/0, 3.7/4.3, 19/21 and 39/43 mg/kg bw/d for P1/P2 males, respectively, during premating; 0/0, 4.2/4.7, 22/24 and 44/49 for P1/P2 females, respectively, during premating; 0/0, 4/4, 21/21 and 43/42 for P1/P2 females, respectively, during gestation; 0/0, 8/7, 36/36 and 74/65 for P1/P2 females, respectively, during lactation)	**Parental** NOAEL: 50 ppm (equal to 3.7/4.0 mg/kg bw/d for M/F) LOAEL: 250 ppm (equal to 19/21 mg/kg bw/d for M/F) **Offspring** NOAEL: 50 ppm (equal to 3.7/4.0 mg/kg bw/d for M/F) LOAEL: 250 ppm (equal to 19/21 mg/kg bw/d for M/F) **Reproductive** NOAEL: 500 ppm (equal to 39/42 mg/kg bw/d for M/F). LOAEL: not determined.	**Parental** ≥250 ppm: lower RBC counts, HGB and HCT (P1/P2 both sexes); lower MCHC (P1/P2 M and P2 F); increased reticulocyte counts (P2 both sexes); increased incidence/severity hemosiderin deposition, extramedullary hematopoiesis and congestion of red pulp in spleen (P1/P2 both sexes). 500 ppm: lower MCHC (P1 females); increased reticulocyte counts (P1 both sexes) and MCV (P1/P2 M); increased spleen weight (P1/P2 both sexes). Hematological/histopathological findings at ≥250 ppm considered indicative of regenerative hemolytic anemia **Offspring** Lower RBC, HGB and HCT for F2 pups on lactation d 21 (only time point evaluated) for both sexes at 250 and 500 ppm. **Reproductive** No treatment-related findings.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
Teratogenicity—rat	25 mated adult female CD (Sprague-Dawley) rats/dose (17 rats/dose for extension study) **Dose levels** Main study: 0, 100, 500 or 1000 mg/kg bw/d Extension study: 0, 5, 25 or 50 mg/kg bw/d	**Maternal toxicity** NOAEL: 50 mg/kg bw/d. LOAEL: 100 mg/kg bw/d **Developmental toxicity** NOAEL: 1000 mg/kg bw/d LOAEL: Not determined.	**Maternal toxicity** ≥ 100 mg/kg bw/d: lower RBC counts, HGB and HCT; increased MCV, MCH and reticulocyte counts; increased spleen weight; increased incidence/severity hemosiderin deposition and extramedullary hematopoiesis in spleen. 500 mg/kg bw/d: lower bw and bwg; increased MCHC. 1000 mg/kg bw/d: increased nucleated RBC counts. Hematological/histopathological findings at 100 mg/kg bw/d and above considered indicative of regenerative hemolytic anemia. **Developmental toxicity** No adverse treatment-related findings. **Teratogenicity** No evidence of any treatment-related irreversible structural changes at any dose level up to and including 1000 mg/kg bw/d (HDT); therefore, under the conditions of this study, AC 900001 Technical Herbicide was not teratogenic.

STUDY	SPECIES/STRAIN AND DOSES	NOAEL and LOAEL mg/kg bw/day	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS
Teratogenicity—rabbit	25 mated adult female New Zealand White rabbits/dose **Dose levels** 0, 5, 20 or 50 mg/kg bw/d	**Maternal toxicity** NOAEL: 5 mg/kg bw/d LOAEL: 20 mg/kg bw/d **Developmental toxicity** NOAEL: 20 mg/kg bw/d LOAEL: 50 mg/kg bw/d	**Maternal toxicity** ≥20 mg/kg bw/d: lower bwg and food consumption; lower RBC, HGB and HCT; elevated MCV and reticulocyte counts; hemosiderin deposition/congestion spleen 50 mg/kg bw/d: increased spleen weight: extramedullary hematopoiesis spleen. Hematological/histopathological findings at 20 and 50 mg/kg bw/d considered indicative of regenerative hemolytic anemia. **Developmental toxicity** Possible slight decrease embryonal-fetal viability manifest as slight increases in abortion (1 on day 21/1 on day 23), postimplantation loss, total number of resorptions (early/late) and mean resorption rate at 50 mg/kg bw/d, findings not statistically significantly different from controls and within historical control values. **Teratogenicity** No evidence of any treatment-related irreversible structural changes at any dose level up to and including 50 mg/kg bw/d (HDT); therefore, under the conditions of this study, AC 900001 was not teratogenic.

