Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Note REG2007-01

Aminopyralid

The active ingredient aminopyralid and associated end-use product Aminopyralid Liquid Concentrate Herbicide for the control of broadleaf weeds and woody plants in rangeland, pasture, industrial and other non-crop areas of Canada as well as of broadleaf weeds in wheat (spring and durum) in the brown soil region of Western Canada have been granted temporary registration under the Pest Control Products Regulations.

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

(publié aussi en français)

17 January 2007

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

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

Internet: pmra_publications@hc-sc.gc.ca
www.pmra-arla.gc.ca
Information Service:
1-800-267-6315 or 613-736-3799
Facsimile: 613-736-3758

ISBN: 978-0-662-44841-9 (978-0-662-44842-6)
Catalogue number: H113-7/2007-1E (H113-7/2007-1E-PDF)

Foreword

Health Canada's Pest Management Regulatory Agency (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 aminopyralid and the associated end-use product Aminopyralid Liquid Concentrate Herbicide .

The PMRA and the United States Environmental Protection Agency (USEPA) reviewed these products within the North American Free Trade Agreement's Technical Working Group on Pesticides' Joint Review Program.

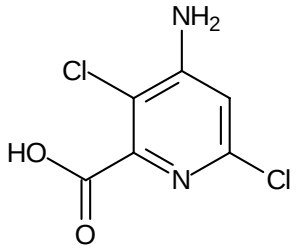
Health Canada has concluded that using aminopyralid and the end-use product Aminopyralid Liquid Concentrate Herbicide in accordance with the label has merit and value consistent with the Pest Control Products Regulations and does not entail an unacceptable risk of harm. Therefore, based on the considerations outlined above, aminopyralid and the end-use product Aminopyralid Liquid Concentrate Herbicide for the control of broadleaf weeds and woody plants in rangeland, pasture, industrial and other non-crop areas as well as of broadleaf weeds in wheat (spring and durum) is proposed for temporary registration pursuant to the Pest Control Products Regulations.

Dow AgroSciences Canada Inc. will be carrying out additional chemistry, storage stability, environmental chemistry and value studies as a condition of this temporary registration. Following the review of this information, the PMRA will publish a proposed registration decision document and request comments from interested parties before proceeding with a final regulatory decision.

Table of Contents

1.0 The Active Substance, its Properties and Uses

1.1 Identity of the Active Substance and Impurities

Active substance		Aminopyralid
Function		Herbicide
Chemical name		
1.	International Union of Pure and Applied Chemistry	4-amino-3,6-dichloropyridine-2-carboxylic acid
2.	Chemical Abstracts Service (CAS)	4-amino-3,6-dichloro-2-pyridinecarboxylic acid
CAS number		150114-71-9
Molecular formula		$C_6H_4Cl_2N_2O_2$
Molecular weight		207.02
Structural formula		
Nominal purity of active		95.3%
Identity of relevant impurities of toxicological, environmental or other significance		Hexachlorobenzene (HCB), a TSMP Track 1 substance, is identified as a possible impurity of toxicological concern. It was not detected in six pilot batches with a detection limit of 0.2 ppm. Pentachlorobenzene (QCB), proposed for addition to the TSMP Track 1 list substance that may be a possible co-contaminant with HCB, was not analyzed at this time. No other impurities of human health or environmental concern as identified in Section 2.13.4 of DIR98-04 and in Appendix II of DIR99-03 are expected to be present in this product.

1.2 Physical and Chemical Properties of the Active Substance and End-use Product

Table 1.2.1 Technical Product: Aminopyralid Technical Herbicide

Property	Result	Comment
Colour and physical state	Off-white powder	—
Odour	Odourless	—
Melting point or range	163.5°C	—
Boiling point or range	Decomposes before boiling	—
Relative density	1.72 g/ml	—
Vapour pressure at 20°C	9.52×10^{-9} Pa (20°C) 2.59×10^{-8} Pa (25°C)	Non-volatile
Henry's law constant at 20°C	7.842×10^{-15} (atm.m^3/mol)	Not expected to be volatile from water and moist soil surfaces
Ultraviolet (UV) – visible spectrum	**pH** / **λ_{max} (nm)** / **ε (L/mol·cm)** Neutral, methanol: 217 / 29 100; 220 / 26 100; 245 / 10 150 12.6: 217 / 22 800; 270 / 9140 1.4 No absorption maxima were observed above 300 nm.	Phototransformation in water can occur based on laboratory studies
Solubility in water at 20°C	**pH** / **Solubility (g/L)** Unbuffered water: 2.48 5: 212 7: 205 9: 203	Very soluble

Property	Result		Comment
Solubility (g/L) in organic solvents at 20°C	**Solvent** Methanol Acetone *n*-Octanol Ethyl acetate 1,2-Dichloroethane Xylene Heptane	**Solubility (g/L)** 52.2 29.2 3.9 3.9 0.2 0.04 <10 mg/L	Soluble in polar organic solvents. Insoluble in non-polar organic solvents
n-Octanol–water partition coefficient (K_{ow})	**pH** Unbuffered water 5 7 9	**log K_{ow}** 0.201 -1.76 -2.87 -2.96	Not expected to bioconcentrate
Dissociation constant (pK_a)	2.56		Dissociates in water, conjugate base will predominate at neutral pH
Stability	The product is compatible with copper, brass, aluminum, stainless steel (304 and 316 grade), ferrous chloride, nickel(II) chloride and cuprous chloride. It is stable at room temperature and at 50°C for 14 days.		—

Table 1.2.2 End-use Product: Aminopyralid Liquid Concentrate Herbicide

Property	Result
Colour	Brown
Odour	Mild odour
Physical state	Liquid
Formulation type	Solution
Guarantee	Aminopyralid, present as the triisopropanolamine (TIPA) salt, 240 g/L
Formulants	The product does not contain any USEPA List 1 formulants or formulants known to be TSMP Track 1 substances.

Property	Result
Container material and description	2.63 L container, plastic
Density	1.14 g/mL (20.0°C)
pH of 1% dispersion in water	7.33 (19.8°C)
Oxidizing or reducing action	The product is not a strong oxidizing agent as evidenced by the lack of reaction with zinc dust. A reaction with potassium permanganate, a strong oxidizing agent, indicates the product may be a weak reducing agent. The product does not react with monoammonium phosphate, a common fire extinguishing agent.
Storage stability	The applicant has indicated that the results of a one-year storage stability study will be provided to the PMRA in August 2005.
Explodability	The product is not explosive.

1.3 Details of Uses

Aminopyralid is formulated in one end-use product, Aminopyralid Liquid Concentrate Herbicide, with a guarantee of 240 g a.i./L. Aminopyralid Liquid Concentrate Herbicide is a contact and residual acting herbicide for use as follows:

- rangeland, pastures, industrial and other non-crop areas in Canada; and
- spring and durum wheat in the brown soil zone region of Western Canada.

1.3.1 Rangeland, Pastures, Industrial and Other Non-crop Areas

For use in rangeland, pastures, industrial and other non-crop areas, Aminopyralid Liquid Concentrate Herbicide may be applied by ground with a minimum spray volume of 100 L water/ha and by air with a minimum spray volume of 19 L water/ha. This product may be applied once per growing season when forage grasses are well-established.

Aminopyralid Liquid Concentrate Herbicide applied at 60 g a.i./ha is effective for suppression of spotted knapweed and Canada thistle. Applied at 70 g a.i./ha, Aminopyralid Liquid Concentrate Herbicide is effective for season long control of spotted knapweed and Canada thistle and suppression of Canada goldenrod and scentless chamomile. Aminopyralid applied at 90 g a.i./ha is effective for season long control of the weeds with the 70 g a.i./ha rate plus scentless chamomile and suppression of absinth wormwood. Aminopyralid applied at 120 g a.i./ha is effective for season long control of the weeds with the 90 g a.i./ha rate plus absinth wormwood and suppression of common tansy and dandelion.

Aminopyralid Liquid Concentrate Herbicide at 70 g a.i./ha may be tankmixed with 2,4-D amine at 840 g a.i./ha for control of annual sowthistle, blue bur, burdock, cocklebur, common plantain, flixweed, goat's beard, prickly lettuce, ragweeds, stinging nettle, sweet clover, curled dock, hawkweed, peppergrass; for season long control of spotted knapweed, scentless chamomile, Canada goldenrod and Canada thistle; and for top growth control of blue lettuce, bull thistle, buttercup, gum weed, hoary cress and perennial sowthistle. Aminopyralid at 90 g a.i./ha may be tankmixed with 2,4-D amine at 1080 g a.i./ha for control of weeds listed above plus season long control of absinth wormwood and dandelion. Aminopyralid at 120 g a.i./ha may be tankmixed with 2,4-D amine at 1440 g a.i./ha for control of weeds listed above plus season long control of western snowberry and common tansy.

1.3.2 Spring and Durum Wheat in the Brown Soil Zone Region of Western Canada

For use in spring and durum wheat in the brown soil zone region of western Canada, Aminopyralid Liquid Concentrate Herbicide may be applied by ground with a minimum spray volume of 100 L water/ha.

Aminopyralid Liquid Concentrate Herbicide may be applied at 10 g a.i./ha for suppression of wild buckwheat or in a tankmix with Starane Herbicide (Registration Number 24815) at 144 g a.i./ha for control of wild buckwheat, cleavers, kochia, round-leaved mallow and volunteer flax in spring wheat (3- to 6-leaf stage) as well as durum wheat (2- to 6-leaf stage).

Fields treated with Aminopyralid Liquid Concentrate Herbicide at 10 g a.i./ha may be seeded to spring wheat and canola with a minimum of 10-month recropping interval.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Substance as Manufactured

Three validated, reverse-phase, high-performance liquid chromatography with ultraviolet detection (HPLC-UV) methods were developed to quantify aminopyralid and its structurally related impurities. The active ingredient and organic impurities were quantified using benzamide as an internal standard with UV detection at 280 nm. HCB was quantitated using an external HCB standard with UV detection at 210 nm. Recoveries for aminopyralid ranged from 99.6 to 100.3% with a method relative standard deviation (RSD) of 0.31%. Recoveries for the impurities present at >0.1% ranged from 94.7 to 98.2% with RSDs ranging from 2 to 8.1%. The detection limits ranged from 1.1 to 11.9 ppm for the impurities. Average recovery for HCB was 97.22% (range 74.66–105.20%) with an RSD of 2%. Chromatograms for blanks, analytical standards and samples showed no analytical interferences in the retention vicinities of the analytes of interest.

Based upon the validation data and the chromatograms, the methods were assessed to be precise, accurate and specific for the determination of the active and its impurities.

2.2 Method for Formulation Analysis

Aminopyralid was determined using a reverse-phase HPLC-UV analytical method. Quantitation was by internal standard (diethylphthalate) with UV detection at 270 nm. Recoveries for aminopyralid ranged from 99.2 to 101.2% with a method RSD of 0.3%. Chromatograms for a blank, aminopyralid analytical standard, internal standard and sample showed no analytical interferences in the retention vicinities of the analytes of interest.

Based upon the validation data and the chromatograms, the method was assessed to be precise, accurate and specific for the determination of aminopyralid. The method is acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

2.3.1 Methods for Environmental Residue Analysis

Aminopyralid was analyzed according to the United States Food and Drug Administration's (USFDA) Multiresidue Method guidelines published in the Pesticide Analytical Manual, Volume I (January 1994). Aminopyralid was tested through protocols A and C, and as a result of Protocol C testing, was also tested through protocols D and E. Based on the results using Protocol E, testing under Protocol F was not required. As methylated aminopyralid provided good response on the column/detector combinations outlined in Protocol C, additional testing was performed with aminopyralid methyl ester under Protocol B.

Aminopyralid is not an *N*-methylcarbamate and was not found to be naturally fluorescent; therefore, further testing under Protocol A was not required. Methylation efficiency was low for aminopyralid using Protocol B. Aminopyralid was not recovered using Protocol D (with no cleanup), or using Florisil cleanup under Protocols E and F. The results of the study indicate that the USFDA Multiresidue Method guidelines are not applicable to aminopyralid.

2.3.1.1 Analytical Methodology (parent compound and transformation products)—Soil and Sediment

A validated high performance liquid chromatography with electrospray ionization and tandem mass spectrometry (HPLC-ESI-MS-MS) analytical method was developed to quantify aminopyralid in a range of soils. Butyl chloroformate was used to derivatize the samples. Quantitation was by a stable isotope internal standard (aminopyralid-1-^{15}N-2,6-^{13}C) with confirmation of identity by electrospray ionization - tandem mass spectrometry. Recoveries over four levels of fortification from 0.0015 to 0.10 µg/g ranged from 80 to 102%, with a mean of 88%. The mean RSD was 5.5% over the validated range. The limit of quantitation (LOQ) was 0.0015 µg/g. The applicant provided chromatograms of spiked and unspiked control samples as well as an analytical standard. Mass spectra of parent and product ions were provided for labelled and unlabelled aminopyralid butyl ester. No analytical interferences were noted in the retention vicinities of the analytes of interest.

Based upon the validation data and the chromatograms, the method was found to be precise, accurate, specific and sensitive for the determination of aminopyralid. It is acceptable for use as a postregistration monitoring method. Although the stable isotope internal standard specified is not commercially available, the method may be modified for postregistration monitoring purposes by using an external standard with HPLC-UV or HPLC-MS.

The PMRA has accepted the data generated in all environmental matrices, which showed that no relevant transformation products result from the application of aminopyralid. Therefore, the analytical data regarding metabolites or transformation products in soil and sediment is not required.

2.3.1.2 Analytical Methodology (parent compound and transformation products)—Water

A validated HPLC-ESI-MS-MS analytical method was developed to quantify aminopyralid in a range of water types (tap, ground, surface). Butyl chloroformate was used to derivatize the samples. Quantitation was by a stable isotope internal standard (aminopyralid-1-^{15}N-2,6-^{13}C) with confirmation of identity by electrospray ionization and tandem mass spectrometry. Recoveries over three levels of fortification from 0.05 to 5.00 µg/L ranged from 92 to 106%, with a mean of 100.3%. The mean RSD was 4.1% over the validated range. The LOQ was 0.05 µg/g. The applicant provided chromatograms of spiked and unspiked control samples as well as an analytical standard. Mass spectra of parent and product ions were provided for labelled and unlabelled aminopyralid butyl ester. No analytical interferences were noted in the retention vicinities of the analytes of interest.

Based upon the validation data and the chromatograms, the method was found to be precise, accurate, specific and sensitive for the determination of aminopyralid. It is acceptable for use as a postregistration monitoring method. Although the stable-isotope internal standard specified is not commercially available, the method may be modified for postregistration monitoring purposes by using an external standard with HPLC-UV or HPLC-MS.

2.3.2 Multiresidue Methods for Residue Analysis

Aminopyralid was analyzed according to the United States Food and Drug Administration's (USFDA) Multiresidue Method guidelines published in the Pesticide Analytical Manual, Volume I (January 1994). Aminopyralid was tested through protocols A and C, and as a result of Protocol C testing, was also tested through protocols D and E. Based on the results using Protocol E, testing under Protocol F was not required. As methylated aminopyralid provided good response on the column/detector combinations outlined in Protocol C, additional testing was performed with aminopyralid methyl ester under Protocol B.

Aminopyralid is not an *N*-methylcarbamate and was not found to be naturally fluorescent; therefore, further testing under Protocol A was not required. Methylation efficiency was low for aminopyralid using Protocol B. Aminopyralid was not recovered using Protocol D (with no cleanup) or using Florisil cleanup under protocols E and F. The results of the study indicate that the USFDA Multiresidue Method guidelines are not applicable to aminopyralid.

2.3.3 Methods for Residue Analysis of Plants and Plant Products

High-performance liquid chromatography with tandem mass spectrometry (LC-MS/MS) Method GRM 02.31 has been proposed by the petitioner as an enforcement method for residues of aminopyralid in plant commodities. The proposed LC-MS/MS method was used to determine residues of free and conjugated aminopyralid in/on grass and wheat samples from the storage stability, field trial and processing studies associated with the currently requested uses.

Briefly, ground samples are extracted with 0.1 N sodium hydroxide, releasing bound residues and hydrolyzing base-labile conjugates to free aminopyralid. The extract is then acidified with hydrochloric acid and heated to release acid-labile conjugates. Following hydrolysis, the extract is cleaned up through an anion-exchange solid-phase extraction (SPE) column. The internal standard, $^{13}C_2{}^{15}N$-aminopyralid, is added to the eluate, and residues are derivatized with butyl chloroformate to form the 1-butyl esters of aminopyralid for LC-MS/MS analysis. The validated LOQ is 0.01 ppm for all matrices, and the calculated limit of detection (LOD) is 0.002 ppm.

Method validation data for LC-MS/MS Method GRM 02.31 demonstrated adequate method recoveries of aminopyralid from barley grain, forage, and straw; grass forage and hay; sorghum grain, forage, and stover; and wheat grain, forage, and straw fortified at the LOQ (0.01 ppm). This method also demonstrated adequate method recoveries of aminopyralid at up to 0.50 ppm for cereal grain, 5.00 ppm for cereal forage and straw, and 20.0 ppm for grasses.

Adequate radiovalidation data have been submitted for the extraction procedures of Method GRM 02.31 using samples of grass and wheat commodities bearing weathered residues, from the respective metabolism studies, in which crops were treated with [2,6-^{14}C]aminopyralid. Adequate independent laboratory validation data have been submitted using grass forage and wheat grain. The PMRA concluded that confirmatory analysis procedures are not required for the proposed enforcement method due to the high specificity of the LC-MS/MS method.

The petitioner is required to show that the proposed enforcement method (GRM 02.31) can differentiate between aminopyralid, clopyralid and picloram, as they are all similar in structure.

2.3.4 Methods for Residue Analysis of Food of Animal Origin

LC-MS/MS Method GRM 03.18 has been proposed by the petitioner as an enforcement method for residues of aminopyralid in ruminant milk and tissues.

Briefly, milk or ground tissue samples are extracted with methanol/sodium bicarbonate. The extract is cleaned up through an anion-exchange SPE plate. The internal standard, $^{13}C_2{}^{15}N$-aminopyralid, is added to the eluate, and residues are derivatized with butyl chloroformate to form the 1-butyl esters of aminopyralid for LC-MS/MS analysis. The validated LOQ is 0.01 ppm for all matrices, and the calculated LOD is 0.003 ppm.

Method validation data for LC-MS/MS Method GRM 03.18 demonstrated adequate method recoveries of aminopyralid from bovine whole milk, cream, skimmed milk, fat, kidney, liver and muscle fortified at the LOQ (0.01 ppm). This method also demonstrated adequate method recoveries of aminopyralid at up to 100× LOQ (1.0 ppm) for milk, fat, liver and muscle, or at 250× LOQ (2.5 ppm) for kidney. The spiking levels and samples used in method validation adequately bracket expected residue levels in ruminant milk and tissues. Two recoveries were below the acceptable 70–120% range: 67% in one kidney sample spiked at the LOQ and 64% in one milk cream sample spiked at the higher level (1.0 ppm). The low recoveries (2 out of 70 samples) were likely due to random error and not systematic error. Acceptable concurrent method recovery data were included with the feeding study.

Adequate independent laboratory validation data have been submitted using bovine milk and kidney. The PMRA concluded that confirmatory analysis procedures are not required for the proposed enforcement method due to the high specificity of the LC-MS/MS method.

A radiovalidation study was not conducted for the LC-MS/MS enforcement method because residues in samples from a goat metabolism study were very low; only kidney samples had a total radioactive residue (TRR) >0.01 ppm. However, the extraction solvent used in the proposed enforcement method is similar to that used in the goat metabolism study. In the goat metabolism study, 76–96% of the TRRs were extracted from milk, liver and kidney samples using methanol (fat and muscle samples were not subjected to extraction procedures due to low residue levels). As noted above for the proposed enforcement method, methanol/sodium bicarbonate is used as the extraction solvent.

The petitioner is required to show that the proposed enforcement method (GRM 03.18) can differentiate between aminopyralid, clopyralid and picloram, as they are all similar in structure.

3.0 Impact on Human and Animal Health

3.1 Integrated Toxicological Summary

Technical aminopyralid and Aminopyralid Liquid Concentrate Herbicide was rapidly absorbed, distributed, and excreted following oral administration in the rat. Tissue distribution and bioaccumulation were minimal, <0.73% of the administered doses were recovered in tissues after dosing for all dosing groups. The highest levels of radioactivity were found in the skin and carcass. Aminopyralid was excreted unchanged indicating the absence of metabolism. In the urine and feces, ≥96 and 100% of the administered dose (AD) were recovered, respectively, as the parent compound.

Technical aminopyralid, 94.5% purity, was of low acute toxicity in rats following oral, dermal or inhalation exposure (oral LD_{50} >5000 mg/kg bw; dermal LD_{50} >5000 mg/kg bw; inhalation LC_{50} >5 mg/L). It was not irritating to the rabbit skin, but was extremely irritating to the rabbit eye. Skin sensitization testing with guinea pigs, using the maximization method, showed that aminopyralid was not a dermal sensitizer.