GENOTOXICITY—AC 900001 Technical Herbicide (picolinafen)

STUDY	SPECIES/STRAIN OR CELL TYPE	DOSE LEVELS	SIGNIFICANT EFFECTS / COMMENTS
Bacterial reverse gene mutation assay (in vitro)	*Salmonella typhimurium* (TA98, TA100, TA1535, TA1537 and TA1538) and *Escherichia coli* (WP2uvrA)	0, 100, 250, 500, 1000 or 2500 µg/plate ± S9 metabolic activation	**NEGATIVE**
Mammalian cell gene mutation assay (in vitro)	Chinese hamster ovary (CHO) cells at the hypoxanthine-guanine-phosphoribosyl transferase (HGPRT) locus	0, 10, 25, 50, 100, 200 or 300 µg/mL ± S9 metabolic activation	**NEGATIVE**

STUDY	SPECIES/STRAIN OR CELL TYPE	DOSE LEVELS	SIGNIFICANT EFFECTS / COMMENTS
Mammalian cytogenetics (in vitro)	Chinese hamster ovary (CHO) cells	0, 10, 25, 100, 200, 400, 600, 800 or 1000 µg/mL (-) S9 metabolic activation; 0, 10, 25, 50, 100, 200, 300, 400 or 600 µg/mL (+) S9 metabolic activation	**NEGATIVE**
Micronucleus Assay (in vivo)	Male mouse bone marrow cells (erythrocytes)	0, 500, 1000 or 2000 mg/kg bw (sacrifice at 24 and 48 hours)	**NEGATIVE**

Appendix II Residues

Table 1 Food Residue Chemistry Overview

DIRECTIONS FOR USE OF PICOLINAFEN ON CEREAL CROPS						
Crop	**Formulation/ type**	**Interval (day)**	**Rate (g a.i./ha)**	**#/ season**	**Maximum rate**	**PHI (days)**
spring wheat, durum wheat, barley	AC 900001/WDG	Not applicable	50	1	50 g a.i. /ha	60
Label Restrictions:	Treated field may be grazed or cut for forage or hay 30 days after application. Do not apply by air. Do not apply more than once per season.					

PHYSICOCHEMICAL PROPERTIES	
Water solubility	**°C** **Solvent** **g/L** 20 pH 5 buffer 3.8×10^{-5} 20 pH 7 buffer 4.7×10^{-5} 20 pH 9 buffer 3.8×10^{-5} 20 deionized water 3.9×10^{-5} 10 deionized water 3.0×10^{-5} 30 deionized water 6.8×10^{-5}
Solvent solubility at 20°C (g/100 mL)	**Solvent** **Solubility** acetone 5.7 dichloromethane 76.4 ethyl acetate 46.4 n-hexane 0.38 methanol 3.04
n-Octanol–water partition coefficient (Log K_{ow})	**Solvent** **log K_{ow}** Deionized water 5.37 pH 5 buffer 5.36 pH 7 buffer 5.43 pH 9 buffer 5.36
Dissociation constant (pKa)	None between the pH values of 2–12.
Vapour pressure	**Temp. (°C)** **Vapour pressure (Pa)** 70 2.36×10^{-4} 80 8.49×10^{-4} 90 2.44×10^{-3} 20 1.6×10^{-7} (estimated)
Relative density (g/mL)	1.45
Melting point or range	107.2–107.6°C

UV–visible absorption spectrum	**λ (nm)** **ϵ (l•mol^{-1}•cm^{-1})** 202 39500 230 (shoulder) 14600 290 13000 No absorption at 350–400 nm was observed.

ANALYTICAL METHODOLOGY			
Parameters	**Plant Matrices**		**Animal Matrices**
Method ID	FAMS 079-01	M 3313	FAMS 109-01
Type	Data gathering	Data gathering and enforcement	Data gathering and enforcement
Analytes	Picolinafen	Picolinafen	Picolinafen and CL 153815
Instrumentation	GC/NPD	GC/MS	HPLC with MS/MS detection
LOQ	0.05 mg/kg	0.05 mg/kg	Milk: 0.01 mg/kg Meat, egg and fat: 0.02 mg/kg
Standard	An external standard method was used for retention time, response and calibration.	An external standard method was used for retention time, response and calibration.	An external standard method was used for retention time, response and calibration.
ILV	Not required	When spiked with picolinafen at the method LOQ of 0.05 mg/kg, recoveries obtained by the independent laboratory were: barley hay, 88 ± 3.8 (n=4); barley forage, 117 ± 10 (n=4); wheat grain, 114 ± 14 (n=4) and wheat straw, 81 ± 6.2 (n=5). The values obtained are indicative that method No. M 3313 is reproducible.	When spiked with picolinafen at the LOQ, the recoveries obtained by the independent laboratory were comparable ranging from 84–90% in milk, 81–90% in meat, 60–66% in eggs and 68–75% in fat. When spiked with CL 153815, recoveries in milk, meat, egg and fat ranged from 95–111%, 69–79%, 69–77% and 68–75%, respectively. These values are indicative of the method having good reproducibility.
Extraction/clean up	Cleaned up by liquid-liquid partitioning with water, saturated sodium chloride and ethyl acetate followed by gel permeation chromatography (GPC) using methanol.	C_{18} SPE column clean-up	Liquid-liquid partitioning with ethyl acetate followed by GPC with cyclohexane:ethyl acetate (50:50, v:v) + 0.5% acetic acid as the eluent.