Aminopyralid Liquid Concentrate Herbicide was of low acute toxicity by the oral, dermal and inhalation routes of exposure in male and female rats (oral LD_{50}, >5000 mg/kg bw; dermal LD_{50}, >5000 mg/kg bw; inhalation LC_{50} >5.79 mg/L, actual concentration). This end-use product was a minimal eye irritant in rabbits and is slightly irritating to the rabbit skin. The formulation was not a dermal sensitizer when tested in guinea pigs based on the maximization method.

The genotoxic potential of aminopyralid was assessed in *in vitro* and *in vivo* systems. It was not mutagenic when tested in Ames microbial and mammalian cell systems, and did not cause chromosomal aberrations in *in vitro* rat lymphocytes or *in vivo* mouse bone marrow cells.

The genotoxic potential of Aminopyralid Liquid Concentrate Herbicide was also assessed in *in vitro* and *in vivo* systems. It was not mutagenic when tested in Ames microbial and mammalian cell systems, and did not cause chromosomal aberrations in *in vitro* rat lymphocytes or *in vivo* mouse bone marrow cells.

The subchronic and chronic toxicity of aminopyralid was investigated in mice, rats and dogs. A series of range-finding 30- and 90-day studies were conducted initially. These studies were used to establish appropriate dose levels to be used in longer term studies. A 28-day dermal study was also carried out in rats. In addition, a 90-day dietary toxicity study of Aminopyralid Liquid Concentrate Herbicide in rats was carried out.

Subchronic and chronic toxicity studies of aminopyralid conducted in the mouse indicated the lack of treatment-related findings at the highest target dose, 1000 mg/kg bw/day, administered in the diet for up to 18 months. The lower white blood cell counts and liver effects observed at 1000 mg/kg bw/day level in the 4-week study were not demonstrated in the 90-day and 18-month studies. Thus, the findings in the 4-week study were probably incidental and unrelated to treatment. Based on the findings, the no observed adverse effect levels (NOAELs) established in the subchronic and chronic studies were 1000 mg/kg bw/day, the highest dose tested. There was no evidence of oncogenic potential of aminopyralid in the mouse.

Subchronic and chronic toxicity studies conducted in the rat indicated a slightly higher sensitivity of the male to the toxic potential of aminopyralid. However, the subchronic and chronic toxicity potential of aminopyralid was slight, even at the limit dose of 1000 mg/kg bw/day in the diet for up to 2 years. The main toxic effect of aminopyralid in the rat was the increased in cecal weight and hyperplasia of the mucosal epithelium of the cecum and ileum. These effects were more pronounced in the male. With prolonged administration for 2 years and at the high dietary dose of 1000 mg/kg bw/day, aminopyralid adversely affected body weight and body-weight gain of male and female rats. Body weight of male rats was also slightly depressed at a dose of 500 mg/kg bw/day administered for 2 years. Based on the hyperplasia of the mucosal epithelium of the cecum and ileum, the NOAELs established in the 90-day study for male and female rats were 500 and 1000 mg/kg bw/day, respectively. On the basis of adverse body weight effects, the NOAELs established in the 2-year study for male and female rats were 50 and 500 mg/kg bw/day, respectively. There was no evidence of oncogenicity.

A 28-day dermal toxicity study of aminopyralid in rats tested at doses up to 1000 mg/kg bw/day did not result in any systemic toxicity. The NOAEL was established at 1000 mg/kg bw/day, the highest dose tested.

A short-term 90-day dietary toxicity study of Aminopyralid Liquid Concentrate Herbicide in rats was available. The only systemic effect observed was an increase in cecal weight unaccompanied with histopathological changes at the two high-dose levels of 1211 and 2421 mg EP/kg bw/day. The only other treatment-related alterations, which were considered secondary to increased resorption of colonic water with compensatory renal excretion, were minimal increases in urine volume for high-dose males and females, and a minimal decrease in urine specific gravity for high-dose females. The NOAEL was 2421 mg/kg bw/day (1000 mg aminopyralid-TIPA/kg bw/day; 520 mg a.e./kg bw/day) for both sexes, the highest dose tested.

Short-term toxicity studies of aminopyralid conducted in the dog indicated that the stomach was the target organ. Treatment-related histopathological changes to the stomach were evident for dogs that received aminopyralid at dietary concentrations of 3.0% for over 90 days. The stomach effect involved slight diffuse hyperplasia and hypertrophy of the mucosal epithelium, slight lymphoid hyperplasia of the gastric mucosa, and/or very slight/slight chronic mucosal inflammation. Based on the stomach effects, the NOAEL for the 90-day study was 0.75% (♂ = 282, ♀ = 232 mg/kg bw/day) and the NOAEL for the 1-year study was 0.30% (♂ = 99.2, ♀ = 93.2 mg/kg bw/day).

There are no subchronic toxicity data in the rabbit.

Reproductive toxicity data available in the rat indicated that aminopyralid did not affect reproductive performance or other reproductive parameters at the limit dose of 1000 mg/kg bw/day in the diet. At 1000 mg/kg bw/day, aminopyralid did not induce systemic toxicity in the parental animals, affect the reproductive performance or cause offspring toxicity. The lowest observed adverse effect levels (LOAELs) were not established since there were no adverse, treatment-related effects. The NOAELs for parental, reproductive and offspring toxicity were all 1000 mg/kg bw/day.

The teratogenic potential of aminopyralid was assessed in the rat and rabbit. In the rat tested at the limit dose of 1000 mg/kg bw/day administered by oral gavage, there was no treatment-related maternal or developmental toxicity. Thus, the NOAELs for both maternal and developmental toxicity were 1000 mg/kg bw/day, the highest dose level tested. There was no evidence of teratogenicity. In the rabbit, a dose of 750 mg/kg bw/day resulted in severe clinical signs and body-weight loss that led to the termination of investigation at this dose level. At the lower dose of 500 mg/kg bw/day, the maternal animals showed incidences of incoordinated gait, which was transient, not persistent, and did not progress in severity subsequently. A single rabbit at 500 mg/kg bw/day group had ulcers/erosions in the glandular mucosa of the stomach. The LOAEL and NOAEL for maternal toxicity in the rabbit were 500 and 250 mg/kg bw/day, respectively. In the rabbit, there were no treatment-related developmental or teratogenic effects noted at any dose level tested. Hence, the developmental LOAEL could not be established. The developmental NOAEL was 500 mg/kg bw/day.

The teratogenicity and developmental toxicity potential of Aminopyralid Liquid Concentrate Herbicide was assessed in the rat and rabbit. Both studies were tested at dose levels of 0, 484, 1211 and 2421 mg EP/kg bw/day (= 0, 200, 500, 1000 mg aminopyralid-TIPA; 0, 104, 260, 520 mg a.e./kg bw/day). Both studies demonstrated the lack of teratogenic potential of Aminopyralid Liquid Concentrate Herbicide. No treatment-related maternal or developmental toxicity was observed in the rat study. For the rabbit study, maternal toxicity was observed at the two high-dose levels. The findings included decreased fecal output and lower food intake and body-weight gains. At 2421 mg EP/kg bw/day, developmental toxicity was demonstrated by the lower fetal weights. The LOAELs for maternal and developmental toxicity for the rat were 2421 mg/kg bw/day (1000 mg aminopyralid-TIPA; 520 mg a.e./kg bw/day). The NOAELs for maternal and developmental toxicity for the rabbit were 484 mg EP/kg bw/day (200 mg aminopyralid TIPA; 106 mg a.e./kg bw/day) and 1211 mg EP/kg bw/day (500 mg aminopyralid TIPA; 260 mg a.e./kg bw/day), respectively.

aminopyralid was assessed for neurotoxicity in the rat following acute oral exposure as well as exposure in the diet for 1 year. The assessment involved an extensive examination of behavioural parameters employing functional observational battery (FOB) and motor activity testing, as well as thorough examination of the nervous tissues. When tested at the high single oral dose of 2000 mg/kg bw, or at the high dietary dose of 1000 mg/kg bw/day for 1 year, aminopyralid did not cause any neurotoxic effects. Thus, the neurotoxicity NOAEL for acute oral exposure was 2000 mg/kg bw and for the 1-year dietary exposure was 1000 mg/kg bw/day.

Available toxicity data did not indicate that aminopyralid or Aminopyralid Liquid Concentrate Herbicide might adversely affect other organ systems, such as endocrine or immune systems. Thus, studies assessing other toxic endpoints are not required.

The toxicological database for aminopyralid is complete and adequate.

3.2 Determination of Acceptable Daily Intake (ADI)

The lowest NOAEL of 50 mg/kg bw/day was established in male rats in the combined 2-year chronic toxicity and oncogenicity study based on reduced body weight. Using this NOAEL and the standard uncertainty factors of 100 (10× for intraspecies variation and 10× for interspecies variation), an ADI of 0.5 mg/kg bw was established.

3.3 Acute Reference Dose (ArfD)

Technical aminopyralid is of low acute toxicity; therefore, no ARfD is needed for the general population.

For women of child-bearing ages (13–50 year of age), a separate ARfD is not required because there is no evidence of reproductive, developmental and offspring toxicity at maternally toxic doses of aminopyralid when tested in the rat and rabbit.

3.4 Toxicological Endpoint Selection—Occupational and Bystander Risk Assessment

In the absence of dermal absorption data, dermal absorption would be assumed to be equivalent to oral exposure (100%). However, as the toxicity endpoint for use in the risk assessment is from a dermal study, an estimate of dermal absorption is not required.

The toxicological database for aminopyralid and Aminopyralid Liquid Concentrate Herbicide did not indicate significant toxic effects. Both the technical grade active ingredient and the formulation are of low acute toxicity by the oral, dermal and inhalation routes of exposure in the rat. Aminopyralid and its formulation are not skin irritants or sensitizers when tested in rabbits and guinea pigs, respectively. The formulation is not an eye irritant in rabbits, but the technical product is a severe eye irritant, probably because of its physical nature, which causes mechanical abrasion when instilled into the eyes of rabbits.

Short- and long-term toxicity data in rats and dogs, but not in mice, demonstrated that the gastrointestinal tract was the target organ. Rats exposed to aminopyralid at high dose levels had increased cecal size and weight. Histopathological findings of the gastrointestinal tract in rats and dogs revealed slight diffuse hyperplasia and hypertrophy of the mucosal epithelium of stomach, slight lymphoid hyperplasia of the gastric mucosa and very slight/slight chronic mucosal inflammation. When tested in rats, aminopyralid did not affect reproductive performance or parameters. Aminopyralid and Aminopyralid Liquid Concentrate Herbicide were not teratogenic when tested in rats and rabbits, and were not genotoxic based on a test battery assessing gene mutation and chromosome aberration in microbial and mammalian *in vitro* and *in vivo* systems. Aminopyralid was not neurotoxic after acute oral exposure or after 1-year dietary exposure in rats.

Based on the above-noted observations, for the short- and intermediate-term occupational exposures and the predominantly dermal route of exposure for workers, it was considered appropriate to base the occupational risk assessment on the 28-day rat dermal toxicity study. This study was well conducted and did not demonstrate any systemic toxic effects at 1000 mg/kg bw/day, the highest dose tested.

A margin of exposure of 100 is considered to be protective of all workers

3.5 Impact on Human or Animal Health Arising from Exposure to the Active Substance or to Impurities Contained in it

3.5.1 Occupational Exposure and Risk

3.5.1.1 Handler Exposure and Risk

Aminopyralid is a new herbicide with one proposed end-use product, Aminopyralid Liquid Concentrate Herbicide. The proposed uses include spring and durum wheat, rangeland, pasture, industrial and other non-crop areas. Farmers and custom applicators, as well as individuals who treat rangeland, pasture, industrial and other non-crop areas, have potential for exposure when applying the end-use product.

Aminopyralid Liquid Concentrate Herbicide is applied at 0.010 kg a.i./ha to wheat and 0.12 kg a.i./ha to other areas (range and pasturelands, industrial sites and other non-crop areas). With the proposed ground and aerial application methods, the typical area treated per day ranges from using 150 L of the spray solution with a backpack sprayer to treating 490 ha aerially. Potential exposure would be short to intermediate term and via the dermal route.

Exposure estimates are based on data from the Pesticide Handlers Exposure Database (PHED), version 1.1. The PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates. The PHED subsets generated compare well with the product/use scenario. Subsets were created with the appropriate formulation (liquid), application equipment and protective clothing for the proposed uses. Exposure estimates are based on the best-fit measure of central tendency for each body part and default values for area treated per day.

For the estimation of worker exposure, it is assumed that a farmer will spray his crop in a day. For custom applicators, it is assumed that spraying will take place over a maximum of 30 days. Assumptions made for the estimates include the following.

- The body weight of the worker is 70 kg.
- The dermal absorption is the default value of 100%.
- All mixer/loaders wear protective clothing consistent with the label-recommended personal protective equipment (coveralls and chemical-resistant gloves).
- Applicators wear coveralls and gloves or no gloves, depending upon the application equipment.

The inhalation exposure would be minimal as the vapour pressure of aminopyralid is low (9.52×10^{-6} kPa at 20° C), which is considered non-volatile and qualifies for a waiver (NAFTA value of 1×10^{-5} kPa) for outdoor use.

For the various short- to intermediate- term exposure scenarios, a NOAEL of 1000 mg a.i./kg bw/day from the rat 28-day dermal study was chosen for risk assessment purposes. Margins of exposure are presented in Table 3.5.1.1.1.

Table 3.5.1.1.1 Handler Exposure Estimates and Margins of Exposure

Scenario	Exposure (mg a.i./kg bw/day)[a]	Margin of Exposure[b]
Groundboom: Farmer (mixer/loader/applicator)	0.0012	833 000
Groundboom: Custom Applicator (mixer/loader/applicator)	0.0024	416 000
Aerial (mixer/loader)	0.0289	34 000
Aerial (applicator)	0.006	166 000
High-pressure handwand (mixer/loader/applicator)	0.1689	5900
Low-pressure handwand (mixer/loader/applicator)	0.002	500 000
Right-of-way sprayer (mixer/loader/applicator)	0.0907	11 000
Backpack sprayer (mixer/loader/applicator)	0.0137	73 000

[a] Calculated as µg a.i./kg a.i. handled × application rate × area treated × 100% dermal absorption / body weight 70 kg).

[b] NOAEL: 1000 mg/kg bw/day (28-day rat dermal study).

3.5.1.2 Postapplication Exposure and Risk

There is the potential for postapplication exposure to workers re-entering treated wheat fields for scouting. Harvesting (swathing) wheat is not expected at the stage of growth when application would occur (preharvest interval [PHI] of 40 days) and is performed mechanically.

As the product will be applied once a season and only when the weeds are at an actively growing stage, postapplication activities in non-cropland areas should be negligible and limited to some scouting. As the product label states to re-enter “when spray has dried”, residues should be dry at the time of any re-entry. Therefore, neither dermal contact nor inhalation exposure should be of concern.

A worst case estimate of postapplication exposure would involve re-entry to the site on the day of application to perform scouting (wheat). For this scenario, the postapplication margin of exposure falls above the target margin of exposure; therefore, it is acceptable for the proposed uses (see Table 3.5.1.2.1).

Table 3.5.1.2.1 Postapplication Exposure Estimates and Margins of Exposure

Postapplication Activity	NOAEL (mg/kg bw/day)[a]	Exposure (mg a.i./kg bw/day)	Margin of Exposure[b]
Scouting	1000	0.0034	294 000

[a] NOAEL from the 28-day dermal toxicity study.
[b] The target margin of exposure is 100.

3.5.2 Bystander Exposure and Risk

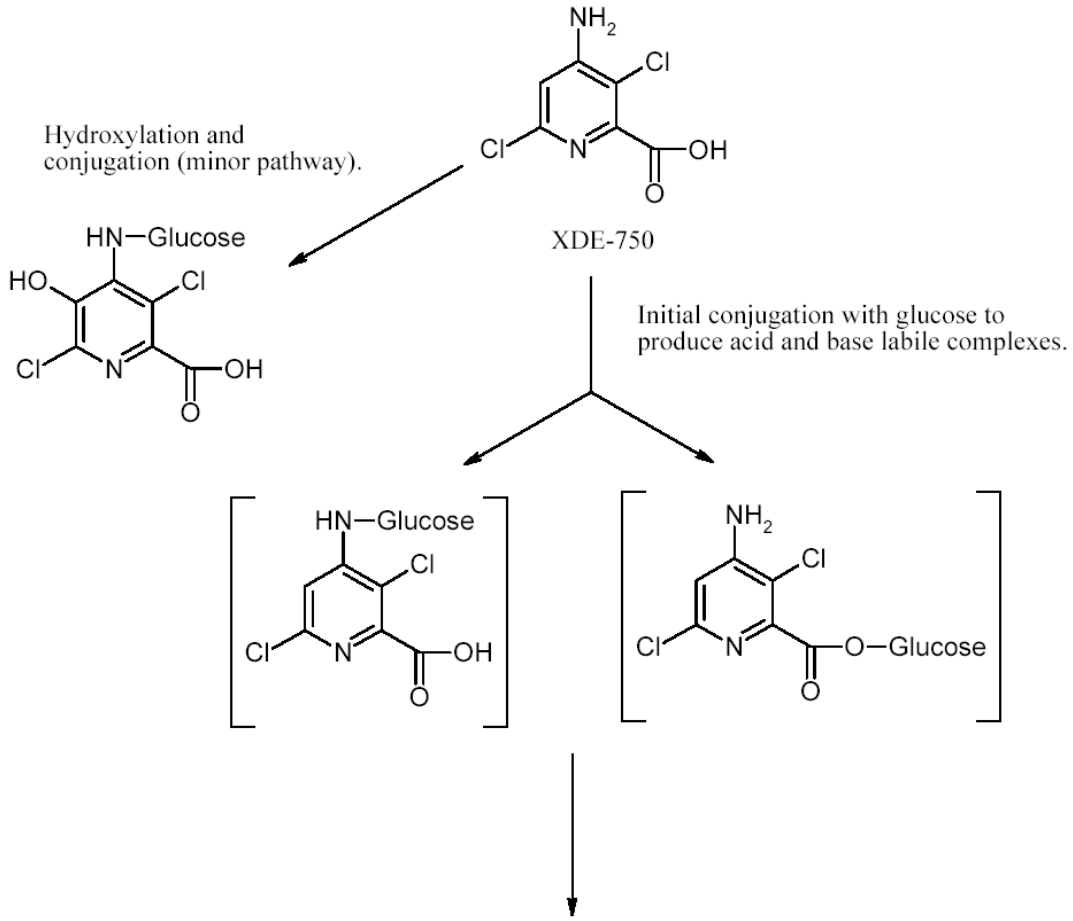
Potential bystander exposure is expected to be negligible with respect to application to wheat in an agricultural cropland area. The spraying to rangelands, pastureland, industrial and other non-crop areas should not result in significant bystander exposure. However, the bystander assessment would be covered off by the scouting assessment for wheat.