Radiovalidation	—	—	—
Multiresidue method	Samples of wheat grain spiked with picolinafen at the LOQ (0.01 mg/kg) and 10 times the LOQ, were analyzed according to the European DFG Multi Residue Method S19 (GC/ECD) with modified extraction. When spiked at the LOQ, recoveries ranged from 85-95% (91 ± 4.6% [CV = 5.1]; n = 5), demonstrating the capability of this method to be used for enforcement purposes.		Samples of milk, meat, egg and fat spiked with picolinafen at the LOQ (0.01 mg/kg for milk and 0.02 mg/kg for meat, egg and fat) and 10 times the LOQ, were analyzed according to the European DFG Multi Residue Method S19 (GC/ECD) with modified extraction. At the LOQ, average recoveries of picolinafen in these matrices were 81 ± 9.3%, 83 ± 6.1%, 87 ± 6.2% and 86 ± 4.3%, respectively, demonstrating the capability of this method to be used for enforcement purposes.

NATURE OF THE RESIDUE IN PLANTS—Wheat	
Radiolabel position	[aniline-^{14}C]-picolinafen and [pyridine^{14}C]-picolinafen
Test site	Test containers each measuring 1 m^2 and kept outdoors in a fenced test site.
Treatment	Postemergence foliar application at end of tillering stage (BBCH-Code 25-29)
Rate	100 g a.i./ha
Seasonal rate	100 g a.i./ha
PHI	27 days (foliage), 86 days (grain, straw)

Based on the wheat metabolism study, there is minimal translocation of picolinafen and the associated metabolites into untreated parts of the plant as demonstrated by the low TRRs in seed. In forage, the predominant residue was the parent compound, picolinafen. The acid metabolite, CL 153815, and the fluoroaniline metabolite accounted for approximately 7% and 4% of the TRRs, respectively, in straw. As the metabolic pathway in wheat is very similar to that found in rat, neither metabolite was considered to be of toxicological significance.

Metabolites Identified	**Major Metabolites (> 10% TRRs)**		**Minor Metabolites (< 10% TRRs)**	
Radiolabel Position	**[aniline-^{14}C]-picolinafen**	**[pyridine^{14}C]-picolinafen**	**[aniline-^{14}C]-picolinafen**	**[pyridine^{14}C]-picolinafen**
Wheat foliage	Picolinafen	Picolinafen, CL 153815	—	—
Wheat straw	Picolinafen	Picolinafen	—	CL 153815
Wheat grain	TRRs were too low for analysis.			

CONFINED ROTATIONAL CROP Study—Carrots, Peas, Sugar Beets, Sunflowers, Soybeans		
Radiolabel position	[aniline-^{14}C]-picolinafen	[pyridine^{14}C]-picolinafen
Test site	Outdoor test plots	
Formulation used for trial	Formulated as an emulsifiable concentrate	
Application rate and timing	Rate: 100 g a.i./ha. Plantback time: 30 days and 11 months	

Metabolites Identified		Major Metabolites (> 10% TRRs)		Minor Metabolites (< 10% TRRs)	
Radiolabel Position		**[aniline-^{14}C]-picolinafen**	**[pyridine^{14}C]-picolinafen**	**[aniline-^{14}C]-picolinafen**	**[pyridine^{14}C]-picolinafen**
Lettuce	PBI 30 days PBI 11 months	When rotational crops harvested at maturity, there was no measurable residue in the RACs; therefore, no attempt was made to identify or characterize the nature of the radioactive residues. Furthermore, the soil metabolism study demonstrated that picolinafen undergoes rapid transformation to CL 153815, classified as slightly to moderately persistent under aerobic conditions, and CL 7693, a minor transformation product that is strongly bound to soil and not expected to be readily available for uptake or transport. The MORs in the rotational crops from the confined crop rotation study did not trigger a need for field accumulation studies.			
Carrots (top and roots)	PBI 30 days PBI 11 months				
Sugar beets (top and roots)	PBI 30 days				
Sunflowers (straw)	PBI 30 days				
Peas (vine/pod)	PBI 30 days				
Soy beans (plant/straw/ seeds)	PBI 30 days PBI 11 months				

NATURE OF THE RESIDUE IN LAYING HEN			
Species	Dose Level	Length of Dosing	Sacrifice
Hen (Hyline W-98)	12.5 ppm for [aniline-^{14}C]-picolinafen and [pyridine^{14}C]-picolinafen. 0.05 ppm for [aniline-^{14}C]-picolinafen	13 days	21–23 hours after the last dose

Greater than 97% of the administered dose was eliminated via the excreta. Combined TRR found in muscle, fat, liver and eggs accounted for < 0.4% of the total administered dose.