4.0 Residues

4.1 Nature of the Residue in Plants

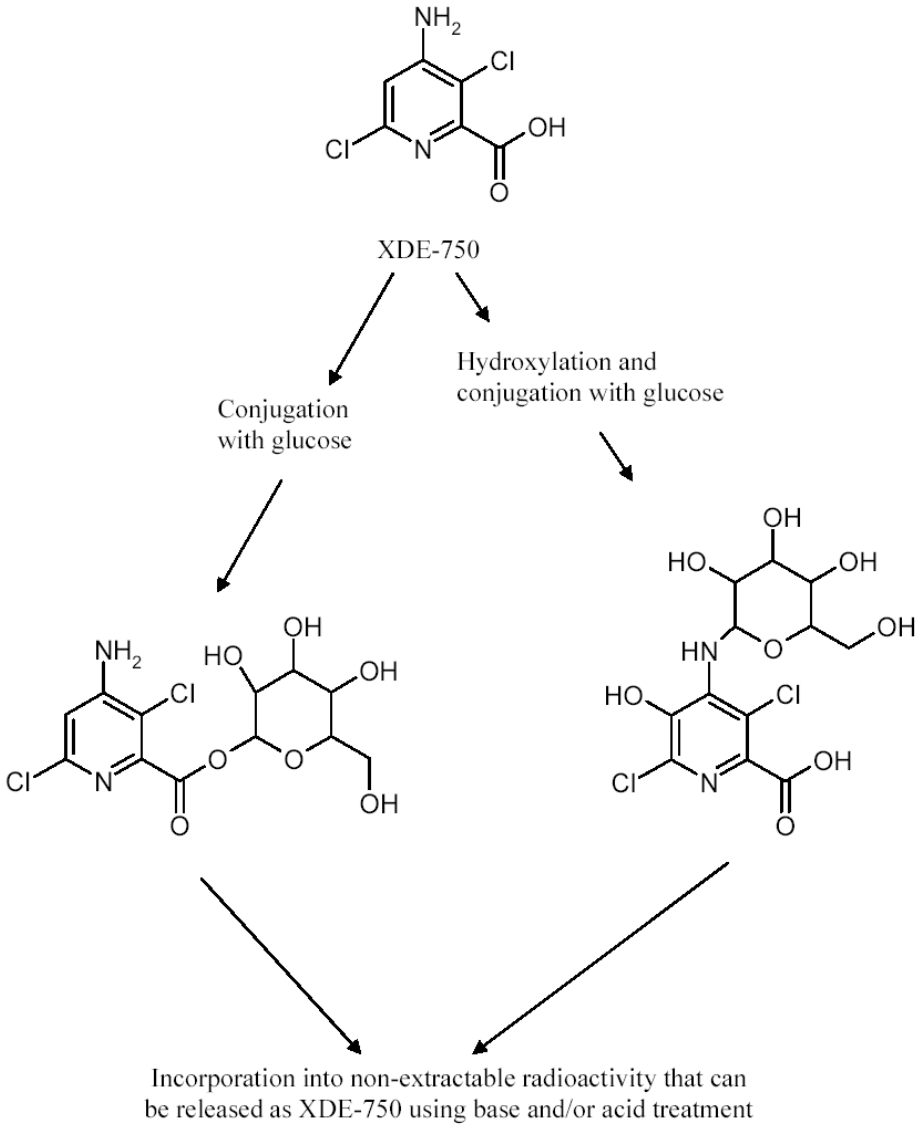
Aminopyralid, radiolabelled at the 2- and 6-positions of the pyridine ring, was foliarly applied once to each of the 3 types of pasture grasses (Big bluestem, Perennial rye grass and *Panicum maximum*) approximately 8–10 weeks after planting at a rate of 360 g a.i./ha. The predominant residue in all three grass species was free aminopyralid which accounted for 23.8–38.0% TRR (3.40–6.68 ppm) in samples collected 21 and 42 days after treatment (DAT). An additional 59.6–69.4% TRR (5.38–14.44 ppm) was characterized as acid- and base-labile conjugates of aminopyralid. The proposed metabolic pathway of aminopyralid in grass is shown in Figure 4.1.1.

Figure 4.1.1 Proposed Metabolic Pathway of Aminopyralid in Grass



Aminopyralid, also radiolabelled at the 2- and 6-positions of the pyridine ring, was foliarly applied once to spring wheat when plants were at the BBCH 26–28 stage (6 to 8 tillers) using 2 treatment rates: a low rate (40.1 g a.i./ha) and a high rate (80.3 g a.i./ha). The predominant residues were free and conjugated aminopyralid (90% of TRR, or 3.703 ppm, in 0-DAT forage; 38% of TRR, 0.332 ppm, in 14-DAT forage; 35.4% of TRR, or 0.244 ppm, in 35-DAT hay; 79% of TRR, 0.489 ppm, in 86-DAT straw; and 60% of TRR, or 0.050 ppm, in 96-DAT grain). The proposed metabolic pathway of aminopyralid in wheat is shown in Figure 4.1.2.

Figure 4.1.2 Proposed Metabolic Pathway of Aminopyralid in Wheat



On the basis of the metabolism in grass and wheat, the residue of concern (ROC) may be defined as free and conjugated aminopyralid. The metabolism of aminopyralid in grass and wheat is well understood.

4.2 Confined Accumulation in Rotational Crops

Aminopyralid, radiolabelled in the 2- and 6- positions of the pyridine ring, was applied to soil at 10 g a.i./ha. Lettuce, sorghum, and turnips were planted at 90- and 120-DAT. The TRRs that were ≥0.01 ppm in 90- and 120-DAT samples included early sorghum forage (0.027 ppm and 0.017 ppm, respectively), 90-day sorghum stover (0.027 ppm) and 120-DAT mature turnip tops (0.010 ppm). The TRR in all other rotational crop commodities were <0.001–0.007 ppm. TTRs were generally found to decrease from the 90-day plantback interval to the 120-day plantback interval.

Only 90-DAT sorghum early forage and stover, and 120-DAT sorghum early forage and turnip tops contained radioactivity ≥0.01 ppm. These were extracted for metabolite characterization. Free aminopyralid was the major residue identified in rotational crop matrices, at 44.2% TRR (0.012 ppm) and 26.9% TRR (0.005 ppm) in 90- and 120-DAT sorghum early forage, respectively, 18.1% TRR (0.005 ppm) in 90-DAT sorghum stover, and 17.2% TRR (0.002 ppm) in 120-DAT turnip tops. Two metabolite fractions were also characterized as conjugated aminpopyralid in each matrix (5.4–20.5% TRR, or 0.001–0.006 ppm, was more polar fraction than aminopyralid; 23.1–67.9% TRR, or 0.006-0.010 ppm, was slightly less polar than aminopyralid). The results of the confined rotational crop study indicate that residues of aminopyralid are metabolized in rotated crops in the same manner as in primary crops.

4.3 Field Accumulation in Rotational Crops

On the basis of the results of the confined crop rotation study described above, it was determined that a field accumulation study is not required.

4.4 Nature of the Residue in Animals

Aminopyralid, radiolabelled at the 2- and 6-positions of the pyridine ring, was orally administered to 1 lactating goat at a nominal dose of ~15 mg/kg in the diet for 6 consecutive days. Total radioactive residues (TRR) in samples of milk and tissues, collected from the treated goat, were <0.01 ppm, except in kidney, which bore a TRR of 0.071 ppm. In kidney, the parent aminopyralid was the only residue identified at 79.9% TRR (0.057 ppm). The study reported that elimination via urine and feces was approximately the same (~46% each). The identity of unchanged aminopyralid was confirmed in urine and feces.

Aminopyralid, also radiolabelled at the 2- and 6-positions of the pyridine ring, was orally administered to 10 white laying hens at ~12 mg/kg in the diet for 7 consecutive days. The TRR in/on all collected samples of eggs and tissues were <0.01 ppm. Due to the low TRR levels in all egg and tissue samples, the residues in these samples were not further characterized/identified. A majority (~79%) of the administered dose was excreted. The day 7 excreta was shown to contain 92.9% TRR as the parent compound aminopyralid. Two poorly resolved fractions (3.3% TRR) were characterized as conjugates of aminopyralid following acid and base hydrolysis.

The available metabolism data from the lactating goat, the laying hen and the rat indicate that the majority of the administered aminopyralid is excreted as unchanged parent compound in all three species. Therefore, the residue of concern in livestock is aminopyralid, *per se*. The metabolism of aminopyralid in animals is well understood.

4.5 Methods for Residue Analysis of Plants and Plant Products

An LC-MS/MS Method (GRM 02.31) was proposed for data gathering and enforcement purposes. The method limit of quantitation (LOQ) for residues of free and conjugated aminopyralid was reported as 0.01 ppm. This method was found to give acceptable recoveries for the analysis of barley grain (102±6.6%, n=20), sorghum grain (103±2.9%, n=6) and wheat grain (105±5.3%, n=10) at the 0.01–0.5 ppm spiking levels. The method also gave acceptable recoveries for the analysis of barley forage (96±6.3%, n=10), barley straw (96±4.0%, n=9), sorghum forage (100±4.6%, n=10), sorghum stover (96±4.1%, n=10), wheat forage (97±6.4%, n=10) and wheat straw (99±5.0%, n=11) at the 0.01–5 ppm spiking levels. The method also gave acceptable recoveries for the analysis of grass forage (97±4.7%, n=29) and grass hay (99±4.1%, n=30) at the 0.01–20 ppm spiking levels. The independent laboratory validation did support the reliability and reproducibility of the enforcement Method GRM 02.31 for the determination of the free and conjugated aminopyralid in grass and wheat matrices.

The petitioner is required to show that the proposed enforcement method (GRM 02.31) can differentiate between aminopyralid, clopyralid, and picloram, as they are all similar in structure.

4.6 Methods for Residue Analysis of Food of Animal Origin

An LC-MS/MS Method (GRM 03.18) was proposed for data gathering and enforcement purposes for ruminants. The method LOQ for residues of aminopyralid *per se* was reported as 0.01 ppm. This method was found to give acceptable recoveries for the analysis of the following at the 0.01–1 ppm spiking level:

- bovine whole milk, milk cream, and skim milk (80±8, n=22);
- bovine fat (93±4, n=12);
- bovine liver (83±5, n=12); and
- bovine muscle (84±7, n=12).

This method was also found to give acceptable recoveries for bovine kidney (81±8, n=12) at the 0.01–2.5 ppm spiking level. The independent laboratory validation did support the reliability and reproducibility of Method GRM 03.18 for the determination of aminopyralid *per se* in bovine matrices. An enforcement method for poultry was not submitted and is not required as no residues are expected in poultry matrices.

The petitioner is required to show that the proposed enforcement method (GRM 03.18) can differentiate between aminopyralid, clopyralid and picloram, as they are all similar in structure.

4.7 Storage Stability Data—Plants/Animals

4.7.1 Plants

The data presented in the freezer storage stability study indicated that residues of aminopyralid were stable at approximately -20°C for up to 187 days (6.2 months) in grass hay and forage, 168 days (5.6 months) in wheat grain as well as 175 days (5.8 months) in wheat straw. Ground samples were spiked with aminopyralid at 0.1 ppm. These interim results were from an 18-month study. There was no evidence of degradation from the interim data.

Freezer storage stability data for residues of aminopyralid in/on grass that covers a period of at least 14.5 months are required to support the conditions under which samples were stored in the crop field trials.

4.7.2 Animals

No freezer storage stability data were submitted for animal matrices.

4.8 Crop Field Trials

Supervised crop field trials in wheat were conducted in Canada and the United States with aminopyralid (as the water emulsion in oil formulation [EO]; the soluble concentrate liquid [SC/L] TIPA salt formulation; and the SC/L potassium salt formulation) at 10 g a.e./ha (the proposed Canadian rate). Wheat forage and hay were sampled 0 and 6–7 days postapplication, and wheat grain and straw were sampled 49–80 days post treatment. The petitioner is limiting use of the end-use product to Region 7 of Western Canada. Therefore, the seven trials submitted in Region 7 (Saskatchewan, Nebraska, North Dakota and South Dakota) satisfy requirements for the number and location of trials (Regulatory Directive DIR98-02, Section 9). From the submitted wheat field trials in Region 7, the maximum aminopyralid (free and conjugated) residues were 0.777 ppm for wheat forage (0 DAT), 2.377 ppm for hay (0 DAT), 0.026 ppm for grain (49- to 56-day PHI) and 0.145 ppm for straw (49- to 56-day PHI). Consequently, an MRL of 0.04 ppm should be established to cover residues of aminopyralid in wheat grain. This MRL is harmonised with the tolerance levels of the United States. Residue decline studies in wheat demonstrated that the proposed MRL for wheat grain will not be exceeded when collected at a PHI of 50 days.

Supervised crop field trials in grass were conducted in Canada and the United States with aminopyralid formulated as the TIPA salt at ~120 g a.e./ha (the proposed Canadian rate). Grass forage was harvested 0, 6–8 and 13–15 days after application, and grass hay was harvested 0, 13–15 and 20–22 days after application. The Canadian and United States trials submitted (2 trials in Region 1; 2 trials in Region 2; 1 trial in Region 4; 2 trials in Region 5; 1 trial in Region 5A; 3 trials in Region 7; 1 trial in Region 8; 1 trial in Region 9; 2 trials in Region 11; 5 trials in Region 14) are in accordance with PMRA Regulatory Directive DIR98-02, Section 9, with the exception of 1 trial in Region 5B and 1 trial in Region 14. The maximum aminopyralid residues in pasture and rangeland grass forage and hay from the submitted grass field trials that are relevant to the Canadian regional requirements (DIR98-02, Section 9) are 14.03 ppm for grass forage and 51.50 ppm for grass hay, both collected 0 DAT.

4.9 Processed Food/Feed

Aminopyralid, formulated as a water emulsion in oil, was applied to wheat at ~50 g a.e./ha and the wheat grain (containing 0.054-0.055 ppm) was subsequently processed into germ, bran, middlings, shorts, and flour using simulated commercial processing procedures. A sample of wheat aspirated grain fractions was also generated. A comparison of the residues in the raw agricultural commodity with those in each processed fraction resulted in concentration factors of 2.6×, 1.2×, 6.1×, ~0.2×, 0.62× and 0.4× for wheat bran, wheat shorts, aspirated grain fractions, wheat flour, middlings, and wheat germ, respectively. An MRL of 0.1 ppm will be needed to cover residues of aminopyralid in wheat bran. This MRL is harmonised with the tolerance levels of United States. No other MRLs are needed to cover residues of aminopyralid in processed fractions.

4.10 Meat/Milk/Poultry/Eggs

Lactating Holstein dairy cattle were orally administered aminopyralid at 32.8, 64.5, 181.5 and 644.7 mg/kg feed. The maximum theoretical dietary burden (MTDB) for cattle is 58 ppm. The expected residues of aminopyralid from cattle feeding at ~1.1× the MTDB is 0.024 ppm in whole milk, 0.012 ppm in cream, 0.015 ppm in skim milk, 0.013 ppm in fat, 0.202 ppm in kidney, 0.014 ppm in liver and <0.01 ppm in muscle. Based on these residues, the following MRLs will be established:

- 0.03 ppm in milk;
- 0.02 ppm in fat (from goat, cattle, horse and sheep);
- 0.02 ppm in meat byproducts excluding kidney (from goat, cattle, horse and sheep); and
- 0.3 ppm in kidney (from goat, cattle, horse and sheep).

These MRLs are harmonised with the tolerance levels of the United States.

A poultry feeding study was not submitted, and is not required on the basis of the results from the aminopyralid metabolism study in the laying hen. In particular, at the feeding level employed (~12 mg/kg aminopyralid in feed, or 66× the MTDB for poultry), residues were <0.01 ppm in all poultry matrices. As such, there is no expectation of residues, and MRLs are not required to cover residues of aminopyralid in poultry commodities.

4.11 Dietary Risk Assessment

The proposed domestic use of aminopyralid on wheat and rangeland and pasture grasses 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 dietary risk assessment included an expected environmental concentration (EEC) of 0.067 mg/L that consisted of aminopyralid in groundwater, and a chronic exposure analysis using an ADI of 0.5 mg/kg/day. For the chronic exposure analysis, 0.3% to 1.0% of the dietary risk from aminopyralid use was attributed to food and water for all of the population subgroups.

5.0 Fate and Behaviour in the Environment

5.1 Physical and Chemical Properties Relevant to the Environment

Residues relevant to the environment are that of the parent chemical, aminopyralid. This new synthetic auxin herbicide is of high water solubility (2.48 g/L) and is non-volatile. Aminopyralid is formulated in the end-use product as a TIPA salt. The aminopyralid-TIPA salt dissociates in water to form the TIPA cation and the conjugate base of aminopyralid, which is a negatively charged molecule and is referred to as the acid equivalent (aminopyralid). Based on the physical and chemical properties of aminopyralid, it is not expected to undergo direct photolysis in water; however, studies of phototransformation in water indicate that phototransformation is rapid. The log K_{ow} of 0.2 is low and bioconcentration is not expected to occur in the environment. See Appendix III, Table 1for a summary of physical and chemical properties of aminopyraid relevant to the environment.

5.2 Abiotic Transformation

Aminopyralid does not hydrolyze at the tested pH values of 5–9; 100% of the test chemical remained as the parent compound at the end of 30 days. The parent compound is not expected to hydrolyze in the environment. The phototransformation of [2,6-^{14}C]-labelled 4-amino-3,6-dichloropyridine-2- carboxylic acid (aminopyralid) was studied on a German silt loam soil for 44 days.

In the irradiated samples, the concentration of the parent compound decreased from 104.2% of the applied at day 0 to 69.3% of the applied amount at test termination. There were no major transformation products formed in the irradiated samples. The predicted environmental half-life on soil is 72.2 days. Photolysis on soil is not a significant route of transformation of aminopyralid in the environment.

The aqueous phototransformation of [2,6-^{14}C]-labelled 4-amino-3,6-dichloropyridine-2-carboxylic acid was studied in sterile aqueous buffer solutions at pH 5 at an initial concentration of 0.2 and 30 µg a.i./mL for 15 days. The concentration of the parent compound decreased from 96.8% at day 0 to 0% of the applied amount at day 2 post-treatment. The only two potentially major transformation products identified, but not quantified, in the irradiated samples were oxamic acid (CAS #471-47-6) and malonamic acid (CAS # 2345-56-4). These two products plus at least four more acid amides (2 or 3 carbons in length) together reached a maximum concentration of 68.8% of applied radioactivity by 12 days post-treatment and decreased to 65.7% of applied radioactivity at study termination. Aminopyralid is expected to undergo phototransformation in the upper layers of surface water on sunny days at 40° N latitude.

5.3 Biotransformation

In most aerobic soils, (Houston clay, Regent loam, Manning sandy loam and Holdrege silt loam) aminopyralid transforms relatively rapidly, having a half-life of 6–39 days (best fit). However, in a clay loam soil (Barnes from North Dakota), the transformation of the active was very slow, with a half-life of 330 days (533 days assuming that non-extractable residues were parent chemical); this difference from the other soils could not be explained by soil properties. The major route of transformation is mineralization to CO_2, while the formation of non-extractable residues is less important. Extractable residues in Houston clay, Regent loam, Manning sandy loam and Holdrege silt loam soils were low at study termination (1.1–3.7%), but were much higher in Barnes clay loam soil (41%). Non-extractable residues were low in Regent loam, Manning sandy loam and Holdrege silt loam soils (0–8%), 14% in Barnes clay loam soil and 24.3% in the clay soil. Evolved CO_2 accounted for only 27% of residues in Barnes clay loam soil, while it was 65–73% in the other four soils. No major transformation products were detected other than CO_2 and non-extractable residues in the five soils.

Under aerobic aquatic conditions, aminopyralid is essentially stable, having a first-order half-life of 866, 462 and 990 days in French, Italian and American water sediment systems, respectively. Emphasis is placed on the results from the French system, as the redox potential and oxygen content was the most appropriate of the three. The parent chemical was 82–90% extractable in the whole system of all three water sediment systems, and was found predominantly in the water layer (52%, 68% and 78.8% for the French, Italian and American systems, respectively). The distribution of the parent molecule after 101 days in sediment was 38.7%, 14.8% and 12% for the French, Italian and American systems, respectively. Non-extractable residues were low in all systems, ranging from 3.2–14.8%. Very little mineralization to CO_2 was observed in any system, ranging from 2–3%. Although all half-lives calculated exceed the duration of the study, it is evident that aminopyralid will be persistent in aerobic aquatic systems.

Aminopyralid is stable in anaerobic water sediment systems, and no transformation occurred in either of the North Dakota or Cuckney systems tested. The parent chemical was primarily detected in the water phase, with 69.5–71.7%. Concentrations of the parent compound in sediment reached 32–36.7%. Non-extractable residues were low at 0.7–2.4%. Very little mineralization was observed (< 1%). No major transformation products were produced.

In summary, aminopyralid underwent rapid microbial transformation in most, but not all (4/5) aerobic soils via mineralization. Aminopyralid is classified as non-persistent to slightly persistent in most soils (half-life of 6–39 days), but can be persistent in others (half-life of 330–533 days). It is persistent in aquatic systems under aerobic and anaerobic conditions. Having a high water solubility and low K_{ow}, it is partitioned mostly to the water phase in water/sediment systems and can be expected to accumulate in water (52–79%) and to a lesser extent in sediment (12–38.7%).

5.4 Mobility

Aminopyralid is not expected to volatilize from dry or moist surfaces under field conditions, based on the vapour pressure and the Henry's Law constant. Based on laboratory data, aminopyralid is expected to be mobile in soil. It is highly water soluble, is stable to hydrolysis and aquatic biotransformation and does not phototransform on soil. Aminopyralid is an anionic molecule that has a soil half-life of >2 weeks (except in 1 soil), a Henry's law constant below 10^{-2} atm × m^3/mol and organic carbon adsorption coefficient (K_{oc}) values below 50. All of these factors indicate that it has the potential to leach through the soil column and reach ground and surface water. Aminopyralid partitions mainly to the water phase in aquatic systems and to a lesser extent to sediment, which is in agreement with low K_{oc} values for soil adsorption.

5.5 Dissipation and Accumulation under Field Conditions

Terrestrial field dissipation of aminopyralid in Canadian field trials was studied in New Brunswick (Ecoregion 5.3, Atlantic Highlands), Ontario (Ecoregion 8.1, Mixed Wood Plains), Manitoba (Ecoregion 9.2, Temperate Prairies), Saskatchewan (Ecoregion 9.3, West Central Semiarid Prairies), and Alberta (Ecoregion 9.2, Temperate Prairies). An American site, in Montana, was also used (Ecoregion 9.3, West Central Semiarid Prairies). The target application rate was set at 120% of the seasonal maximum rate. Field dissipation was rapid, having dissipation time 50% (DT_{50}) values of 9–54 days, resulting in a classification of non-persistent to moderately persistent (DT_{50} < 6 months, Goring et al. 1975). The results of the field study are in good agreement with those of the aerobic soil laboratory study, except for one soil type, which resulted in a half-life of 330 days (or 533 days if it is assumed that non-extractable residues were parent chemical) under laboratory conditions.

The main route of dissipation in the field is thought to be primarily due to mineralization and to leaching. Aminopyralid was detected in the soil column with a LOQ of 1.5 ng/g almost exclusively in the top 15-cm layer in 3 of 5 soils, despite irrigation to achieve the 30-year average precipitation rate (which ranged from 98–154% of mean). In the Montana soil, it was detected in the 75- to 90-cm layer at a concentration of 9.4% of the applied amount; however, there was much higher than short-term average rain fall at this site on two occasions. These results indicate that movement through the soil profile can occur and may be expected under certain field conditions. Leachate water samples were not collected and, thus, the extent and depth to which aminopyralid can leach in soil is not fully characterized. However, leaching is expected to be mitigated by the low application rates, interception by ground cover and rapid biotransformation in soil. Residues remaining at the end of the growing season were 2.6–8.6%, except in Alberta (23.8%). Carryover one year post treatment is likely to be non-existent or may

be limited, as in the case of Alberta. Residues were not detectable after less than one year in three soils, while in the Ontario test site there was 2.1% carryover and in Alberta 22.4% carryover after one year. Accumulation in soil is not expected to occur because of rapid biotransformation and dissipation.

5.6 Bioaccumulation

A study was not submitted, as the parent chemical is a highly water soluble negatively charged molecule and has a very low log K_{ow} (0.2). Aminopyralid is not expected to bioconcentrate and a fish bioconcentration study is not triggered.

5.7 Summary of Fate and Behaviour in the Terrestrial Environment

Aminopyralid is resistant to hydrolysis, while it will photolise slowly on soil with a half-life of 72.2 days. Phototransformation is not relevant in the environment. It is not expected to volatilize from dry or moist surfaces under field conditions based on the vapour pressure and the Henry's Law constant. Because of aminopyralid's physical and chemical properties including high water solubility, low K_{oc} (<24) and a negative charge, mobility in soil is classified as "very high" according to McCall et al. (1981). In most soils, aminopyralid is non-persistent to slightly persistent (half-life of 6–39 days) under laboratory conditions, but can be persistent as evidenced in one soil (half-life of 330 days). Soil biotransformation results in mineralization to CO_2 (up to 73%), and relatively low levels of bound residues are produced (mostly less than14%, up to 25% in one soil). No major transformation products are formed other than CO_2 and bound residues in the terrestrial environment. Field dissipation is rapid with DT_{50} values ranging from 9–54 days, with a resulting classification of non-persistent to moderately persistent. Limited carryover occurs from one growing season to another (2.6–8.6%, 23.8% in Alberta soil), while little to no carryover of parent chemical occurs to one year postapplication (only 1 in 6 soils had more than 5% carryover after one year [22.4% in Alberta]). Leaching will be a factor in the field dissipation of aminopyralid and can reach a depth of 90 cm or more with significant rain events close to application time, having up to 10% of the active ingredient detected in soil at this depth. Groundwater and surface water exposure to aminopyralid may be expected due to its high solubility and low adsorption to soil. Leaching modelling results over 20 years predict detectable concentrations in groundwater and in surface water. Accumulation in the field should not occur due to rapid dissipation from soil.

5.8 Summary of Fate and Behaviour in the Aquatic Environment

Entry to aquatic systems can occur from spray drift, runoff and leaching in soil resulting in surface water recharge. Aminopyralid does not hydrolyze, but can be expected to phototransform in clear shallow water on sunny days based on the laboratory study. However, under environmental conditions, slower phototransformation is expected due to light interception by suspended matter and attenuation in deeper water as well as cloud cover. The two major phototransformation products identified in water were oxamic and malonamic acids, which, with other 2–3 carbon molecules (containing only C, N, H, O), accounted for 65% of the applied parent material. Aminopyralid is very persistent in the aquatic environment based on aerobic and anaerobic biotransformation studies and does not transform to any extent in either the water or

sediment phase. Therefore, no major transformation products were produced in aquatic systems. Under aerobic aquatic conditions, aminopyralid has a half-life of 462–990 days, while in anaerobic systems it is stable. The parent chemical partitions predominantly to the water phase (52–78.8% in aerobic and 69–72% in anaerobic systems). The distribution to sediment was 12–38.7% in aerobic and 32–37% in anaerobic systems. Non-extractable residues were low, ranging from 3.2–14.8%. Aminopyralid can accumulate in deep water in aquatic systems; however, entry to the aquatic environment should be limited based on its terrestrial fate and use pattern. Bioconcentration is not expected to occur due to a low Log K_{ow}.

5.9 Expected Environmental Concentrations

5.9.1 Soil

Aminopyralid is applied to wheat at 10 g a.i./ha, and to range and pasture and other non-crop lands at 120 g a.i./ha, once a year. Assuming a soil density of 1.5 g/cm^3, the following EECs were determined:

- wheat—0.0044 mg a.i./kg
- range and pasture—0.0533 mg a.i./kg

5.9.2 Aquatic Systems

Direct Application to Surface Water
The EEC of aminopyralid from a direct over spray of 30 cm deep water body is 0.04 mg a.i./L based on non-crop use rates, and 0.0033 mg a.i./L based on wheat use rates. (See Appendix III for tables).

Drinking Water
Estimated environmental concentrations (EECs) of aminopyralid in potential drinking water sources (groundwater and surface water) were estimated using computer simulation models. An overview of how EECs are estimated is provided in the PMRA's Science Policy Notice SPN2004-01, *Estimating the Water Component of a Dietary Exposure Assessment*. EECs of aminopyralid in groundwater were calculated using the Leaching Estimation and Chemistry Model (LEACHM), which simulates leaching through a layered soil profile over a multi-year period (20 years). The concentrations calculated using LEACHM are estimates of the flux, or movement, of pesticide into shallow groundwater (2-m or 5-m depth) with time. EECs of aminopyralid in surface water were calculated using the combined Pesticide Root Zone Model and Exposure Analysis Modeling System (PRZM/EXAMS), which simulate pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in two types of vulnerable drinking water sources, a small reservoir (57-year simulation) and a prairie dugout (81-year simulation).

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The Level 1 EEC estimate is expected to allow for future use expansion into other crops at this application rate. Appendix III, Table 5 lists the application information and main environmental fate characteristics used in the models. The models were run to simulate fate and transport of aminopyralid. Appendix III, Table 6 provides the EECs calculated in the Level 1 drinking water assessment.

5.9.3 Vegetation and Other Food Sources

The EECs of aminopyralid in vegetation and food sources were based on the maximum annual application rate of Aminopyralid Liquid Concentrate Herbicide (120 g a.i./ha). This did not account for any transformation of aminopyralid on the foliage. A direct overspray scenario using a nomogram developed by the USEPA from the data of Hoerger and Kenaga (1972), Kenaga (1973), and modified according to Fletcher et al. (1994) for use in ecological risk assessment (Urban and Cook 1986) was used (Appendix III, Table 7 and 8).

6.0 Effects on Non-target Species

6.1 Effects on Terrestrial Organisms

6.1.1 Invertebrates

Aminopyralid is not acutely toxic to earthworms. The 14-day LC_{50} was >1000 mg a.i./kg dw soil. The 14-day no observed effect concentration (NOEC) based on survival, sublethal effects and weight loss was 1000 mg a.i./kg dw soil. Similarly, bees are not sensitive by either contact or ingestion. The LD_{50} and NOEC was >100 and 100 µg a.i./bee, respectively for contact exposure and the LD_{50} and NOEC was > 117 and 117 µg a.i./bee for oral exposure. As a result, aminopyralid is categorized as relatively non-toxic to honeybees.

6.1.2 Birds

The acute oral LD_{50} was >2250 mg a.i./kg bw, the highest level tested, which categorizes aminopyralid as practically non-toxic to Northern bobwhite quail on an acute oral basis. Clinical signs of toxicity (the most sensitive endpoint) were observed in birds from all treatment levels. The no observed effect level (NOEL) for sublethal effects was 14 mg a.i./kg bw and the lowest observed effect level (LOEL) was 23 mg a.i./kg bw.

In the acute dietary toxicity study of aminopyralid in Northern bobwhite quail, no mortality was observed. The subsequent 5-day acute dietary LC_{50} was > 5556 mg a.i./kg diet, which categorizes aminopyralid as practically non-toxic to Northern bobwhite quail on an acute dietary basis. No clinical signs of toxicity or treatment-related effects on body weight or food consumption were observed. The NOEC was 5556 mg a.i./kg diet and the LOEC was >5556 mg a.i./kg diet. Mallard ducks were also not affected by aminopyralid in the diet. No mortality was observed during the study. The subsequent 5-day acute dietary LC_{50} was >5496 mg ai./kg diet, which categorizes aminopyralid as practically non-toxic to mallard duck on an acute dietary basis. The NOEC was 5496 mg a.i./kg diet, and the LOEC was >5496 mg a.i./kg diet.

The reproductive toxicity study of aminopyralid in Northern bobwhite quail revealed no difference in body weight or feed consumption for the parental generation and no treatment related adverse effects were observed in offspring. The NOEC of aminopyralid for the bobwhite quail based on the reproductive parameters is 2610 mg a.i./kg dw of diet, and the LOEC is > 2610 mg a.i./kg dw of diet, the highest tested concentration. In mallard duck, no significant treatment-related effects on any adult or offspring toxicity endpoint were observed. The NOEC and LOEC were 2623 and >2623 mg a.i./kg diet, respectively.

6.1.3 Mammals

Mammalian toxicity studies with rats and mice showed no acute toxicity and no adverse effects up to 1000 mg a.i./kg bw and in rabbits at 250–500 mg a.i./kg bw. The most sensitive endpoint for rats was the 90-day dietary NOAELs (6750 mg a.i./kg diet) and for mice 6520 mg a.i./kg diet. No oncogenicity or teratogenic effects were found in the mammalian studies, and neurotoxicity was also not observed.

Rat
In the 90 day dietary toxicity study, there were no adverse, treatment-related effects on mortality, and sublethal effects other than urine pH. The NOAEL was 14 100 mg a.i./kg diet (1000 mg/kg bw/day) for females and 6750 mg a.i./kg diet (500 mg/kg bw/day) for males, indicating differences in gender sensitivity. The LOAEL was not determined in females and was 13 100 mg a.i./kg diet (1000 mg/kg bw/day) for males.

In the multigeneration reproduction study, there were no treatment-related effects for parent animals on mortality, clinical signs, body weight and body-weight gain, food intake, reproductive function, reproductive parameters or histopathology. For parental toxicity, reproductive toxicity, and offspring toxicity, the LOAELs were not established as there were no adverse, treatment-related effects. The NOAELs were 15 400 ppm (1000 mg/kg bw/day).

Mouse
The 90-day dietary NOAEL was 6520 mg a.i./kg diet (1000 mg/kg bw/day) in males and females. No effects were observed on mortality, clinical signs, body weight, food intake, hematology, clinical chemistry, organ weight and gross pathology.

6.1.4 Vascular Plants

Vegetative vigour and seedling emergence were adversely affected (EC_{25}) in the most sensitive plant, soybean at 0.39 and 1.4 g aminopyralid/ha, respectively, rates which are only 0.32 and 1.16% of the seasonal label application rate. For seedling emergence, a 27.4% reduction in soybean dry shoot weight was observed at the LOEC of 0.93 g aminopyralid/ha. Vegetative vigour was also most sensitive in soybean, with a 30.5% reduction in shoot length at the LOEC of 0.93 g aminopyralid/ha. (See Appendix III for tables).

6.2 Effects on Aquatic Organisms

None of the aquatic organisms tested are acutely sensitive to aminopyralid. Acute toxicity to animal species is classified as practically non-toxic, while algae and vascular plants are somewhat susceptible to aminopyralid in laboratory studies, but only at concentrations higher than the EEC (water 0.04 mg a.i./L). Freshwater fish rainbow trout and bluegill sunfish were acutely insensitive to the highest test concentrations, but showed significant adverse effects in early life stage of fish (fathead minnows).

The most sensitive aquatic species, the fathead minnow, had hatchling survival reduced to 67.3% of control and growth was affected at 2.44 mg a.i./L (LOEC) with a NOEC of 1.36 mg a.i./L. The second most sensitive group of aquatic organisms were freshwater and marine algae, having NOECs of 6 to 13 mg a.i./L, respectively. The growth rate of the green alga *Pseudokirchneriella* was reduced by 50% at 30 mg a.i./L. This species had a NOEC of 23 mg a.i./L for all endpoints. Cell density was reduced by 99% at the LOEC of 46 mg a.i./L. The alga *Navicula* was slightly more sensitive with an NOEC of 6 mg a.i./L, while cell density was reduced by 28% at the LOEC of 12 mg a.i./L. The aquatic vascular plant *Lemna*, a monocot, had a low sensitivity to aminopyralid (EC_{50} > 88 mg a.i./L). The marine diatom *Skeletonema* showed a cell density reduction of 32% at the LOEC of 25 mg a.i./L, and had a NOEC of 13 mg a.i./L. Chronic and subchronic toxicity was also low. Freshwater invertebrates such as chironomids are not sensitive from exposure to the test chemical in sediment (28-day NOEC = 123 mg a.i./L) while for pelagic crustaceans such as *Daphnia magna*, chronic toxicity is very low and reproduction is not affected (21-day NOEC = 102 mg a.i./L). A summary of effects of aminopyralid on aquatic organisms is presented in Appendix III, Table 12.

6.2.1 Freshwater Invertebrates—*Daphnia magna*

In the 48-hour acute toxicity study of aminopyralid to the water flea, *Daphnia magna*, no immobilization or sublethal effects were observed in the 98.6 mg a.i./L treatment group. The 48-hour EC_{50} was >98.6 mg a.i./L, which categorizes aminopyralid as practically non-toxic to the water flea. The 48-hour NOEC and LOEC concentrations were 98.6 and >98.6 mg a.i./L, respectively.

In the chronic toxicity study to *Daphnia magna*, cumulative mortality was 0% in the treatment groups after 21 days of exposure. The 21-day LC/EC_{50} was estimated as >102 mg a.i./L The EC_{50} for reproduction was estimated as > 102 mg a.i./L . The LOEC was >102 mg a.i./L for all endpoints. The NOEC for mortality, reproduction and growth (length) were 102 mg a.i./L, the highest concentration tested.

6.2.2 Freshwater Benthic Invertebrates—Chironomids

In the 28-day chronic toxicity study of aminopyralid to a midge, *Chironomus riparius*, a significant reduction in mean percent emergence (the most sensitive endpoint) was observed at the 88 mg a.i./kg. Mean percent emergence was 94% for the control group, compared to 88, 86, 80, 75 and 0% at the sediment-exposures 17, 33, 88, 186 and 540 mg a.i./kg, respectively. The 28-day EC_{50}, based on sediment concentrations and midge emergence, was 229 mg a.i./kg. The NOEC for development rate was 88 mg a.i./kg . The NOEC for percent emergence was 33 mg a.i./kg (123 mg a.i./L initial measured concentration in overlying water).

6.2.3 Freshwater Fish

No mortality was observed in rainbow trout at 100 mg a.i./L after 96 hours. The LC_{50} was >100 mg a.i./L, which categorizes aminopyralid as practically non-toxic to juvenile rainbow trout. The NOEC and LOEC based on mortality were 100 and >100 mg a.i./L, respectively. In bluegill sunfish (*Lepomis macrochirus*), the LC_{50} was >100 mg a.i./L, which categorizes aminopyralid as practically non-toxic to juvenile bluegill sunfish. The NOEC and LOEC values based on the lack of mortality and sublethal effects were 100 and >100 mg a.i./L, respectively. The early life-stage of Fathead Minnow (*Pimphales promelas*) was two orders of magnitude more sensitive compared to other fish species. The NOEC for time-to-hatch and hatching success was 11.4 mg a.i./L. Survival of minnow larvae was statistically-reduced at the 2.44 mg a.i./L treatment level. The NOEC for larval survival was 1.36 mg a.i./L. Statistically significant treatment-related sublethal signs of toxicity were reported at 2.44 mg a.i./L. Sublethal effects included pale coloration, immobility, deformed/underdeveloped body and scoliosis. The NOEC for sublethal effects and growth was 1.36 mg a.i./L, the most sensitive aquatic endpoint.

6.2.4 Freshwater Green Algae and Vascular Plants

Navicula pelliculosa cell density and biomass were significantly reduced at 12, 23, 48 and 100 mg a.i./L, and the growth rates were significantly reduced at the 48 and 100 mg a.i./L. No other signs of toxicity were observed after 120 hours. For the cell density and biomass endpoints, the NOEC was 6.0 mg a.i./L. *Pseudokirchneriella subcapitata* showed inhibition in biomass of -6, 11, -9, 101 and 103% at 5.6, 12, 23, 46 and 94 mg a.i./L, respectively. All endpoints were significantly reduced at the 46 and 94 mg a.i./L treatment levels. No other signs of toxicity were observed after 96 hours. Growth rate was the most sensitive endpoint, with an EC_{50} of 30 mg a.i./L; the NOEC was 23mg a.i./L for all endpoints. Duckweed, *(Lemna gibba)* had a growth rate inhibition of 2, 4, 2, -2 and 2% at 5.2, 11, 21, 44 and 88 mg a.i./L, respectively. The growth rate percent inhibitions were 0, 8, 16, 2 and 12% at 5.2, 11, 21, 44 and 88 mg a.i./, respectively. The frond number endpoint was most sensitive; the EC_{50} was >88 mg a.i./L for all endpoints and the NOEC was 44 mg a.i./L.

6.2.5 Amphibians

Larvae of the Northern leopard frogs (*Rana pipiens*) were not sensitive to aminopyralid as no mortalities and sublethal effects were observed. The LC_{50} was >95.2 mg a.i./L, which categorizes aminopyralid as practically non-toxic. The NOEC and LOEC values based on mortality and sublethal effects were 95.2 and >95.2 mg a.i./L, respectively.

6.2.6 Marine Invertebrates

No mortalities or sublethal effects were seen in the saltwater mysid, *Americamysis bahia*. The 96-hour LC_{50} was > 100 mg a.i./L, which categorizes aminopyralid as practically non-toxic to the saltwater mysid. Based on mortality and sublethal effects, the NOEC and LOEC values were 100 and > 100 mg a.i./L, respectively. Eastern oyster (*Crassostrea virginica*) exhibited no mortalities or sublethal effects. Shell growth was inhibited by 12% in the 89 mg a.i./L treatment group. No statistically significant reductions in shell growth were identified. The NOEC is 89 mg a.i./L and the 96-hour EC_{50} are >89 mg a.i./L. Aminopyralid is classified as slightly toxic to the Eastern oyster.

6.2.7 Marine Fish

Sheepshead minnow (*Cyprinodon variegatus*) showed no mortalities or sublethal effects after a 96-hour exposure period. The LC_{50} was determined to be >120 mg a.i./L, which categorizes aminopyralid as practically non-toxic. The NOEC and LOEC values were determined to be 120 and >120 mg a.i./L, respectively.

6.2.8 Marine Algae

The marine diatom *Skeletonema costatum* was not acutely sensitive to aminopyralid, having an EC_{50} of 70 mg a.i./L for biomass, the most sensitive endpoint. The percent inhibitions for biomass were -15, 1, 32, 33 and 58% in the 6.2, 13, 25, 50 and 100 mg a.i./L treatment groups, respectively. The percent inhibitions for growth rates were 0, 2, 14, 15 and 26% in the 6.2, 13, 25, 50 and 100 mg a.i./L treatment groups, respectively. The growth rates and biomass were significantly reduced in the 25, 50 and 100 mg a.i./L treatment groups. The NOEC for growth rate and cell density were 13 and 100 mg a.i./L (the highest concentration tested), respectively, and the EC_{50} was >100 mg a.i./L for both endpoints. (See Appendix III for tables).

6.3 Effects on Biological Methods of Sewage Treatment

Not required.

6.4 Risk Characterization

Risk assessment integrates the environmental 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 risk quotient (RQ) method, which is the ratio of the expected environmental concentration (EEC) divided by

the toxicity endpoint. The EECs used to calculate the RQ are described in Section 5.10, and generally the toxicity endpoint used is the no observed effect concentration or level (NOEC or NOEL; if a NOEC or NOEL is not available, one-tenth of the LC_{50} or LD_{50} is used to approximate a no effect level) or an EC_{25} (for terrestrial plants). Risks are then classified based on the scheme presented in Appendix III, Table 13.