Metabolites Identified	Major Metabolites (> 10% TRRs)		Minor Metabolites (< 10% TRRs)	
Radiolabel Position	**[pyridine^{14}C]-picolinafen**	**[aniline-^{14}C]-picolinafen**	**[pyridine^{14}C]-picolinafen**	**[aniline-^{14}C]-picolinafen**
Liver	CL 153815, CL 952711	M700H01	Picolinafen	Picolinafen, CL 44167
Fat	Picolinafen, CL 952711	Picolinafen	—	CL 44167
Muscle	Picolinafen, CL 153815	—	—	—
Egg	Picolinafen	Picolinafen, CL 44167	CL 153815	—

NATURE OF THE RESIDUE IN RUMINANT			
Species	Dose Level	Length of Dosing	Sacrifice
Goat (La Mancha strain)	For both [aniline-^{14}C]-picolinafen and [pyridine^{14}C]-picolinafen High dose: 47.2–65.1ppm Low dose: 6.3–10.8 ppm	7 days	20–21 hours after last dose

Picolinafen was rapidly metabolized and excreted via the urine and feces. Greater than 90% of the administered radioactive dose was eliminated within 48 hours regardless of dose rate or radiolabelling position. Radioactivity found in tissues and blood accounted for < 0.5% of the total applied dose. The total amount of radioactivity excreted in milk accounted for 0.1% of the administered dose in the pyridine label goats (low and high dose) and 0.2% and 0.3% of the administered dose for the aniline-label goats at the low and high dose levels, respectively.

Metabolites Identified	**Major Metabolites (> 10% TRRs)**		**Minor Metabolites (< 10% TRRs)**	
Radiolabel Position	**[pyridine^{14}C]-Picolinafen**	**[aniline-^{14}C]-picolinafen**	**[pyridine^{14}C]-picolinafen**	**[aniline-^{14}C]-picolinafen**
Kidney (high and low dose)	CL 153815	CL 1009718, CL 6497, CL 44167	—	Picolinafen, CL 1009639, CL 410142
Liver (high dose)	CL 153815	CL 1009718, CL 44167	—	CL 1009639, CL 6497
Liver (low dose)	CL 153815	CL 1009639, CL 6497, CL 44167	—	CL 1009718
Fat (high dose)	Picolinafen	Picolinafen, CL 44167	—	—
Milk (high dose)	CL 153815	CL 6497	—	CL 44167

CROP FIELD TRIALS—Wheat, Barley

Supervised crop field trials on wheat (20) and barley (16) were conducted in sites located throughout Manitoba, Saskatchewan and Alberta, Canada, as well as North and South Dakota, USA (zones 5, 7, 7A and 14).

Commodity	Total Rate (g a.i./ha)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	Min	Max	HAFT	Mean	SDEV
Wheat forage	50	21–28	Picolinafen	2	≤ 0.05	0.0059	0.054	0.054	—
Wheat hay	50	64–108	Picolinafen	6	≤ 0.05	0.194	0.177	0.092	0.06
Wheat straw	50	64–108	Picolinafen	42	≤ 0.05	≤ 0.05	≤ 0.05	≤ 0.05	—
Wheat grain	50	57–115	Picolinafen	54	≤ 0.05	≤ 0.05	≤ 0.05	≤ 0.05	—
Barley forage	50	27–28	Picolinafen	4	≤ 0.05	0.0078	0.077	0.064	0.02
Barley hay	50	61–79	Picolinafen	10	≤ 0.05	0.066	0.058	0.052	0.005
Barley straw	50	62–93	Picolinafen	33	≤ 0.05	≤ 0.05	≤ 0.05	≤ 0.05	—
Barley grain	50	54–93	Picolinafen	46	≤ 0.05	≤ 0.05	≤ 0.05	≤ 0.05	—

RESIDUE DECLINE

Three wheat field trials in Zone 5 (1 trial) and Zone 7 (2 trials) and three barley field trials one each in zones 5, 7 and 14 were also conducted as residue decline studies.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	Min	Max	HAFT	Mean	SDEV
Wheat forage	50	0.1714	Picolinafen	66 66 4 	2.33 0.227 ≤ 0.05 ≤ 0.05 ≤ 0.05	3.34 0.544 0.173 0.259 0.059	3.63 0.479 0.160 0.188 0.054	2.675 0.326 0.092 0.096 0.052	0.387 0.126 0.054 0.084 0.004
Barley forage	50	0.1714	Picolinafen	66 54 	1.175 0.148 ≤ 0.05 ≤ 0.05	3.81 0.486 0.104 ≤ 0.05	3.73 0.441 0.100 ≤ 0.05	2.503 0.289 0.071 ≤ 0.05	1.059 0.133 0.027 —

MAXIMUM RESIDUE LIMITS

Wheat, barley	0.05 ppm

FIELD ACCUMULATION IN ROTATIONAL CROPS

The MORs in the rotational crops from the confined crop rotation study did not trigger a need for field accumulation studies.

PROCESSED FOOD AND FEED

There were no measurable residues of picolinafen in wheat and barley grain when treated according to the proposed use pattern. Furthermore, the wheat metabolism study demonstrated that when treated at twice the label rate, residues in seed were low (0.004 ppm). Therefore, the processing study, to determine residues in processed fractions (bran, germ, shorts and middlings), was not required.

LIVESTOCK FEEDING

Livestock feeding studies were not required in support of this petition based on the findings from the livestock metabolism studies which demonstrated that no measurable transfer of residues of picolinafen from treated feed into the livestock tissues, milk and eggs.