In addition to the RQ, an indicator of risk in birds and mammals is the number of feeding days on contaminated food required to reach the toxicity endpoint of concern (acute oral toxicity NOEL). Risk based on the number of feeding days is classified as follows: if the number of feeding days is less than one, then there is a risk, and conversely, if the number of feeding days is greater than or equal to one day then there is negligible risk (Days < 1 = Risk; Days $\geq$1 = Negligible risk).

6.4.1 Environmental Behaviour

In the terrestrial environment, aminopyralid is non-persistent to moderately persistent and undergoes aerobic soil biotransformation. Dissipation in soil occurs mainly through microbial mineralization, while binding to organic matter as non-extractable residues is generally low. Leaching can also be expected to be a mode of transport in the environment if application coincides with precipitation. Adsorption K_{oc} values indicate that soil binding is low and mobility, based on laboratory data classification, may be expected to be high. Modelling of groundwater concentrations using LEACHM indicates it will reach groundwater and modelling with PRZM/EXAMS indicates that it will reach surface water by runoff. In field studies, the parent chemical was detected almost exclusively in the top 15-cm layer in three soils, but was detected in one study up to the lowest sampling depth of 90 cm. Thus, groundwater contamination may occur under field conditions. However, because of the low application rate of 10–120 g a.i./ha once a year, a Canadian use pattern mostly on grass/plant covered areas (wheat use is restricted to the prairies and the crop is treated when it is well emerged) and rapid soil biotransformation, groundwater contamination may be offset. No major transformation products other than CO_2 and bound residues are formed in soils. Accumulation in soil is not expected to occur and carryover to the next year will be negligible, but up to 23.8% of the active ingredient has been observed at the end of the growing season in one study.

Susceptible non-target plants such as broadleaf and woody plants, including crops, growing in fields adjacent to sites where aminopyralid is used may be exposed. The parent chemical can be taken up by plant surfaces and from the soil. Plant toxicity from soil exposure in subsequent seasons is not of concern because of the low carryover rate in most soils.

Aminopyralid can enter aquatic systems by spray drift, runoff and leaching. In water, no transformation occurs from biotic or abiotic sources other than phototransformation. Phototransformation leads to the formation of the expected major transformation products oxamic and malonamic acids, and other 2–3 carbon molecules containing only C, N, O and H. As this herbicide is very persistent in aquatic systems and partitions mostly to the water phase, it has the potential to accumulate in the aquatic environment especially under anaerobic conditions. Although significant accumulation in aquatic environments is not expected, fish, invertebrates, algae, macrophytes and benthic organisms may be exposed to aminopyralid. In summary,

aminopyralid dissipates relatively rapidly in the field. It is persistent in the aquatic environment, but it is not expected to accumulate significantly based on water modelling.

6.4.2 Terrestrial Organisms

6.4.2.1 Earthworms

The EEC in soil was estimated using the maximum label rate for use on range, pasture and non-crop lands (120 g a.i./ha) (see Section 5.9.1) The EEC in soil for aminopyralid was 0.0533 mg a.i./kg soil. The earthworm 14-day acute NOEC was > 1000 mg a.i./kg dw soil. The risk quotient is (EEC/NOEC) << 0.1. Therefore, aminopyralid poses a negligible risk to earthworms at the proposed application rates.

6.4.2.2 Honeybees

The acute oral and contact LD_{50} values for aminopyralid are >100 and >117µg a.i./bee, respectively. Aminopyralid is relatively non-toxic to bees on both an acute contact and oral basis according to the classification system of Atkins (1981) (if LD_{50} >11 µg/bee). The LD_{50} (µg/bee) can be converted to the equivalent application rate in kilogram per hectare by multiplying µg/bee by 1.12 (Atkins 1981). Therefore, the field LD_{50}s range from >112 to >131 kg a.i./ha, which is significantly higher than the proposed application rate of 0.120 kg a.i./ha.

6.4.2.3 Predators and Parasites

Not required for use pattern.

6.4.2.4 Birds

Wild birds will be exposed to aminopyralid in sprayed food items including vegetation, insects, seeds, etc. Acute toxicity was not observed in the bobwhite quail oral/dietary and mallard duck dietary studies. Aminopyralid is classified as practically non-toxic to these birds on an acute basis. No reproductive effects were seen in bobwhite quail. Based on a diet of 30% small insects, 15% forage crops, and 55% grain and seeds and the maximum seasonal application rate of 120 g a.i./ha (rangeland and pasture uses), the EEC of aminopyralid in the bobwhite quail's diet is 21.02 mg a.i./kg dw. For mallard duck, having a diet of 30% large insects and 70% grain and seeds, the EEC in the diet is 4.06 mg a.i./kg dw (Appendix III, Table 5 and 6).

The acute oral toxicity study with bobwhite quail determined that the reported LD_{50} and NOEL (sublethal effects such as loss of coordination) values were >2250 and 14 mg a.i./kg bw, respectively, while the LOEC was 23 mg a.i./kg bw. The mean body weight per individual (BWI) of bobwhite quail in the control treatment was 0.212 kg/individual, while the mean food consumption (FC) for males and females was 0.024 kg dw diet/individual/day. The daily intake (DI = FC × EEC) is, therefore, 0.5 mg a.i/individual/day. When expressed on a per individual basis, the $LD_{50(individual)}$ (LD_{50} × BWI) was 477 mg a.i/individual, and the $NOEL_{(individual)}$ (NOEL × BWI) was 2.97 mg a.i./individual. Based on the dietary intake and the $LD_{50(individual)}$, it would take a bobwhite quail greater than 954 continuous days of feeding to attain the dose

equivalent to the LD_{50} as determined for the laboratory population. Similarly, based on the dietary intake and the $NOEL_{(individual)}$, the number of days of continuous intake by a bobwhite quail to attain a dose equivalent to the NOEL derived from the laboratory population is 5.9 days. Therefore, aminopyralid does not present an acute risk (risk of mortality and sublethal effects is negligible) to the bobwhite quail at the proposed application rates.

Acute dietary studies with bobwhite quail indicated that the NOEC for mortality and sublethal effects (5556 mg a.i./kg dw of diet) was greater than the EECs (21.02 mg a.i./kg dw.). Dietary studies with mallard duck produced an NOEC of 5496 mg a.i./kg dw of diet, indicating that they are equally non-sensitive to this herbicide. Reproductive endpoints were not significantly affected from exposure to aminopyralid in either the bobwhite quail or mallard duck, having NOECs of 2610 and 2623 mg a.i./kg dw of diet, respectively. The acute dietary and chronic reproductive risk was determined as the risk quotient (RQ = EEC/NOEC), which was <0.1 for both mallard duck and bobwhite quail in all cases, indicating that the acute dietary and chronic reproductive risk to birds is negligible.

Aminopyralid can be expected to pose negligible dietary and reproductive risk (RQ < 0.1) to wild birds consuming similar proportions of contaminated feed to bobwhite quail and mallard duck when aminopyralid is applied at the maximum rate.

6.4.2.5 Small Wild Mammals

Wild mammals such as rats, mice and rabbits could be exposed to aminopyralid residues as a result of consumption of sprayed vegetation and/or contaminated prey. The rat diet consists of approximately 70% short grass, 20% grain/seed and 10% large insects. Therefore, the EEC in the rat diet is 60.54 mg a.i./kg dw diet.

The acute oral risk to rats was determined based on the number of feeding days required to reach the toxicity endpoints (LD_{50} and NOAEL). The LD_{50} and NOAEL were >5000 mg/kg and 500 mg/kg bw, respectively (NOAEL was estimated as 1/10th the LD_{50}). The default values were used for rat food consumption, 0.06 kg dw diet/individual/day, and for body weight per individual (BWI), 0.35 kg/individual. The daily intake (DI = FC × EEC) was, therefore, 3.63 mg a.i./individual/day for crop and turf uses, respectively, which is equivalent to 10.38 mg a.i./kg bw/day. When expressed on a per individual basis, the $LD_{50(individual)}$ (LD_{50} × BWI) was 1750 mg a.i/individual, and the $NOAEL_{(individual)}$ (NOAEL × BWI) was 175 mg a.i./individual. Based on the dietary intake and the $LD_{50(individual)}$, it would take a rat greater than 482 continuous days of feeding to attain the dose equivalent to the LD_{50} as determined for the laboratory population. Based on the dietary intake and the $NOAEC_{(individual)}$, it would take a rat greater than 48.2 continuous days of feeding to attain the dose equivalent to the NOAEC as determined for the laboratory population. Therefore, aminopyralid presents a negligible risk to the rat at the proposed maximum application rate.

The dietary risk to rats was assessed based on the 90-day dietary NOAEC of 6750 mg/kg dw diet. Risk to rat on a short-term dietary basis was estimated as negligible (EEC/NOAEC = 60.54/6750 = 0.0089). Dietary risk to mice was assessed based on the 90-day dietary NOAEC of 6520 mg/kg dw diet. The shorter term dietary risk to mice was estimated as negligible (EEC/NOAEC = 60.18/6520 = 0.009).

The reproductive risk to small mammals was assessed based on the rat multigeneration reproductive study (NOAEC parent, offspring and reproduction: 15 400 mg/kg dw diet). Risk to the parents, offspring and reproduction was estimated as negligible (EEC/NOAEC = 60.54/15 400 = 0.0039). This indicates that exposure of small mammals to aminopyralid contaminated food is expected to pose a negligible acute and chronic reproductive risk.

6.4.2.6 Terrestrial Vascular Plants

Toxicity to plants was observed in both seedling emergence and vegetative vigour studies. The most sensitive species in both of these studies was the dicot soybean, while onion was the most sensitive monocot. For seedling emergence, the EC_{25} for soybean fresh shoot weight was 1.4 g aminopyralid/ha. The EC_{25} for onion was 15 g aminopyralid/ha, indicating an order of magnitude lower toxicity in monocots. Based on the proposed application rate of 120 g aminopyralid/ha, the RQ (EEC/EC_{25}) for seedling emergence was 85.7 and 8 for soybean and onion, respectively, indicating a high risk to dicots and a moderate risk to monocot terrestrial plants.

In the vegetative vigour study, the EC_{25} for soybean fresh shoot length was 0.39 g aminopyralid/ha. The EC_{25} for onion was 27.5 g aminopyralid/ha, indicating close to two orders of magnitude higher toxicity in dicots. Based on the proposed application rate (EEC) of 120 g aminopyralid/ha, the RQ (EEC/EC_{25}) for vegetative vigour was 308 and 4.4 for soybean and onion, respectively, indicating a very high risk to dicots and a moderate risk to monocot terrestrial plants. Therefore, non-target terrestrials plants (especially dicot plants) in or near treated areas will be adversely affected if mitigative measure are not taken.

6.4.2.7 Summary of Risk to Terrestrial Organisms

The environmental risk assessment of the new herbicide active ingredient aminopyralid and associated end-use product Aminopyralid Liquid Concentrate Herbicide at the proposed maximum application rate of 120 g a.i./ha has indicated a negligible risk to earthworms, birds and small wild mammals and a very high to moderate risk to vascular plants. Aminopyralid is relatively non-toxic to adult honeybees. Because of the very high toxicity of and exposure to aminopyralid in or near treated areas, susceptible non-target plant species are at risk; as such, mitigative measures must be taken to minimize adverse effects on plant populations. Risk mitigation is discussed in Section 6.5.

The risk characterization to terrestrial organisms is summarized in Appendix III, Table 14.

6.4.3 Aquatic Organisms

6.4.3.1 Freshwater

Invertebrates
The freshwater crustacean invertebrate *Daphnia magna* and benthic invertebrate *Chironomus riparius* were not sensitive to aminopyralid either acutely or chronically. The NOECs were 98.6 and 123 mg a.i./L for these species. Risk was calculated based on the direct overspray of a 30-cm deep water body at the maximum application rate of 120 g a.i./ha, resulting in an EEC of 0.04 mg a.i./L. The acute and chronic risk quotients (EEC/NOEC) were << 0.1; therefore, the risk from the use of aminopyralid at the maximum rate is estimated to be negligible to freshwater invertebrates.

Fish and Amphibians
Rainbow trout and bluegill sunfish survival was not affected by aminopyralid at 100 mg a.i./L, although 7% of rainbow trout exhibited loss of equilibrium. This level of effect is considered to be low and within the acceptable range in the control group; therefore, this is not considered a biologically significant effect, and the NOEC is 100 mg a.i./L. The acute risk quotients were << 0.1. The early life-stage of fathead minnow was the most sensitive aquatic endpoint determined. The 32-day NOEC for growth, survival and other sublethal effects was 1.36 mg a.i./L, while the LOEC was 2.44 mg a.i./L. The subchronic risk quotient (EEC/NOEC) for fathead minnow hatchlings was 0.029. Therefore, the risk from the use of aminopyralid at the maximum rate is estimated to be negligible to freshwater fish. Aminopyralid was not acutely toxic to the tadpoles of the leopard frog (NOEC = 95.2 mg a.i./L). The RQ was << 0.1; thus, the risk to amphibians is expected to be negligible.

Aquatic Plants
Algae and the vascular plant *Lemna* showed moderate sensitivity to aminopyralid. As these aquatic plant species are not dicots, they are not very susceptible to this synthetic auxin herbicide. The NOECs ranged from 6 to 13 mg a.i./L for algae and was 44 mg a.i./L for *Lemna*. Therefore, the risk from the use of aminopyralid at the maximum rate is estimated to be negligible to algae and floating aquatic plants (RQ = 0.07–0.009). However, toxicity studies with rooted dicot aquatic plant species were not conducted, and the risk to these species is not known. Based on the high toxicity observed in terrestrial dicot plants, it is possible that aquatic dicots would be similarly sensitive to aminopyralid. Examples of aquatic plants that may be adversely affected by concentrations less than the maximum application rate include dicots such as water lily and water milfoil as well as other rooted plants that can be emergent or submerged. These plants play a vital role in aquatic environments in providing food and shelter for fish, invertebrates and water fowl among others. Because of the lack of data on rooted aquatic plants and associated uncertainty in the risk assessment, mitigative measures to reduce exposure of aquatic environments to aminopyralid are recommended (Section 6.5).

6.4.3.2 Marine

Aminopyralid was slightly toxic to practically non-toxic to the marine invertebrates Eastern oyster and mysid shrimp and to the marine fish sheepshead minnow (NOECs = 89, 100 and 120 mg a.i./L, respectively). The diatom *Skeletonema sp.* exhibited low acute sensitivity, having an NOEC of 13 mg a.i./L. The RQ for all of the marine species tested were << 0.1, and the risk to these organisms from the use of aminopyralid at the maximum rate is expected to be negligible.

6.4.3.3 Summary of Risk to Aquatic Organisms

The risk characterization to aquatic organisms is presented in Appendix III, Table 15. The aquatic risk assessment determined that there is negligible risk to freshwater and marine invertebrates, fish and algae from the proposed uses and use rate of Aminopyralid Liquid Concentrate Herbicide. The risk to potentially susceptible aquatic plants such as submerged or emergent dicots and monocots is unknown as no data are available. These plants are an important part of the aquatic ecosystem, providing food and shelter for many species both aquatic and terrestrial. Aquatic dicot and monocot rooted plants may be susceptible to aminopyralid based on studies with terrestrial plants (high to very high risk). Therefore, in lieu of new data requirements, it is recommended that mitigative measures similar to those for terrestrial habitats (i.e. use of buffer zones) be taken.

6.5 Risk Mitigation

An assessment of the environmental risk associated with the use of aminopyralid and the end-use product, Aminopyralid Liquid Concentrate Herbicide, at the maximum application rate of 120 g a.i./ha has been conducted. Aminopyralid Liquid Concentrate Herbicide is expected to pose a risk to terrestrial vascular plants and may be expected to pose a risk to aquatic rooted vascular plants.

6.5.1 Non-Target Organisms

Mitigative measures to reduce non-target plant toxicity include observing buffer zones (for aerial and ground application to range and pasture lands and for ground application to wheat) and using spray nozzles that produce coarse spray droplets to minimize drift. As the risk to rooted aquatic plants is not known, a precautionary statement to protect both terrestrial and aquatic plants is recommended. The following statement is recommended for addition to the ENVIRONMENTAL HAZARDS section of the label to mitigate risk to terrestrial and aquatic plants.

> TOXIC to terrestrial and aquatic plants. Observe terrestrial buffer zones specified under DIRECTIONS FOR USE.

Buffer zones to protect sensitive terrestrial and aquatic plants from spray drift are recommended to mitigate risk. Buffer zones were determined based on the proposed application rate of 10 and 120 g a.i./ha, and the toxicity to the most sensitive terrestrial plant species (soybean EC_{25} = 0.39 g a.i./ha). The following statement and buffer zones are recommended for the protection of terrestrial and aquatic habitats.

> The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of non-target sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows and shrublands), aquatic habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Ground Application Buffer Zones

Method of Application	Crop	Buffer Zone (metres) Required for the Protection of Terrestrial and Aquatic Habitat
Field sprayer*	Wheat	2
	Rangeland, pasture, industrial and other non-crop areas	10

* For field sprayers, buffer zones can be reduced by 70% when using shrouds or 30% when using cones

Aerial Application Buffer Zones

Spray Quality	Buffer Zone (metres) Required for the Protection of Terrestrial and Aquatic Habitat:	
	Aircraft Type	
	Fixed-Wing Aircraft	Rotary-Wing Aircraft
ASAE Coarse (VMD = 385.22 µm)	175	150
ASAE Coarse - Very Coarse (VMD = 439.39 µm)	125	100
ASAE Very Coarse (VMD = 477.94 µm)	100	90
ASAE Very Coarse - Extremely Coarse (VMD = 521.38 µm)	80	70

The following text must also be added to DIRECTIONS FOR USE:

> Field sprayer application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply with spray droplets smaller than the ASAE coarse classification.
>
> Aerial application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply when wind speed is greater than 16 km/h at flying height at the site of application. DO NOT apply with spray droplets smaller than the ASAE coarse classification.

The following statement is recommended for addition to the DIRECTIONS FOR USE section of the label.

> DO NOT apply this product directly to fresh water habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands), estuaries or marine habitats. DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

6.5.2 Leaching and Surface Runoff

The parent chemical aminopyralid has the potential to leach to groundwater and enter surface water based on its characteristics, including very high soil mobility and water solubility. Modelling results indicated the parent chemical may leach to shallow groundwater (Section 5.0). Aminopyralid leached to a maximum soil depth of 75 cm in Ontario and it leached to 90 cm after significant rain events in Montana at 7- to 28-days after application. In New Brunswick, Alberta and Saskatchewan, soil plots augmented with irrigation to bring precipitation levels to the 30-year average; however, the parent chemical was mostly detected in the 0- to 15-cm layer. It is possible that residue concentrations in field soil core samples did not accurately reflect the degree of leaching of aminopyralid, as it is highly soluble and may have leached beyond the maximum depth sampled. This may have occurred only in the Ontario and Montana soils, where, within the first 14 days after application, parent chemical residues were distributed deep into the soil column, while 23–34% of the parent chemical was not accounted for. Some of this loss would have been due to microbial transformation, but some may have been due to leaching, given the short time period. Because leaching and surface runoff may be expected to occur if application is closely followed by significant rain fall, there are precautionary measures that should be included on product labels to minimize the risk of aquatic contamination.

The following precautionary measures are recommended to be included in the DIRECTIONS FOR USE section of the label:

> To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to, heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g., soils that are compacted or fine textured such as clay). To reduce leaching and runoff, avoid application of this product when heavy rain is forecast. Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body. The use of this product may result in contamination of groundwater particularly in areas where soils are permeable (e.g., sandy soil) and/or the depth to the water table is shallow.

6.6 Data Requirements

Aquatic plants such as algae and duckweed are not sensitive to aminopyralid. Rooted aquatic macrophytes may be sensitive to aminopyralid based on the results of the terrestrial plant studies. At this time, no information is available to the PMRA on the sensitivity of rooted aquatic macrophytes. It was demonstrated that the aquatic macrophyte *Lemna*, a monocot species, was not sensitive (RQ < 0.1), which was expected as aminopyralid is specifically active against broadleaf dicot plants. Emergent and submerged dicot macrophytes are expected to be susceptible to aminopyralid based on the mode of action of this herbicide and the high degree of toxicity observed in terrestrial dicot vascular plants. Therefore, toxicity studies with rooted aquatic macrophytes such as the emergent plant nodding smartweed (*Polygonum muhlenberg*) and the submerged dicot water milfoil (*Myriophyllum sibiricum*) would more accurately characterize the risk posed by aminopyralid to the aquatic plant community. In the absence of this information, aquatic buffer zones to protect rooted macrophytes will be based on the terrestrial plant species.

7.0 Efficacy

7.1.1 Intended Use

Aminopyralid is formulated in one end-use product, Aminopyralid Liquid Concentrate Herbicide, with a guarantee of 240 g a.i./L. Aminopyralid Liquid Concentrate Herbicide is a contact and residual acting herbicide for use as follows:

- rangeland, pastures, industrial and other non-crop areas in Canada; and
- spring and durum wheat in the brown soil zone region of Western Canada.

7.1.2 Mode of Action

Aminopyralid is classified as a pyridine carboxylic acid (Group 4). As with all pyridine group herbicides, aminopyralid is a growth regulator herbicide that possesses auxin-like qualities causing uncontrolled cell division and growth usually in meristematic regions. Aminopyralid is readily absorbed by plant foliage and roots as well; it translocates in both the xylem and phloem and accumulates in meristematic areas. It results in cell elongation and tissue proliferation, followed by chlorosis, which progresses into necrosis within a few days, followed by plant death within one to six weeks after application. Injury symptoms are most obvious on newly developing leaves. Like many other herbicides in this group, aminopyralid is effective on perennial and annual broadleaf weeds.

7.2 Effectiveness Against Pest

7.2.1 Aminopyralid in Rangeland, Pasture, Industrial and Other Non-crop Areas

The performance of Aminopyralid Liquid Concentrate Herbicide applied as an alone treatment at 60, 70, 90 and 120 g a.i./ha in rangeland, pasture, industrial and non-crop areas was assessed in a total of 74 Canadian trials conducted in Alberta, Manitoba, Saskatchewan, Ontario and British Columbia as well as 4 American trials conducted in Iowa, Missouri, Washington (state), and Montana over a 3-year period (2001, 2002 and 2003). Adequate data were provided to establish the lowest effective rate for the alone treatment of Aminopyralid Liquid Concentrate Herbicide and support weed claims as presented in Table 7.2.1.1.

Table 7.2.1.1 Supported Weed Control/Suppression Claims for Aminopyralid Liquid Concentrate Herbicide Alone Treatment

Rate (g a.i./ha)	Supported Weed Claims	
	Season Long Control	Suppression
60	—	Canada thistle, spotted knapweed
70	Canada thistle, spotted knapweed	Canada goldenrod, scentless chamomile
90	Weeds listed above plus scentless chamomile	Absinth wormwood, Canada goldenrod
120	Weeds listed above plus absinth wormwood	Common tansy, dandelion, Canada goldenrod

7.2.2 Aminopyralid + 2,4-D Amine in Rangeland, Pasture, Industrial and Other Non-crop Areas

The performance of Aminopyralid Liquid Concentrate Herbicide + 2,4-D amine tankmix was also assessed in those trials. Adequate data were provided to support weed claims for aminopyralid + 2,4-D amine tankmix as presented in Table 7.2.2.1.

Table 7.2.2.1 Supported Weed Control Claims for Aminopyralid Liquid Concentrate Herbicide + 2,4-D Amine Tankmix

Rate (g a.i./ha)	Supported Weed Claims
70 + 840	Control of annual sowthistle, blue bur, burdock, cocklebur, common plantain, flixweed, goat's beard, prickly lettuce, ragweeds, stinging nettle, sweet clover, curled dock, hawkweed, peppergrass, and season long control of Canada thistle, spotted knapweed, scentless chamomile, Canada goldenrod, and top growth control of blue lettuce, bull thistle, buttercup, gum weed, hoary cress, perennial sowthistle
90 + 1080	All weeds listed above plus season long control of absinth wormwood and dandelion
120 + 1440	All weeds listed above plus season long control of western snowberry and common tansy

7.2.3 Aminopyralid in Spring and Durum Wheat in the Brown Soil Zone Region of Western Canada

The performance of Aminopyralid Liquid Concentrate Herbicide applied as an alone treatment at 10 g a.i./ha in spring and durum wheat was assessed in 10 Canadian trials conducted in Alberta and Saskatchewan and 7 American trials conducted in North Dakota and Montana over a 2-year period (2002 and 2003). Adequate data were provided to support the suppression of wild buckwheat for the alone treatment of Aminopyralid Liquid Concentrate Herbicide at 10 g a.i./ha.

7.2.4 Aminopyralid Liquid Concentrate Herbicide + Starane Herbicide in Spring and Durum Wheat in the Brown Soil Zone Region of Western Canada

The performance of Aminopyralid Liquid Concentrate Herbicide + Starane Herbicide tankmix was also assessed in those trials. Adequate data were provided to support control claims of wild buckwheat, cleavers, kochia, round-leaved mallow and volunteer flax for Aminopyralid Liquid Concentrate Herbicide at 10 g a.i./ha + Starane Herbicide at 144 g a.i./ha.

7.3 Phytotoxicity to Target Plants or Target Plant Products

7.3.1 Aminopyralid in Rangeland and Pastures

Phytotoxicity of various forage grasses to the maximum application rate of Aminopyralid Liquid Concentrate Herbicide at 120 g a.i./ha and twice this rate were evaluated in a total of 69 Canadian field trials conducted in British Columbia, Alberta, Saskatchewan, Manitoba and Ontario over a 2-year period (2002 and 2003). Herbicide treatments were applied on actively growing forage grasses from the 3-leaf stage to the pre-heading stage. The forage grass species—including crested wheatgrass, meadow bromegrass, intermediate wheatgrass, smooth bromegrass, orchardgrass, tall fescue, creeping red fescue, perennial ryegrass, timothy grass, kentucky bluegrass, blue grass species and/or wheatgrass—were planted either separately or in mixed sward. Crop ratings of visual injury, chlorosis and necrosis, epinasty growth and growth inhibition of forage grasses to the alone treatment of Aminopyralid Liquid Concentrate Herbicide are acceptable.

Forage grass biomass yield reported confirms the tolerance claim for forage grasses in pasture and rangeland with the application of Aminopyralid.

7.3.2 Aminopyralid + 2,4-D Amine in Rangeland and Pastures

Phytotoxicity of the forage grasses to Aminopyralid Liquid Concentrate Herbicide + 2,4-D amine tankmix at the maximum application rate of 120 + 1440 g a.i./ha and twice this rate was also evaluated in the forage trials. Crop ratings of visual injury, chlorosis and necrosis, epinasty growth and growth inhibition of forage grasses to Aminopyralid Liquid Concentrate Herbicide + 2,4-D amine tankmix are acceptable.

Forage grass biomass yield reported confirms the tolerance claim for forage grasses in pasture and rangeland with the application of Aminopyralid Liquid Concentrate Herbicide + 2,4-D amine.

7.3.3 Aminopyralid in Spring Wheat

Phytotoxicity of spring wheat to an alone treatment of Aminopyralid Liquid Concentrate Herbicide at 10 g a.i./ha and the higher rates of 15, 20, 30 and 40 g a.i./ha were evaluated in a total of 12 Canadian field trials conducted in Alberta and Saskatchewan and 12 American trials conducted in North Dakota and Montana over a 2-year period (2002 and 2003). Herbicide treatments were applied from the 3- to 6-leaf stage of 10 spring wheat varieties (Abbey, AC Barrie, AC Crystal, Briggs, Intrepid, McNeal, Norpro, Splendor, Teal and Utopia). Crop ratings of visual injury, chlorosis and necrosis, epinasty growth and growth inhibition of spring wheat to the alone treatment of Aminopyralid Liquid Concentrate Herbicide are acceptable.

Yield of spring wheat reported confirms the tolerance claim for spring wheat in the brown soil zone region of western Canada with the application of Aminopyralid Liquid Concentrate Herbicide.

7.3.4 Aminopyralid Liquid Concentrate Herbicide + Starane Herbicide in Spring Wheat

Phytotoxicity of spring wheat to Aminopyralid Liquid Concentrate Herbicide + Starane Herbicide tankmix at the maximum application rate of 10 + 144 g a.i./ha and higher rates, including twice this rate, were also evaluated in the spring wheat trials. Crop ratings of visual injury, chlorosis and necrosis, epinasty growth and growth inhibition of spring wheat to Aminopyralid Liquid Concentrate Herbicide + Starane Herbicide tankmix are acceptable.

Yield of spring wheat reported confirms the tolerance claim for spring wheat in the brown soil zone region of western Canada with the application of Aminopyralid Liquid Concentrate Herbicide + Starane Herbicide.

7.3.5 Aminopyralid in Durum Wheat

Phytotoxicity of durum wheat to an alone treatment of Aminopyralid Liquid Concentrate Herbicide at 10 g a.i./ha and the higher rates of 15, 20, 30 and 40 g a.i./ha were evaluated in 10 Canadian field trials conducted in Alberta and Saskatchewan and 13 American trials conducted in North Dakota and Montana over a 2-year period (2002 and 2003). Herbicide treatments were applied from the 2- to 6-leaf stage of 11 durum wheat varieties (Abbey, Avonlea, Belzer, Kyle, Lebsock, Mountrail, Navigator, Pierce, Penville, Rugby, and Utopia). Crop ratings of visual injury, chlorosis and necrosis, epinasty growth and growth inhibition of durum wheat to the alone treatment of Aminopyralid Liquid Concentrate Herbicide are acceptable.

Yield of durum wheat reported confirms the tolerance claim for durum wheat in the brown soil zone region of western Canada with the application of Aminopyralid.

7.3.6 Aminopyralid Liquid Concentrate Herbicide + Starane Herbicide in Durum Wheat

Phytotoxicity of durum wheat to Aminopyralid Liquid Concentrate Herbicide + Starane Herbicide at the maximum application rate of 10 + 144 g a.i./ha and higher rates, including twice this rate, was also evaluated in those durum wheat trials. Crop ratings of visual injury, chlorosis and necrosis, epinasty growth and growth inhibition of durum wheat to Aminopyralid Liquid Concentrate Herbicide + Starane Herbicide are acceptable.

Yield of durum wheat reported confirms the tolerance claim for durum wheat in the brown soil zone region of western Canada with the application of Aminopyralid + Starane Herbicide.

7.4 Impact on Succeeding Crops

7.4.1 Spring Wheat

Crop visual injury and grain yield of spring wheat planted as a rotational crop in the year following application of Aminopyralid Liquid Concentrate Herbicide at 10 g a.i./ha and the higher rates of 15, 20, 30, 40 and 60 g a.i./ha was assessed in 5 trials conducted in Alberta and Saskatchewan over a 2-year period (2001 and 2002). The herbicides were applied as postemergence treatments to spring wheat in all five trials. Spring wheat was planted as a rotational crop 10 to 11 months after herbicide treatments.

The visual crop injury and grain yield data provided support the claim of spring wheat as a rotational crop with a minimum 10-month recropping interval.

7.4.2 Canola

Crop visual injury and grain yield of canola planted as a rotational crop in the year following application of Aminopyralid Liquid Concentrate Herbicide at the proposed rate of 10 g a.i./ha and at the higher rates of 15, 20, 30, 40 and 60 g a.i./ha was assessed in 6 trials conducted in Alberta, Saskatchewan and North Dakota over a 2-year period (2001 and 2002). The herbicides were applied as postemergence treatments to spring wheat or bare soil. Canola was planted as a rotational crop from 10 to 11 months after herbicide treatments.

The crop visual injury and seed yield data provided support the claim of canola as a rotational crop with a minimum 10 month recropping interval.

7.5 Economics

Invasive plants produce a wide range of detrimental impacts on the agriculture industry. Many act as hosts for insects and crop disease. They reduce crop quality and market opportunities, and similarly decrease farm income by reducing yields by an average of 10–15 percent (Fraser Basin Council [N.D.]). Across Canada, more than 26 million hectares are set aside annually for ruminate grazing and forage production. Of this, about 16 million hectares are native pasture, 4 million hectares are tame or seeded pasture, and 6 million hectares are cultivated tame hay and fodder crops.

Aminopyralid Liquid Concentrate Herbicide may be used in wheat, rangeland, pasture and industrial use patterns to control a number of annual and perennial broadleaf weeds, including noxious/invasive weeds and woody plants in rangeland and pastures.

7.6 Sustainability

7.6.1 Survey of Alternatives

7.6.1.1 Non-chemical Control Practices

Prevention
Human activity is a major cause of invasive, noxious plant spread. As a result, prevention is an important and inexpensive management program component for noxious and invasive plants.

Mechanical Control
Mechanical treatments include either removal of plant tissue above ground or removal of enough of the root and crown to kill the plant. Hand pulling or mowing before fruits mature and viable seeds form can effectively suppress some plants. In contrast, mowing plants that have the capability to reproduce vegetatively can actually exacerbate weed interference by stimulating production of new stems from vegetative buds below the cut surface. Perennial plants that have the capacity to reproduce vegetatively can be severely damaged or killed by tillage, bulldozing, root-plowing or grubbing. Their high cost limits use of these mechanical treatments.

Cultural Methods
Cultural practices include fire, grazing, re-vegetation or re-seeding, and plant competition. These practices enhance desirable vegetation, minimizing weed invasion.

7.6.1.2 Chemical Control Practices

Herbicides are important tools to control invasive and noxious weeds and assist in establishing desired vegetation, especially when used in concert with other control methods.

Several Group 4 herbicides are currently registered for use in rangeland, pastures and industrial vegetation management areas in Canada to control invasive and woody species (Table 7.6.1.2.1).

There are numerous postemergent broadleaf weed herbicides, with different modes of action, that may be used alone or in various tank mix combinations for use in wheat in western Canada (Table 7.6.1.2.2).

Table 7.6.1.2.1 Alternative Postemergent Herbicides for Control of Broadleaf Weeds in Rangeland, Pastures, Industrial and Other Non-crop Areas

Technical Grade Active Ingredient	End-use Products (Example)	Herbicide Classification	
		Group	Mode of Action
Metsulfuron-methyl	Escort Herbicide	2	ALS inhibitor
2,4-D amine	2,4-D Amine 600 Liquid Herbicide	4	Synthetic auxin
2,4-D ester	2,4-D Ester LV 600	4	Synthetic auxin
2,4-DB	Caliber 400	4	Synthetic auxin
Picloram	Tordon 22K	4	Synthetic auxin
Clopyralid	Transline	4	Synthetic auxin
Triclopyr	Remedy	4	Synthetic auxin
Dicamba	Banvel II	4	Synthetic auxin
MCPA amine	MCPA Amine 500	4	Synthetic auxin
MCPA ester	MCPA Ester 500	4	Synthetic auxin

Table 7.6.1.2.2 Alternative Postemergent Herbicides for Wild Buckwheat Control/Suppression in Wheat (Spring and Durum)

Technical grade active ingredient	End-use products (example)	Herbicide Classification	
		Group	Mode of Action
Metsulfuron methyl	Ally Herbicide	2	ALS inhibitor
Florasulam	Florasulam SC Herbicide	2	ALS inhibitor
Thifensulfuron methyl	Freedom WSB 75DF	2	ALS inhibitor
Imazamethabenz-methyl	Assert SG Herbicide	2	ALS inhibitor
Triasulfuron	Unity 75 WG	2	ALS inhibitor
2,4-D ester	2,4-D Ester LV 600	4	Synthetic auxin
Clopyralid	Lontrel 360 Herbicide	4	Synthetic auxin
Dicamba	Banvel II	4	Synthetic auxin
MCPA	MCPA Ester 500	4	Synthetic auxin
Fluroxypyr	Starane Herbicide	4	Synthetic auxin
Bromoxynil	Pardner	6	Inhibitors of photosystem II at Site A
Linuron	Lorox DF Herbicide	7	Inhibitors of photosystem II at Site B

7.6.2 Compatibility with Current Management Practices Including Integrated Pest Management

Application of Aminopyralid Liquid Concentrate Herbicide would not exclude the sequential use of other herbicides for control of annual, perennial or woody species not controlled by the product alone or when tank mixed.

Aminopyralid Liquid Concentrate Herbicide is compatible with integrated pest management (IPM) programs. Using a herbicide in conjunction with grazing is the preferred management practice for controlling invasive weeds in rangeland and pastures. The application of Aminopyralid Liquid Concentrate Herbicide following renovation, mowing or mechanical brush control is an example of using both chemical and manual control methods.

7.6.3 Contribution to Risk Reduction

Aminopyralid Liquid Concentrate Herbicide is a low-use rate product (10 g a.i./ha for use in wheat and 60–120 g a.i./ha for use in rangeland, pasture, industrial and other non-crop areas) that will reduce the number of kilograms of herbicide active ingredients in the environment compared to high-rate herbicide alternatives.

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

Group 4 mode-of-action herbicides help to manage resistant weed species. The mode of action of Group 4 is not conducive to the formation of site specific, target enzyme, or metabolism based resistance. The use of Aminopyralid Liquid Concentrate Herbicide with the tank mix of fluroxypyr will help to control of ALS-resistance kochia and wild buckwheat, which are major broadleaf weed control issues in the brown soil zone region. The extensive use of the Group 2 ALS chemistry to control kochia has now significantly reduced the effectiveness of Group 2 chemistry due to resistance.

In the interest of resistance management, the label of Aminopyralid Liquid Concentrate Herbicide has include the following statements, as outlined in Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

Resistance Management Recommendations
For resistance management, Aminopyralid is a Group 4 herbicide. Any weed population may contain or develop plants naturally resistant to Aminopyralid or other Group 4 herbicides. The resistant biotypes may dominate the weed population if these herbicides are used repeatedly in the same area. 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 Aminopyralid or other Group 4 herbicides with different herbicide groups that control the same weeds in a given treatment area.
- 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, cultural, biological and other chemical control practices.
- Monitor treated weed populations for resistance development.
- 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 Dow AgroSciences Canada Inc. at 1-800-667-3852.

7.7 Conclusions

Table 7.7.1 Accepted Crops, Application Rates and Crop Growth Stage for Aminopyralid Liquid Concentrate Herbicide

Crop	Maximum Application Rate	Crop Stage at Application
Forage grasses	120 g a.i./ha	Once forage grasses are well established (have developed a good secondary root system and show good vigor)
Spring wheat	10 g a.i./ha	3- to 6-leaf stage
Durum wheat	10 g a.i./ha	2- to 6-leaf stage

Table 7.7.2 Accepted Weed Claims for Aminopyralid Liquid Concentrate Herbicide

Weed	Control/Suppression	Rate (g a.i./ha)
Rangeland, pastures, industrial and other non-crop areas		
Canada thistle, spotted knapweed	Suppression	60
	Control	70
Canada goldenrod	Suppression	70
Scentless chamomile	Suppression	70
	Control	90
Absinth wormwood	Suppression	90
	Control	120
Common tansy, dandelion	Suppression	120
Spring and durum wheat		
Wild buckwheat	Suppression	10

Table 7.7.3 Accepted Crop Rotation Options for Aminopyralid Liquid Concentrate Herbicide in Wheat

Crop	Interval
Spring wheat and canola	Year following application (10-11 months)

Table 7.7.4 Accepted Tankmix Partners for Aminopyralid Liquid Concentrate Herbicide

Aminopyralid Rate	Tankmix Partner Product Rate
Rangeland, pastures, industrial and other non-crop areas	
70, 90 or 120 g a.i./ha	2,4-D amine at 840, 1080 or 1440 g a.i./ha
Spring wheat and durum wheat	
10 g a.i./ha	Starane Herbicide at 144 g a.i./ha

8.0 Toxic Substances Management Policy

During the review of Aminopyralid Technical and Aminopyralid Liquid Concentrate Herbicide, the PMRA has taken into account the federal Toxic Substances Management Policy[1] and has followed its Regulatory Directive DIR99-03[2]. It has been determined that this product does not meet TSMP Track 1 criteria for the following reasons.

- Aminopyralid meets the criteria for persistence. Its values for half-life in soil (330–533 days; aerobic biotransformation) are above the TSMP Track 1 cut-off criteria for soil (≥182 days). Also, in water/sediment systems, aminopyralid is persistent (half-life 462–990 days) and exceeds the TSMP Track 1 cut-off criteria for sediment (≥365 days) . Although data on the persistence in air were not available, the vapour pressure and Henry's Law constant indicate that aminopyralid will not volatilize from water or moist soil under field conditions; thus, long-range atmospheric transport is not expected to occur.

- Aminopyralid is not expected to be bioaccumulative based on its log K_{ow} of 0.2, which is below the TSMP Track 1 cut-off criterion of 5.

- Aminopyralid does not meet the criteria for toxicity (see sections 3.6, 4.7 and 6.4).

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

- Technical grade aminopyralid 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 known to contain TSMP Track 1 substances.

---

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

9.0 Regulatory Decision

Health Canada's PMRA has concluded that the use of aminopyralid and the end-use product Aminopyralid Liquid Concentrate Herbicide in accordance with the label has merit and value consistent with the Pest Control Products Regulations and do not entail an unacceptable risk of harm. Therefore, based on the considerations outlined above, the use of aminopyralid and the end-use product Aminopyralid Liquid Concentrate Herbicide for the control of broadleaf weeds and woody plants in rangeland, pasture (without legumes), industrial and other non-crop areas as well as the control of broadleaf weeds in wheat (spring and durum) is proposed for temporary registration pursuant to the Pest Control Products Regulations, pending submission of chemistry, storage stability and environmental chemistry studies.