Table 2 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES		
ROC FOR ENFORCEMENT **Primary crops** **Rotational crops**	Picolinafen Picolinafen	
ROC FOR RISK ASSESSMENT **Primary crops** **Rotational crops**	Picolinafen Picolinafen	
METABOLIC PROFILE IN DIVERSE CROPS	None	
ANIMAL STUDIES		
ANIMALS	**Poultry**	**Ruminant**
ROC FOR ENFORCEMENT	Picolinafen and CL 153815	Picolinafen and CL 153815
ROC FOR RISK ASSESSMENT	Picolinafen	Picolinafen
METABOLIC PROFILE IN ANIMALS	Similar	Similar
FAT SOLUBLE RESIDUE	Yes	Yes

DIETARY RISK from Food and Water			
Chronic non-cancer dietary risk **ADI = 0.014 mg/kg bw** **EEC = 0.08 µg/L (Picolinafen)** **EEC = 0.61 µg/L (CL 153815)** **Chronic dietary exposure analyses were performed to determine the exposure and risk estimates which resulted from the use of picolinafen on wheat and barley in Canada. The assessment used the maximum residue limits and assumed 100% crop treated.**	**POPULATION**	**ESTIMATED RISK (% of ADI)**	
		Food (MRL)	**Food + combined EECs**
	All infants < 1 year	0.2	0.8
	Children 1–6 years	1.4	1.6
	Children 7–12 years	0.9	1.1
	Females 13–50 years	0.5	0.6
	Males 13–19 years	0.7	0.8
	Males 20+ years	0.6	0.7
	Seniors 55+ years	0.4	0.5
	Total population	0.6	0.8

Appendix III Environmental Assessment

Table 1 Physical and Chemical Properties of the Transformation Product, CL 153815, That Are Relevant to the Environment

Property	Value	Comments
Solubility in water	pH 5 120 mg/L pH 7 18 400 mg/L pH 9 72 400 mg/L (estimated)	Estimates indicate CL 153815 is very soluble in water. Empirical data are required.
Vapour pressure	7.87×10^{-6} mm Hg (estimated)	Slightly volatile. Empirical data are required.
Henry's Law constant	1.6×10^{-8} atm.m^3/mol (estimated)	Non-volatile from moist soil and water surfaces.
log K_{ow}	2.95 at pH 5 1.15 at pH 7 0.66 at pH 9 (estimated)	Not likely to bioaccumulate. Empirical data are required.
pK_a	3.25	Relatively strong acid. Anion at environmentally relevant pH conditions (pH 5 to pH 9). Potential for leaching.
UV–visible absorption	$\lambda_{max} < 290$ nm	Photolysis is not expected to be an important route of transformation.

Table 2 Summary of Abiotic Transformation Rates of AC 900001 Technical Herbicide and the Major Transformation Product, CL 153815

Fate Process	AC 900001 Technical Herbicide	CL 153815	Interpretation
Hydrolysis	Stable at pH 4, pH 7 and pH 9	Not expected between pH 5 and pH 9.	Hydrolysis in soil is not a transformation pathway for AC 900001 Technical Herbicide or CL 153815.
Photolysis—soil	DT_{50} = 30 d, 1st order	No data	Photolysis in soil is not an important transformation pathway for AC 900001 Technical Herbicide.
Photolysis—water	DT_{50} = 12.1 d DT_{50} = 24.8 d, pH 5 DT_{50} = 31.4 d, pH 7 DT_{50} = 22.6 d, pH 9	Very slowly photolysed; stable under alkaline conditions.	Photolysis in water is not an important transformation pathway for AC 900001 Technical Herbicide or CL 153815.

Table 3 Summary of Biotransformation Rates of AC 900001 Technical Herbicide and its Major Transformation Product, CL 153815

Fate Process	Picolinafen	CL 153815	Interpretation[a]
Aerobic soil	DT_{50} < 2–14 d DT_{90} = 34–149 d	DT_{50} = 30–77 d	AC 900001 Technical Herbicide is non-persistent. CL 153815 is slightly to moderately persistent.
Anaerobic soil	Data inconclusive	No dissipation	CL 153815 is persistent.
Aerobic water layer	DT_{50} = 1.1–1.4 d $DT_{80\text{-}90}$ = 4.5–5.8 d	DT_{50} = 10.9–24.4 d DT_{90} = 36.3–81 d	AC 900001 Technical Herbicide is non-persistent. CL 153815 is slightly persistent.
Aerobic water / anaerobic sediment	DT_{50} = 6.2 d DT_{90} = 20.5–20.6 d	DT_{50} = 45.3–70.1 d DT_{90} = 151–233 d	AC 900001 Technical Herbicide is non-persistent. CL 153815 is moderately persistent.
Anaerobic water / anaerobic sediment	DT_{50} = 18.7 d DT_{90} = 62.2 d	Persistent in both phases	AC 900001 Technical Herbicide is non-persistent. CL 153815 is persistent.
Anaerobic water layer	DT_{50} = 15.4 d DT_{90} = 51.2 d	DT_{50} = 197 d DT_{90} = 654 d	AC 900001 Technical Herbicide is slightly persistent. CL 153815 is persistent.
Anaerobic sediment layer	DT_{50} = 6.4–12.7 d DT_{90} = 21.3–42.2 d	DT_{50} = 645 d	AC 900001 Technical Herbicide is non-persistent. CL 153815 is persistent.