The applicant will be carrying out additional chemistry, storage stability, environmental chemistry and value studies as a condition of this temporary registration. Following the review of this information, the PMRA will publish a proposed registration decision document and request comments from interested parties before proceeding with a final regulatory decision.

The following confirmatory studies must be submitted to the PMRA for review:

- Batch data
- Storage stability
- Corrosion characteristics
- Enforcement analytical methodology

List of Abbreviations

AD	administered dose
ADI	acceptable daily intake
ALS	acid-labile subunit
a.e.	acid equivalent
a.i.	active ingredient
ARfD	acute reference dose
ASAE	American Society of Agricultural Engineers
AUC	area under the curve
BBCH	BASF, Bayer, Ciba-Geigy and Hoechst
bw	body weight
BWI	body weight per individual
CAS	Chemical Abstracts Service
CHO	Chinese hamster ovary
CO_2	carbon dioxide
cm	centimetre(s)
DAT	day(s) after treatment
DI	dietary intake
DT_{50}	dissipation time 50%
eq-h	equivalent-hour
EO	water emulsion in oil
EP	end-use product
EXAMS	Exposure Analysis and Modeling System
g	gram(s)
FC	food consumption
FOB	functional observational battery
ha	hectare(s)
HCB	hexachlorobenzene
HGPRT	hypoxanthine guanine phosphoribosyl transferase
HPLC	high performance liquid chromatography
HPLC-MS	high performance liquid chromatography with mass spectrometry
HPLC-UV	high performance liquid chromatography with ultraviolet detection
HPLC-ESI-MS-MS	high performance liquid chromatography with electrospray ionization and tandem mass spectrometry
kg	kilogram(s)
K_{oc}	organic carbon adsorption coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration 50%
LC-MS/MS	high-performance liquid chromatography method with tandem mass spectrometry
LD_{50}	limit of detection
LEACHM	Leaching Estimation and Chemistry Model
LOAEL	lowest observed adverse effect level
LOD	limit of detection

LOEC	lowest observed effect concentration
LOEL	lowest observed effect level
LOQ	limit of quantitation
MAS	maximum average score
MIS	maximum irritation score
mg	milligram(s)
mol	mole
MRL	maximum residue limit
MTDB	maximum theoretical dietary burden
N/A	not available
nm	nanometre
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
Pa	Pascal(s)
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
PMRA	Pest Management Regulatory Agency
PRZM	Pesticide Root Zone Model
QCB	pentachlorobenzene
ROC	residue of concern
RSD	relative standard deviation
SC/L	soluble concentrate liquid
SD	standard deviation
SPE	solid phase extraction
TIPA	triisopropanolamine
TSMP	Toxic Substances Management Policy
TRR	total radioactive residue
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Agency
UV	ultraviolet
VMD	volume median diameter

Appendix I Toxicology

METABOLISM

In a metabolism study, ^{14}C-aminopyralid (radiochemical purity 98.6%) was administered to Fischer 344 rats, 4 ♂/dose, as a single gavage dose of 50 or 1000 mg/kg bw, or 14 daily doses (50 mg/kg bw/day) of unlabelled aminopyralid (purity 99.5 %) followed by a single gavage dose of 50 mg/kg bw ^{14}C-aminopyralid on day 15. Excreta were collected at 0, 6 (urine only), 12 (urine only), 24, 48, 72, 96, 120, 144 and 168 hours postdosing. Study results indicated that ^{14}C-aminopyralid was rapidly absorbed, distributed, and excreted following oral administration in rats. Total 24-h recoveries of the radioactivity were high for all groups (~41-59 % and 33-43 % of administered dose (AD) in urine and feces, respectively). The absorption and excretion patterns of the ^{14}C moiety were similar among all groups. The findings indicated that aminopyralid was not metabolized to volatile compounds, including CO_2. The average α-phase elimination half-lives ($T_{½}\alpha$) of ^{14}C-aminopyralid equivalents were 2.85, 3.27 and 3.78 hours for the single low, repeat low, and single high dose groups, respectively. The average β-phase urinary elimination half-lives ($T_{½}\beta$) of ^{14}C-aminopyralid equivalents were 10.23, 12.25 and 10.88 hours for the single low, repeat low, and single high dose groups, respectively. Tissue distribution and bioaccumulation of aminopyralid were minimal; <0.73 % of the AD was recovered in tissues 7 days after oral administration for all dosing groups. Highest levels of radioactivity were found in the skin and carcass. Aminopyralid was excreted unchanged indicating an absence of metabolism. Aminopyralid represented ≥96 % of the AD in the urine and 100 % of the AD in feces. Three unknown components (≤4 %) found in urine were also detected in similar quantities in the analysis of the dose formulation, suggesting that they were trace impurities in the radiolabelled material.

In a metabolism study, ^{14}C-aminopyralid (radio-chemical purity 98.25 %) or ^{14}C-aminopyralid-TIPA (radiochemical purity 98.25 %) was administered to Fischer 344 rats, 4 ♂/dose, as a single gavage dose of 50 or 96 mg/kg bw. Excreta were collected at 0, 6 (urine only), 12 (urine only), 24, 48, 72, 96 and 120 hours postdosing. Blood samples were collected at 0.25, 0.5, 1, 2, 4, 6, 8, 10, 12, 24, 36, 48 and 120 hours postdosing. A single oral dose of ^{14}C-aminopyralid or ^{14}C-aminopyralid-TIPA was rapidly absorbed by the rat. The excretion of 38.3 % (for ^{14}C-aminopyralid) and 34.6 % (for ^{14}C-aminopyralid-TIPA) of the administered radioactivity in the urine within 6 hours confirmed that the amino-dichloro-picolinate (or anion) portion of the molecule was rapidly absorbed regardless of whether it was administered as the acid or as the TIPA salt formulation. Plasma AUCs were 23.0 and 19.0 µg eq-h/g plasma; half-lives from the α phase of plasma elimination were 0.338 and 0.509 hours; and half-lives from the β phase of plasma elimination were 8.8 and 13.0 hours for the aminopyralid and aminopyralid-TIPA dosed groups, respectively. These data indicated that pharmacokinetic behaviour was similar between the two compounds. Based on the amount of radioactivity recovered in the urine through 120 hours, a minimum of 46.3 % and 42.5 % of the orally administered ^{14}C-aminopyralid and ^{14}C-aminopyralid-TIPA was absorbed. Radioactivity was rapidly eliminated with 93.5% (44.7 % in urine; 48.8 % in feces) and 93.3 % (41.5 % in urine; 51.8 % in feces) of the AD of ^{14}C-aminopyralid and ^{14}C-aminopyralid-TIPA recovered in excreta within 24 hours postdosing. Urinary rates of elimination calculated for the two compounds were also similar. Half-lives estimated for the rapid initial (α) phase of the urinary elimination curve were 2.8 hours for the ^{14}C-aminopyralid dosed group and 2.5 hours for the ^{14}C-aminopyralid-TIPA dosed group. Half-lives estimated for the slower terminal (β) phase were 7.8 hours for the ^{14}C-aminopyralid dosed group and 10.7 hours for the ^{14}C-aminopyralid-TIPA dosed group. The amino-dichloro-picolinate portion of the molecule(s) was excreted primarily unchanged following a single oral administration of either compound. Parent aminopyralid represented >99 % of the radioactivity detected in the urine and feces of both dose groups. The only unidentified metabolite was detected in urine from the ^{14}C-aminopyralid-TIPA dosed group, and represented 0.34 % of the administered dose. The results from this study indicate that ^{14}C-aminopyralid and ^{14}C-aminopyralid-TIPA, when administered orally to rats, were bioequivalent in terms of absorption, distribution, metabolism and excretion of the amino-dichloro-picolinate portion of the molecule(s).

STUDY	**TGAI, PURITY; DOSES SPECIES/STRAIN**	**LD_{50}, LC_{50}, LOAEL, NOAEL mg/kg bw/day**	**TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS**
ACUTE STUDIES—Technical Active (aminopyralid, 94.5 % purity)			
Acute oral LD_{50}	Rat	♂/♀ > 5000 mg/kg bw	1 ♂ died; clinical signs: perineal, perioral, perinasal soiling, watery feces; recovery by days 4–7; low acute toxicity
Acute dermal LD_{50}	Rat	♂/♀ > 5000 mg/kg bw	Clinical signs: perineal and/or periocular soiling (1♂/2♀); recovery by day 3; low acute toxicity
Acute inhalation LC_{50}; 4-hour nose-only	Rat	♂/♀ > 5.5 mg/L (actual) > 8.6 mg/L (nominal)	Clinical signs: gasping immediately following exposure; low acute toxicity
Primary eye irritation	Rabbit	MAS = 53.5/110 MIS = 59.3/110 (24 hour)	Corneal vascularization from day 15 to 35 (study termination) **DANGER—CORROSIVE TO EYES**
Primary skin irritation	Rabbit	MAS = 0/8 MIS = 0/8	Basically non-irritating
Dermal sensitization (maximization assay)	Guinea pig	No skin reactions 24 and 48 hours after topical challenge	Not a dermal sensitizer

STUDY	TGAI, PURITY; DOSES SPECIES/STRAIN	LD_{50}, LC_{50}, LOAEL, NOAEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
ACUTE STUDIES—Aminopyralid Liquid Concentrate Herbicide (containing 41.3 % aminopyralid TIPA)			
Acute oral LD_{50}	Rat	♂/♀ > 5000 mg/kg bw	Clinical signs: cloudy eyes, lacrimation, watery or soft feces, perineal/periocular soiling; low acute toxicity
Acute dermal LD_{50}	Rat	♂/♀ >5 000 mg/kg bw	Clinical signs: perineal soiling (1 ♂), reddening of test skin sites (2 ♂) low acute toxicity
Acute inhalation LC_{50}; 4-hours nose-only	Rat	♂/♀ > 5.79 mg/L (actual) > 14.95 mg/L (nominal)	Clinical signs: soiling of hair-coat during exposure; perioral, periocular, perineal, perinasal, and/or body soiling; normal by day 4; low acute toxicity
Primary eye irritation	Rabbit	MAS = 0.0/110 MIS = 1.33/110 (1 hour)	Minimally irritating
Primary skin irritation	Rabbit	MAS = 0.45/8 MIS = 0.67/8 (48, 72 hours)	Slightly irritating
Dermal sensitization (maximization assay)	Aminopyralid Liquid Concentrate Herbicide containing 21.3 % aminopyralid Guinea pig	No induction scores were presented; no skin reactions 24 and 48 hours after topical challenge	Not a dermal sensitizer
SHORT-TERM—Technical Active (aminopyralid, 94.5% purity)			
Mouse 30-day dietary	Mouse, CD-1, 5/sex/group Target doses: 0, 10, 100, 500, 1000 mg/kg bw/d actual doses in mg/kg bw/d: ♂ = 0, 11.0, 102.0, 524.7, 1038.0 ♀ = 0, 10.8, 105.0, 530.4, 1058.0	NOAEL ♂/♀ = 1000 mg/kg bw/day	No effects on mortality, clinical signs, bw, food intake, hematology, clinical chemistry, organ weight, gross pathology 1000: hepatocyte – ↑ size, altered cytoplastic staining, ↓ glycogen
Rat 30-day dietary	Rat, Fischer 344, 5/sex/group Target doses: 0, 10, 100, 500, 1000 mg/kg bw/d Actual doses in mg/kg bw/d: ♂ = 0, 11.4, 113.7, 561.1 1125.6 ♀ = 0, 12.2, 110.2, 550.5, 1093.7	NOAEL ♂/♀ = 1000 mg/kg bw/day	No effects on mortality, bw, food intake, clinical signs, ophthalomoscopy, hematology, clinical chemistry, urinalysis, organ weights or histopathology. ≥500: ♂/♀ cecum – ↑ size
Dog 30-day dietary	Dog, beagle, 2/sex/group 0, 1500, 4500, 15000 ppm Actual doses in mg/kg bw/d: ♂ = 0, 62, 93, 543 ♀ = 0, 62, 177, 556	NOAEL ♂ = 543 ♀ = 556 mg/kg bw/day	No effects on bw, food intake, clinical and ophthalmologic observations, hematology, clinical chemistry, organ weight, gross and histopathology
Mouse 90-day dietary	Mouse, CD-1, 10/sex/group Target doses: 0, 10, 100, 500, 1000 mg/kg bw/d Actual doses in mg/kg bw/d: ♂ =0, 10.2, 101, 512, 1020 ♀ = 0, 10.2, 103, 515, 1020	NOAEL ♂/♀ = 1000 mg/kg bw/day	No effects on mortality, clinical signs, bw, food intake, hematology, clinical chemistry, organ weight, gross and histopathology

STUDY	TGAI, PURITY; DOSES SPECIES/STRAIN	LD_{50}, LC_{50}, LOAEL, NOAEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
Rat 90-day dietary (with 4-week recovery)	Rat, Fischer 344 Main groups: 10/sex/group Targeted doses: 0, 10, 100, 500, 1000 mg/kg bw/d Actual doses in mg/kg bw/d: ♂ = 0, 10.9, 109, 543, 1090 ♀ = 0, 10.7, 108, 540, 1060 Recovery groups: 10/sex/group Target doses: 0, 1000 mg/kg bw/d	NOAEL ♂ = 500; ♀ = 1000 mg/kg bw/day (based on mucosal epithelium hyperplasia of the cecum and ileum) LOAEL ♂ = 1000 mg/kg bw/day ♀ = not determined Terminal (day 91) bw (g) and food intake (g/rat/day) of control rats, N = 10/group: bw – ♂ = 331.2±20.1, ♀ = 183.6±7.0 food – ♂ = 17.1±0.7, ♀ = 11.0±0.5	No effects on mortality, bw, food intake, clinical signs, ophthalmoscopy, hematology, clinical chemistry, or urinalysis. ≥500: ♂/♀ ↑ full cecal weight, ♂ ↑ empty cecal weight 1000: ♂/♀ cecum ↑ size; ♂ cecum/ileum - mucosal epithelium hyperplasia 4-week recovery: complete recovery of mucosal epithelium hyperplasia of the cecum and ileum, and partial recovery of the increased cecal weights in 1000 mg/kg bw/day group.
Dog 90-day dietary	Dog, beagle, 4/sex/group 0, 1500, 7500, 30 000 ppm Actual doses in mg/kg bw/d: ♂ = 0, 54.5, 282, 1070 ♀ = 0, 52.7, 232, 929	NOAEL ♂ = 282; ♀ = 232 mg/kg bw/d (based on stomach histopathology) LOAEL ♂ = 1070 ♀ = 929 mg/kg bw/d Terminal (d 92) bw (kg) and food intake (kg/dog/d) of control dogs, N = 4/group: bw – ♂ = 9.66±1.39, ♀ = 7.94±1.02 food – ♂ = 0.32±0.05, ♀ = 0.22±0.02	No effects on bw, food intake, clinical and ophthalmologic observations, hematology, clinical chemistry, gross pathology 30000: ♂/♀ – ↑ liver weight, slight diffuse hyperplasia/hypertrophy of stomach mucosal epithelium
Dog 1-year dietary	Dog, beagle, 4/sex/group 0, 300, 3000, 30 000 ppm Actual doses in mg/kg bw/day: ♂ = 0, 9.9, 99.2, 967 ♀ = 0, 9.2, 93.2, 1038	NOAEL ♂ = 99.2 ♀ = 93.2 mg/kg bw/day (based on stomach histopathology) LOAEL ♂ = 967 ♀ = 1038 mg/kg bw/day	No effects on bw, food intake, clinical signs, ophthalmoscopy, hematology, clinical chemistry, organ weight, gross and histopathology ≥967: ♂/♀ – ↑ liver weight, very slight hepatocyte hypertrophy; slight diffuse hyperplasia and hypertrophy of the mucosal epithelium of stomach, slight lymphoid hyperplasia of the gastric mucosa and very slight/slight chronic mucosal inflammation ♀ – diffuse thickening of stomach mucosa
Rat 28-day dermal	Rat, Fischer 344; 10/sex/group 0, 100, 500, 1000 mg/kg bw/day	NOAEL Systemic: ♂/♀ = 1000 mg/kg bw/day Dermal: ♂ = 100, ♀ = 1000 mg/kg bw/day (based on slight epidermal hyperplasia)	No deaths; no effects on bw, food intake, clinical and ophthalmologic observations, hematology, clinical chemistry, organ weight, gross pathology ≥500: ♂ – slight epidermal hyperplasia
SHORT-TERM—Aminopyralid Liquid Concentrate Herbicide (an aqueous formulation containing 41.3% aminopyralid TIPA)			
Rat 90-day dietary toxicity	Targeted doses: 0, 465, 1211, 2421 mg EP/kg bw/d; or 0, 192, 500, or 1000 mg aminopyralid TIPA/kg bw/d; or acid equivalent (a.e.) doses:0, 100, 260, 520 mg a.e./kg bw/d 10/sex/group	NOAEL 2421 mg EP/kg bw/day, or 1000 mg aminopyralid/kg bw/day, or 520 mg a.e./kg bw/day Terminal (day 90) bw (g) and food intake (g/rat/day) of control rats, N = 10/group: bw – ♂ = 331.0±18.2, ♀ = 185.4±8.6 food – ♂ = 17.4±1.3, ♀ = 12.3±0.6	≥1211: ♂/♀ – ↑ cecal weight 2421: ♂/♀ – slight ↑ urine volume, slight ↓ urine specific gravity

STUDY	TGAI, PURITY; DOSES SPECIES/STRAIN	LD_{50}, LC_{50}, LOAEL, NOAEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
CHRONIC TOXICITY/ONCOGENICITY—Technical Active (aminopyralid, 94.5% purity)			
Mouse 18-month dietary oncogenicity	Mouse, CD-1, 50/sex/group Target doses: 0, 50, 250, 1000 mg/kg bw/day Actual doses in mg/kg bw/day: ♂ = 0, 50.2, 251, 1000 ♀ = 0, 50.9, 252, 1010	NOAEL ♂/♀ = 1000 mg/kg bw/day Not oncogenic	No effects on mortality, clinical signs, bw, food intake, food efficiency, hematology, organ weight, gross and histopathology; no evidence of oncogenicity
Rat 2-year dietary / oncogenicity	Rat, Fischer 344, 65/sex/group Target doses: 0, 5, 50, 500, 1000 mg/kg bw/day Actual doses in mg/kg bw/day: ♂ = 0, 5.1, 50.5, 505, 1001 ♀ = 0, 5.1, 51.2, 507, 1018 10 rats/sex/ group for interim sacrifice at 12 month	NOAEL ♂ = 50 mg/kg bw/day ♀ = 500 mg/kg bw/day (based on lowered bw) LOAEL ♂ = 500 ♀ = 1000 mg/kg bw/day Not oncogenic	Rats survived to study termination: ♂ = 31, 36, 33, 33, 33; ♀ = 41, 38, 39, 38, 39, respectively No effects on mortality, clinical signs, ophthalmoscopy, hematology, clinical chemistry 1000: ♂/♀ - ↓ bw; ↑ cecal weight ≥500: ♂/♀ - ↑ urine volume, ↓ urine SP 500: ♂ - ↓ bw
REPRODUCTION / DEVELOPMENTAL TOXICITY—Technical Active (aminopyralid, 94.5% purity)			
13-Week dietary reproduction probe			
Rat 2-generation (1 litter/generation) dietary	Rat, Sprague Dawley; 30/sex/group Targeted doses: 0, 50, 250, 1000 mg/kg bw/day Actual doses in mg/kg bw/day: ♂ = 0, 52.0, 259, 1030 ♀ = 0, 49.3, 245, 973 Note: test concentrations based on homogeneity analysis data for 50 and 1000 mg/kg bw/day groups were 0.0725±0.0016 and 1.59±0.0399%, respectively; no ppm information on the 250 mg/kg bw/day dose level	NOAEL for maternal, offspring, and reproductive toxicity = 1000 mg/kg bw/day	**Parent Toxicity** ≥250: P_1 ♂/♀ – ↑ cecal weight P_1 & P_2 ♂/♀ – ↑ cecal size 1000: P_2 ♂/♀ – ↑ cecal weight 250: P_2 ♂ – ↑ cecal weight 50: P_2 ♂ – ↑ cecal weight No on mortality, clinical signs, bw, bw gain, food intake, reproductive function, reproductive parameters or histopathology. **Offspring Toxicity** No effects on clinical signs, viability/litter parameters, pup bw, bw gain, organ weight, or gross pathology
Rat teratogenicity	Rat, CD-1; 25 mated ♀/group aminopyralid in 0.5% Methocel A4M at 0, 100, 300, 1000 mg/kg bw/day by oral gavage from gestation days 6–20	NOAEL, maternal and developmental toxicity = 1000 mg/kg bw/day no evidence of teratogenicity	No effects on mortality, bw, bw gain, food intake, organ weights, gross pathology or reproductive parameters
Rabbit teratogenicity	Rabbit, New Zealand white 26 mated ♀/group aminopyralid in 0.5% Methocel A4M at Phase 1: 0, 25, 100, 250 Phase 2: 0, 500, 750 mg/kg bw/day by oral gavage from gestation days 7–27	NOAEL, mg/kg bw/day Maternal toxicity = 250 Developmental toxicity = 500 LOAEL, mg/kg bw/day Maternal toxicity = 500 Developmental toxicity = not determined	**Maternal Toxicity** 750: 2 moribund sacrifice (incoordinated gait, significant bw losses, ↓ food intake); ↓ fecal output; this group was removed from the study on day 20 due to bw decreases and severity of clinical signs; ↑ incidence of pale kidneys, ↑ ulcers/erosions in glandular mucosa of the stomach at necropsy ≥500: ↑ incidence of incoordinated gait, which was transient, with complete resolution within two hours postdosing, and did not appear to progressively worsen on subsequent days; initial bw loss 500: ulcers/erosions in glandular mucosa of stomach in 1 ♀