[a] Classification of Goring et al. (1975) for persistence in soil and classification of McEwen and Stephenson (1979) for persistence in aquatic systems.

Table 4 Properties of CL 153815 that Support its Potential to Leach and Contaminate Groundwater

Property	CL 153815 Value	Cohen et al. (1984) Criterion	Meets Criterion?
Solubility in water	≥ 120 mg/L	> 30 mg/L	Yes
K_d	≥ 6.3	< 5	No
K_{oc}	160–783	< 300	Yes
Henry's Law constant	1.6×10^{-8} atm·m^3/mol	$< 10^{-2}$ atm·m^3/mol	Yes
Ionic state	Negatively charged at ambient pH	Negatively charged at ambient pH	Yes
Hydrolysis half-life	Stable	> 20 weeks	Yes
Photolysis half-life	Stable	> 1 week	Yes
Half-life in soil	> 4 weeks	> 2–3 weeks	Yes

Table 5 Summary of the Field Dissipation of AC 900001 Technical Herbicide and its Major Transformation Product, CL 153815

System	AC 900001 Technical Herbicide	CL 153815	Interpretation
Terrestrial	$t_{1/2}$ = 59–62 d $t_{9/10}$ = 195–208 d ND 147 DAT Fairview, Alberta	Max 9.2 µg/kg 90 DAT 6.9 µg/kg 148 DAT Fairview, Alberta	AC 900001 Technical Herbicide is slightly to moderately persistent, and is not expected to carry over to the next growing season.
	$t_{1/2}$ = 44 d $t_{9/10}$ = 148 d ND 359 DAT Lethbridge, Alberta	Max 11.1 µg/kg 60 DAT 5.9 µg/kg 359 DAT ND 451 DAT Lethbridge, Alberta	53–64% of CL 153815 carried over to the next growing season. No leaching under typical field conditions.
	$t_{1/2}$ = 15 d $t_{9/10}$ = 50 d ND 361 DAT Minto, Manitoba	Max 9.8 µg/kg 90 DAT 6.3 µg/kg 361 DAT ND 453 DAT Minto, Manitoba	
	No residues below 15-cm soil depth	No residues below 15-cm soil depth	

Table 6 Water Modelling Input Parameters

Parameter	AC 900001 Technical Herbicide	CL 153815
Maximum allowable rate per year	0.05 kg a.i./ha	0.05 kg a.i./ha (assumed 100% conversion)
Maximum number of applications per year	1	1
Minimum interval between application	Not applicable	Not applicable
Timing of applications	April 20 (earliest date)	April 20 (earliest date)
Method of application	Groundboom	Groundboom
Molecular weight	376.3	283.21
Solubility in water at pH 7	4.7×10^{-8} mg a.i./L	18 400 mg/L (estimated)
Vapour pressure	1.24×10^{-9} mm Hg	7.87×10^{-6} mm Hg (estimated)
Henry's Law constant	1.6×10^{-8} atm.m^3/mol	1.6×10^{-8} atm.m^3/mol (estimated)
K_{ow} at pH 7	269153	14.125 (estimated)
Hydrolysis half life	Stable	Stable
Photolysis half-life in soil	Stable	Stable
Photolysis half-life in water	31 d	Stable

Parameter	AC 900001 Technical Herbicide	CL 153815
Aerobic soil biotransformation	DT_{50} = 14 d (longest value)	DT_{50} = 77 d (longest value)
Aerobic aquatic biotransformation	Whole system DT_{50} = 6.4 d (longest value)	Whole system DT_{50} = 71.1 d (longest value)
Anaerobic aquatic biotransformation	Whole system DT_{50} = 18.7 d	Stable
Adsorption K_d	248 L/kg (smallest value)	6.3 L/kg (smallest value)
Adsorption K_{oc}	15 100 L/kg (smallest value)	160 L/kg (smallest value)

Table 7 Maximum EEC in Vegetation and Insects after a Direct Overspray

Matrix	EEC (mg a.i./kg fw)[a]	Fresh / dry weight ratios	EEC (mg a.i./kg dw)
Short range grass	11	3.3[b]	35
Leaves and leafy crops	5.6	11[b]	62
Long grass	4.9	4.4[b]	22
Forage crops	6.0	5.4[b]	32
Small insects	2.6	3.8[c]	9.9
Pods with seeds	0.54	3.9[c]	2.1
Large insects	0.44	3.8[c]	1.7
Grain and seeds	0.44	3.8[c]	1.7
Fruit	0.67	7.6[c]	5.1

[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 8 Maximum EEC in Diets of Birds and Mammals

Organism	Matrix	EEC (mg a.i./kg dw diet)
Bobwhite quail	30% small insects 15% forage crops 55% grain	8.8
Mallard duck	30% large insects 70% grain	1.7
Rat	70% short grass 20% grain/seeds 10% large insects	25

Organism	Matrix	EEC (mg a.i./kg dw diet)
Mouse	25% short grass 50% grain/seeds 25% leaves and leafy crops	25
Rabbit	25% short grass 25% leaves and leafy crops 25% long grass 25% forage crops	38

Table 9 Effects on Terrestrial Organisms

Organism	Exposure	Test Substance	Endpoint Value	Degree of Toxicity[a]
Invertebrates				
Earthworm	Acute (14-day)	AC 900001 Technical Herbicide	LC_{50} >1000 mg a.i./kg NOEC 111 mg a.i./kg (B)	—
		CL 153815	LC_{50} 476.5 mg a.i./kg NOEC 125 mg a.i./kg (M)	—
Bee	Oral	AC 900001 Technical Herbicide	LD_{50} > 150 µg a.i./bee NOEC 150 µg a.i./bee*	Relatively non-toxic[c]
	Contact	AC 900001 Technical Herbicide	LD_{50} > 200 µg a.i./bee NOEC 200 µg a.i./bee*	Relatively non-toxic[c]
Predatory mite	Contact inert substrate	AC 900001 Water-Dispersible Granular Herbicide (74.7%) 133 g product/ha (twice the field rate)	0% (M) 10% (F)	Harmless[b]
		AC 900001 Water-Dispersible Granular Herbicide (74.7%) 0.8 g product/ha (0.012 times field rate)	0.4% (M) 13.5% (F)	
Ground dwelling predator (spider)	Contact inert substrate	AC 900001 Water-Dispersible Granular Herbicide (74.7%) 133 g product/ha (twice the field rate)	0% (M) +1% (N)	Harmless[b]
		AC 900001 Water-Dispersible Granular Herbicide (74.7%) 0.8 g product/ha (0.012 times field rate)	5% (M) 7% (N)	

Organism	Exposure	Test Substance	Endpoint Value	Degree of Toxicity[a]
Ground dwelling predator (beetle)	Contact inert substrate	AC 900001 Water-Dispersible Granular Herbicide (74.7%) 133 g product/ha (twice the field rate)	0% (M) 0% (N)	Harmless[b]
Parasitoid	Contact inert substrate	AC 900001 Water-Dispersible Granular Herbicide (74.7%) 133 g product/ha (twice the field rate)	0% (M) 6% (P)	Harmless[b]
		AC 900001 Water-Dispersible Granular Herbicide (74.7%) 0.8 g product/ha (0.012 times field rate)	0% (M) 24% (P)	
Birds				
Bobwhite quail	Acute	AC 900001 Technical Herbicide	LC_{50} > 2250 mg a.i./kg bw NOEL 1350 mg a.i./kg bw (B)	Practically non-toxic
	Acute dietary (8-day)	AC 900001 Technical Herbicide	LC_{50} > 5314 mg a.i./kg diet NOEC 270 mg a.i./kg diet (B)	Practically non-toxic
	Chronic dietary (28-day)	AC 900001 Technical Herbicide	LC_{50} > 2700 mg a.i./kg diet NOEC 2700 mg a.i./kg diet*	—
	Reproduction	AC 900001 Technical Herbicide	NOEC 864 mg a.i./kg diet*	—
Mallard duck	Acute	AC 900001 Technical Herbicide	LC_{50} > 2250 mg a.i./kg bw NOEL 2250 mg/kg bw*	Practically non-toxic
	Acute dietary (8-day)	AC 900001 Technical Herbicide	LC_{50} > 5314 mg a.i./kg diet NOEC 729 mg a.i/kg diet (B, N)	Practically non-toxic
	Chronic dietary (28-day)	AC 900001 Technical Herbicide	LC_{50} > 2700 mg a.i./kg diet NOEC 300 mg a.i./kg diet (E)	—
	Reproduction	AC 900001 Technical Herbicide	NOEC 864 mg/kg diet*	—
Mammals				
Rat	Acute	AC 900001 Technical Herbicide	LD_{50} > 5000 mg a.i./kg bw NOEL 5000 mg a.i./kg bw*	Practically non-toxic
	Dietary (2-year)	AC 900001 Technical Herbicide	LC_{50} > 500 mg a.i./kg diet NOEC 50 mg a.i./kg diet (T)	—
	Reproduction (1-generation)	AC 900001 Technical Herbicide	LC_{50} > 500 mg a.i./kg diet NOEC 500 mg a.i./kg diet*	—

Organism	Exposure	Test Substance	Endpoint Value	Degree of Toxicity[a]
Mouse	Dietary (78-week)	AC 900001 Technical Herbicide	LC_{50} > 800 mg a.i./kg diet NOEC 40 mg a.i./kg diet (T)	—
Vascular Plants				
Vascular plant (lettuce)	Seedling emergence	AC 900001 Water-Dispersible Granular Herbicide (74.7%)	EC_{25} 102 g formulation/ha	—
	Vegetative vigour	AC 900001 Water-Dispersible Granular Herbicide (74.7%)	EC_{25} 60 g formulation/ha	—

* = highest dose tested; B = body weight; M = mortality; N = food uptake (+ indicates increase, otherwise decrease); F = fertility; P = parasitisation; E = egg number; T = tissue effects

[a] USEPA classification, where applicable

[b] Classification by Hassan et al. (1994) for laboratory tests conducted with inert substrates: < 30% harmless; 30–79% slightly harmful; 80–99% moderately harmful; > 99% harmful

[c] Atkins et al. (1981) classification

Table 10 Effects on Aquatic Organisms

Organism	Exposure	Test substance	Endpoint value (mg/L)	Degree of toxicity[a]
Freshwater species				
Daphnia magna	Acute (48-hour)	AC 900001 Technical Herbicide	LC_{50} > 0.45 NOEC 0.45*	Not toxic at solubility limit
		CL 153815	LC_{50} > 98 NOEC 6.0 (M)	Practically non-toxic
	Chronic (21-day)	AC 900001 Technical Herbicide	LOEC 0.0149 (S, R, G) NOEC 0.00706 (S, R, G)	—
Sediment dwelling midge	Chronic (28-day)	AC 900001 Technical Herbicide	LC_{50} > 0.69 NOEC 0.18 (G)	Not toxic at solubility limit
Rainbow trout	Acute (96-hour)	AC 900001 Technical Herbicide	LC_{50} > 0.68 NOEC 0.68*	Not toxic at solubility limit
	Acute (96-hour)	CL 153815	LC_{50} > 100 NOEC 100*	Practically non-toxic
	Early life stage	AC 900001 Technical Herbicide	LOEC 0.012 (G) NOEC 0.0064 (G)	—
	Subchronic (28-day)	AC 900001 Technical Herbicide	NOEC 0.094*	—

Organism	Exposure	Test substance	Endpoint value (mg/L)	Degree of toxicity[a]
Bluegill sunfish	Acute (96-h)	AC 900001 Technical Herbicide	LC_{50} > 0.57 NOEC 0.57*	Not toxic at solubility limit
Blue-green alga	Chronic (120-hour)	AC 900001 Technical Herbicide	EC_{50} 0.34 (B) NOEC 0.017 (B)	—
Green alga	Chronic (72-hour)	AC 900001 Technical Herbicide	EC_{50} 0.00018 (B) NOEC 0.000068 (B)	—
		CL 153815	EC_{50} 27 (B, G) NOEC 12 (B, G)	—
Vascular plant	Chronic (14-day)	AC 900001 Technical Herbicide	EC_{25} 0.026 (F) EC_{50} 0.046 (F) NOEC 0.006 (F)	—

* = highest concentration tested; M = mortality; S = survival; R = reproduction; G = growth; B = biomass, F = frond number

[a] USEPA classification, where applicable

Table 11 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 12 Margin of Safety Values for Terrestrial Organisms

Organism	Test Substance	EEC	Toxicity	MOS	Degree of Risk
Short-term Risk of Mortality					
Earthworm	AC 900001 Technical Herbicide	0.022 mg/kg soil	LC_{50} > 1000 mg/kg soil	45 454	Negligible
	CL 153815	0.026 mg/kg soil	LC_{50} 476.5 mg/kg soil	18 326	Negligible
Bobwhite quail	AC 900001 Technical Herbicide	8.8 mg/kg diet	LC_{50} > 5314 mg/kg diet	603	Negligible
Mallard duck	AC 900001 Technical Herbicide	1.7 mg/kg diet	LC_{50} > 5314 mg/kg diet	3 125	Negligible
Rat	AC 900001 Technical Herbicide	25 mg/kg diet	LC_{50} > 500 mg/kg diet	20	Negligible
Short-term Risk of Sublethal Effects					
Earthworm	AC 900001 Technical Herbicide	0.022 mg/kg	NOEC 111 mg/kg	5045	Negligible
	CL 153815	0.026 mg/kg	NOEC 125 mg/kg	4 807	Negligible
Bobwhite quail	AC 900001 Technical Herbicide	8.8 mg/kg diet	NOEC 270 mg/kg diet	30	Negligible
Mallard duck	AC 900001 Technical Herbicide	1.7 mg/kg diet	NOEC 729 mg/kg diet	428	Negligible
Rat	AC 900001 Technical Herbicide	25 mg/kg diet	NOEC 40 mg/kg diet	1.6	Low
Lettuce	AC 900001 Technical Herbicide	67 g product/ha	EC_{25} 60 g product/ha	0.8	Moderate

Table 13 Margin of Safety Values for Aquatic Species

Organism	EEC (mg a.i./L)	Toxicity (mg a.i./L)	MOS	Degree of Risk
Short-term Risk to Most Sensitive Species				
S. capricornutum	0.0167	NOEC 0.000068	0.004	Very high
Short-term Risk to Other Species				
L. gibba	0.0167	NOEC 0.006	0.35	Moderate
A. flos-aquae	0.0167	NOEC 0.017	1	Low
D. magna	0.0167	NOEC 0.45	26	Negligible
O. mykiss	0.0167	NOEC 0.68	40	Negligible
L. macrochirus	0.0167	NOEC 0.57	34	Negligible

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