STUDY	TGAI, PURITY; DOSES SPECIES/STRAIN	LD_{50}, LC_{50}, LOAEL, NOAEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
REPRODUCTION/DEVELOPMENTAL TOXICITY—Aminopyralid Liquid Concentrate Herbicide (an aqueous formulation containing 41.3% aminopyralid TIPA)			
Teratogenicity—rat	0, 484, 1211, 2421 mg EP/kg bw/day, or 0, 200, 500, 1000 mg aminopyralid TIPA/kg bw/day, or 0, 104, 260, 520 mg a.e./kg bw/day); oral gavage 25 mated ♀/group	NOAEL = 2421 mg EP/kg bw/day, or 1000 mg aminopyralid TIPA/kg bw/day, 520 mg a.e./kg bw/day	No treatment-related effects
Teratogenicity—rabbit	0, 484, 1211, 2421 mg EP/kg bw/day, or 0, 200, 500, 1000 mg aminopyralid /kg bw/day, or 0, 104, 260, 520 mg a.e./kg bw/day oral gavage 26 mated ♀/group	NOAEL Maternal toxicity = 484 mg EP/kg bw/day, or 200 mg aminopyralid TIPA/kg bw/day, 104 mg a.e./kg bw/day Developmental toxicity = 1211 mg EP/kg bw/day, or 500 mg aminopyralid TIPA/kg bw/day, 260 mg a.e./kg bw/day LOAEL Maternal toxicity = 1211 mg EP/kg bw/day, or 500 mg aminopyralid TIPA/kg bw/day, 260 mg a.e./kg bw/day Developmental toxicity = 2421 mg EP/kg bw/day, or 1000 mg XDE-750 TIPA/kg bw/day, 520 mg a.e./kg bw/day	**Maternal Toxicity** (based on XDE-750 TIPA) 1000: ↓ food intake, bw; mild incoordination (transient, sporadic) ≥500: ↓ fecal output **Developmental Toxicity** 1000: ↓ fetal bw
GENOTOXICITY—Technical Active (aminopyralid, 94.5% purity)			
Salmonella/Ames Test	*Salmonella typhimurium* – TA98, 100, 1535, 1537; *Escherichia coli* WP2uvrA	±S9: 0, 100, 333, 1000, 3300 and 5000 µg/plate	Negative
Mammalian cell CHO/HGPRT gene mutation assay	Chinese hamster ovary cells	±S9: 0, 31.25, 62.5, 125, 250, 500, 1000, 1500 and 2070 µg/mL	Negative
In vitro mammalian chromosomal aberration	Rat lymphocytes	Assay 1: ±S9 - 0, 32.3, 64.7, 129.4, 258.8, 517.5, 1035 or 2070 µg/mL (4-hour treatment, 24-hour harvest) Assay 2: -S9 - 0, 125, 250, 500, 750, 1000, 1400, 1700 or 2070 µg/mL; +S9 - 0, 62.5, 125, 500, 1000 or 2070 µg/mL (24-hour treatment, harvest at end of treatment) Assay 3: -S9 - 400, 600, 800, 1000, 1200, 1400, 1600, 1700, 1800 or 2070 µg/mL (24-hour treatment, harvest at end of treatment)	Negative in assays with S9 activation; Clastogenic in assays without S9 activation at cytotoxic doses (≥50% reduction in mitotic indices)
In vivo mouse micronucleus assay	CD-1 mouse; 6♂/group 0, 500, 1000, 2000 mg/kg bw/day for 2 days by oral gavage	Bone marrow cells harvested 24 hours after dosing	Negative

STUDY	TGAI, PURITY; DOSES SPECIES/STRAIN	LD_{50}, LC_{50}, LOAEL, NOAEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
GENOTOXICITY—Aminopyralid Liquid Concentrate Herbicide (an aqueous formulation containing 41.3% XDE-750 TIPA)			
Ames microbial mutation	*Salmonella typhimurium* – TA98, TA100, TA1535, TA1537 *Escherichia coli* WP2uvrA	±S9: 0, 33.3, 100, 333, 1000, 3330, 5000 µg XDE-750 TIPA/plate	Negative
Gene mutation in mammalian cells	CHO cells / HGPRT locus	±S9: 0, 250, 500, 1000, 2000, 4000 XDE-750 TIPA/mL	Minimal cytotoxicity negative
In vitro chromosome aberration	Rat lymphocytes	-S9: 0, 1000, 2000, 4000 µg XDE-750 TIPA/mL, 4 and 24 hours treatment +S9: 0, 500, 1000, 2000 µg XDE-750 TIPA/mL, 4 hours treatment	-S9, 4000 µg/mL - moderate cytotoxicity Negative
In vivo mouse micronucleus	CD-1 mouse, 6 ♂/group; oral gavage at 0, 500, 1000, 2000 mg XDE-750 TIPA/kg bw/day for 2 days	Bone marrow cells harvested 24 hours after dosing	Negative
SPECIAL STUDIES—Technical Active (aminopyralid, 94.5% purity)			
Rat acute neurotoxicity	Rat, Fischer 344, 10/sex/group XDE-750 in 0.5% aqueous Methocel® at 0, 500, 1000, 2000 mg/kg bw	NOAEL ♂/♀ = 1000 mg/kg bw LOAEL ♂/♀ = 2000 mg/kg bw No evidence of acute neurotoxicity	No effects on ophthalmoscopy, bw, FOB, motor activity, gross pathology, or on neuropathologic evaluation 2000: ♂/♀ – ↑ fecal/urine soiling, normal within 3–4 days
1-Year dietary neurotoxicity	Rat, Fischer 344, 10/sex/group; 0, 50, 500, 1000 mg/kg bw/day	NOAEL ♂/♀ = 1000 mg/kg bw/day LOAEL not established No evidence of neurotoxicity	No effects on ophthalmoscopy, bw, FOB, motor activity, gross pathology, or on neuropathologic evaluation

Compound-induced Mortality
Acute studies: no compound induced mortality in rats at limit dose of 5000 mg/kg bw.
30- and 90-day studies in mice, rats and dogs: no compound induced mortality at limit dose of ~1000 mg/kg bw/day.
18-month mouse and 2-year rat studies: no compound induced mortality at dose up to 1000 mg/kg bw/day.
Reproductive toxicity and teratology studies in rats: no compound induced mortality at dose up to 1000 mg/kg bw/day.
Teratology study in rabbits: compound induced mortality (moribund kill) at 750 mg/kg bw/day.

Recommended ARfD
Not required

Recommended ADI
0.5 mg/kg bw/day, based on the NOAEL of 50 mg/kg bw/day established in the 2-year chronic toxicity/oncogenicity study and a standard uncertainty factor of 100.

Margin of Exposure for Other Critical Endpoint(s)
A margin of exposure of 100 is considered to be protective of all workers.

Appendix II

Table 1 Residue Summary

DIRECTIONS FOR USE OF PESTICIDE ON CROPS						
Crop	**Formulation/ Type**	**Interval (day)**	**Rate (g a.i./ha)**	**#/ Season**	**Maximum Rate**	**PHI (days)**
Forage grasses in rangeland, pasture (without legumes)	Soluble concentrate liquid (SC/L)	Not applicable	120	1	120 g a.e./ha/season	Not specified
Wheat (spring and durum in brown soil zone range in Western Canada)	Soluble concentrate liquid (SC/L)	Not applicable	10	1	10 g a.e./ha/season	50 (grain and straw) 0 (hay)

Label Restrictions

Forage Grasses in Rangeland, Pasture
There is no grazing restriction on livestock or lactating dairy animals grazing in treated areas.

Wheat (spring and durum)
There is no grazing restriction on livestock or lactating dairy animals grazing in treated areas. There is no restriction on harvest of wheat for hay following application of Aminopyralid Liquid Concentrate. Fields previously treated with Aminopyralid Liquid Concentrate can be seeded the following year to spring wheat and canola. Fields cannot be seeded to all other crops than those just listed in the calender year following treatment.

PHYSICOCHEMICAL PROPERTIES	
Water solubility	**pH** — **Solubility (g/L)** Unbuffered water at 18°C — 2.48 5 at 20°C — 212 7 at 20°C — 205 9 at 20°C — 203
Solvent solubility at 20°C, g/L	**Solvent** — **Solubility (g/L)** Methanol — 52.2 Acetone — 29.2 *n*-Octanol — 3.9 Ethyl acetate — 3.9 1,2-Dichloroethane — 0.2 Xylene — 0.04 Heptane — <10 mg/L
n-Octanol–water partition coefficient (Log K_{ow}) at 19°C	**pH** — **Solubility (g/L)** Unbuffered water — 0.201 5 — -1.76 7 — -2.87 9 — -2.96
Dissociation constant (p*K*a)	2.56
Vapour pressure	2.59×10^{-8} Pa (at 25°C) 9.52×10^{-9} Pa (at 20°C)
Relative density	1.72 g/mL (at 20°C)
Melting point	163.5°C

UV–Visible absorption spectrum	**Solution**	**Wavelength λ max, nm**	**Extinction coefficient ϵ, (L/mol·cm)**
	Neutral MeOH	217	29 100
	Basic (pH 12.6)	220	26 100
		245	10 150
	Acidic (pH 1.4)	217	22 800
		270	9140

ANALYTICAL METHODOLOGY		
Parameters	**Plant Matrices**	**Animal Matrices**
Method ID	**GRM 02.31**	**GRM 03.18**
Type	Data gathering and enforcement	Data gathering and enforcement
Analytes	Aminopyralid (free and conjugated)	Aminopyralid *per se*
Instrumentation	LC/MS/MS	LC/MS/MS
LOQ	0.01 ppm	0.01 ppm
Standard	Internal standardization with $^{13}C_2{}^{15}N$-aminopyralid	Internal standardization with $^{13}C_2{}^{15}N$-aminopyralid
Independent Laboratory Validation	Independent laboratory validation was successfully completed using grass forage and wheat grain	Independent laboratory validation was successfully completed using milk and kidney
Extraction/ cleanup	Ground samples are extracted with 0.1 N sodium hydroxide, releasing bound residues and hydrolyzing base-labile conjugates to free aminopyralid; the extract is isolated by centrifugation. An aliquot of the supernatant is acidified and heated to hydrolyze acid-labile conjugates. Following hydrolysis, the extract is cleaned up through by SPE. The internal standard, $^{13}C_2{}^{15}N$-aminopyralid, is added to the SPE eluate. The eluate is then evaporated to dryness, residues are reconstituted in acetonitrile/pyridine/1-butanol (22:2:1, v/v/v) and derivatized with butyl chloroformate to form the 1-butyl esters of aminopyralid and the internal standard.	Samples are extracted with methanol/sodium bicarbonate (20:1, v/w). The extract is diluted in water and cleaned up by SPE. Residues are eluted with ethyl acetate/trifluoroacetic acid (99:1, v/v), the internal standard, $^{13}C_2{}^{15}N$-aminopyralid, is added to the SPE eluate. The eluate is evaporated and reconstituted in acetonitrile/pyridine/1-butanol (22:2:1, v/v/v). Derivatized with butyl chloroformate is carried out to form the 1-butyl esters of aminopyralid and the internal standard.
Radiovalidation	Adequate radiovalidation data have been submitted for the extraction procedures of Method GRM 02.31 using samples of grass and wheat containing bioincurred residues of aminopyralid.	None submitted for aminopyralid, but the extraction solvent used in the proposed enforcement method (GRM 03.18) is similar to what was used in the goat metabolism study (where 76-96 % TRRs were extracted from milk, liver and kidney using methanol).
Multiresidue method	Not applicable	Not applicable
Interference Study	The petitioner is required to show that Methods GRM 02.31 and GRM 03.18 can differentiate between aminopyralid, clopyralid and picloram, as they are all similar in structure.	

NATURE OF THE RESIDUE IN WHEAT (SPRING)		
Radiolabel position	^{14}C in the 2- and 6-positions of the pyridine ring	
Test site	Wheat was grown in outdoor test plots.	
Treatment	Plants were treated by foliar application at BBCH 26–28 stage (6 to 8 tiller)	
Rate	Low rate (1 × 40.1 g a.i./ha); High rate (1 × 80.3 g a.i./ha)	
PHI	0 days (early forage); 14 days (forage); 35 days (hay); 86 days (straw and grain)	
Residues were highest in plants treated at the higher application rate, but metabolism was similar in all matrices for both rates. For the low and high rates, TRR was highest in early forage collected 0 DAT and lowest in grain collected 86 DAT. The TRRs in the straw samples collected 86 DAT were approximately 7× less than in the corresponding grain samples, also collected 86 DAT.		
Metabolites Identified	**Major Metabolites (>10% TRRs)**	**Minor Metabolites (<10% TRRs)**
Radiolabel	**^{14}C in the 2- and 6-positions of the pyridine ring**	**^{14}C in the 2- and 6-positions of the pyridine ring**
Forage (0 and 14 DAT)	Aminopyralid	None
Hay (35 DAT)	Aminopyralid Aminopyralid-glucose (characterized)	Hydroxylated aminopyralid glucose (characterized)
Straw (86 DAT)	Aminopyralid	None
Grain (86 DAT)	Aminopyralid	None
NATURE OF THE RESIDUE IN GRASS (Big Bluestream, Perennial Rye Grass, *Panicum maximum*)		
Radiolabel position	^{14}C in the 2- and 6-positions of the pyridine ring	
Test site	Plants were germinated in a greenhouse and were subsequently moved outdoors.	
Treatment	Plants were treated by foliar application 8-10 weeks after planting.	
Rate	1 × 360 g a.i./ha	
PHI	0, 7, 14, 21, and 42 days for forage; 42 days for hay	
Residues were highest in forage collected 0 DAT and decreased with time. Hay samples contained significantly higher (~4×) TRRs than corresponding forage samples that were also collected 42 DAT. Metabolism of aminopyralid was similar for all three grass species.		
Metabolites Identified	**Major Metabolites (>10% TRRs)**	**Minor Metabolites (<10% TRRs)**
Radiolabel	**^{14}C in the 2- and 6-positions of the pyridine ring**	**^{14}C in the 2- and 6-positions of the pyridine ring**
Grass forage (collected 21 DAT, all 3 species of grass)	Aminopyralid Conjugates of aminopyralid (characterized)	Conjugates of aminopyralid (characterized)
Grass hay (collected 42 DAT, all 3 species of grass)	Aminopyralid Conjugates of aminopyralid (characterized)	Conjugates of aminopyralid (characterized)

CONFINED ROTATIONAL CROP STUDY—Lettuce, Sorghum, Turnip	
Radiolabel position	^{14}C in the 2- and 6-positions of the pyridine ring
Test site	Wooden boxes, 0.914 m × 1.524 m (3' × 5'), lined with plastic and maintained outdoors
Treatment	Bare soil
Rate	10 g a.i./ha
PBI	90 and 120 days
Samples of sorghum (early forage 90- and 120-day PBI; stover 90-day PBI) and turnip tops (120-day PBI) contained TRRs that were > 0.010 ppm. These samples were extracted and residues were identified as free aminopyralid as follows: 0.012 ppm for 90-day sorghum early forage, 0.005 ppm for 120-day sorghum early forage, 0.005 ppm for 90-day sorghum stover and 0.002 ppm for 120-day turnip tops. A plantback interval is not necessary because the end-use product label for Canada indicates a one- or two-year interval between treatment and planting of rotational crops.	

NATURE OF THE RESIDUE IN LAYING HEN			
Species	**Radiolabel**	**Dose Level**	**Sacrifice**
Gallus domesticus	^{14}C in the 2- and 6-positions of the pyridine ring	~12 ppm in diet for 7 days	Within ~24 hours of administration of last dose
~79 % AD eliminated in excreta; <0.01 % AD in egg, muscle, fat, liver, skin, and fat.			
Metabolites Identified	**Major Metabolites (>10% TRRs)**	**Minor Metabolites (<10% TRRs)**	
Radiolabel	**^{14}C in the 2- and 6-positions of the pyridine ring**	**^{14}C in the 2- and 6-positions of the pyridine ring**	
Excreta	Aminopyralid	<LOQ	
Egg	<LOQ	<LOQ	
Muscle	<LOQ	<LOQ	
Fat	<LOQ	<LOQ	
Liver	<LOQ	<LOQ	
Skin with subcutaneous fat	<LOQ	<LOQ	

NATURE OF THE RESIDUE IN LACTATING GOAT			
Species	**Radiolabel**	**Dose Level**	**Sacrifice**
Goat (Toggenburg breed)	^{14}C in the 2- and 6-positions of the pyridine ring	~15 ppm in diet for 6 days	Within 24 hours of administration of last dose
95.5 % AD eliminated in urine and feces; 0.01 % AD in milk, kidney, and liver; not detected in muscle and fat. Aminopyralid is highly excreted, with low tissue burden and transfer to milk.			
Metabolites Identified	Major Metabolites (>10% TRRs)	Minor Metabolites (<10% TRRs)	
Radiolabel	^{14}C in the 2- and 6-positions of the pyridine ring	^{14}C in the 2- and 6-positions of the pyridine ring	
Milk	<LOQ	<LOQ	
Liver	<LOQ	<LOQ	
Kidney	Aminopyralid	<LOQ	

CROP FIELD TRIALS—Wheat (Canadian Region 7)

The petitioner is limiting the use of the end-use product to Region 7 of Western Canada. A total of seven trials were conducted in Canada and the United States in Region 7 (Saskatchewan, Nebraska, North Dakota, South Dakota).

Commodity	**Rate (g a.i./ha)**	**PHI (days)**	**Residue (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median**	**Mean**	**SD**
Forage*	9.7–10.5	0	10	0.158	0.777	0.719	0.428	0.418	0.211
Hay*	9.7–10.5	0	10	0.259	2.377	2.318	1.257	1.167	0.79
Grain**	9.4–10.5	49–56	24	0	0.026	0.022	0.013	0.013	0
Straw**	9.4–10.5	49–56	24	0.05	0.145	0.128	0.073	0.082	0.03

* SC/L TIPA salt formulation
** EO TIPA salt, SC/L TIPA salt, SC/L K salt formulations

CROP FIELD TRIALS—Wheat (Canadian and American Trials)

A total of 22 wheat field trials were conducted in Canada and the United States during the 2003 growing season. For the water emulsion in oil (EO) formulation, 2 Canadian wheat field trials were conducted in Region 7 (Saskatchewan; 2 trials) and 20 American wheat field trials were conducted in Region 2 (Virginia; 1 trial), Region 4 (Arkansas; 1 trial), Region 5 (Indiana, Minnesota, Nebraska, North Dakota and South Dakota; 5 trials), Region 6 (Oklahoma; 1 trial), Region 7 (Nebraska, North Dakota and South Dakota; 5 trials), Region 8 (Kansas and Texas; 6 trials) and Region 11 (Washington; 1 trial). For the SC/L TIPA salt formulation and SC/L K salt formulation, a total of seven trials were conducted with each formulation in Region 7 (two trials in Canada and five trials in the United States).

Commodity	Total Rate (g a.i./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	SD
Forage	9.4–10.4	0	72	0.105	0.883	0.85	0.4	0.42	0.186
Hay		0	72	0.259	2.608	2.358	0.956	1.05	0.557
Grain		49–80	72	0	0.026	0.025	0.01	0.012	0
Straw		49–80	72	0	0.17	0.136	0.052	0.057	0.04

RESIDUE DECLINE—Wheat

Residues of aminopyralid declined with time in all matrices.

CROP FIELD TRIALS—Grass

A total of 20 grass field trials were conducted in Canada and the United States during the 2002 growing season. Seven Canadian grass field trials were conducted in Region 7 (Alberta and Saskatchewan; 2 trials) and Region 14 (Alberta, Manitoba and Saskatchewan; 5 trials). Thirteen American grass field trials were conducted in Region 1 (New York and Pennsylvania; 2 trials), 2 (Georgia and Virginia; 2 trials), Region 4 (Louisiana; 1 trial), Region 5 (North Dakota and Ohio; 2 trials), Region 5A (Wisconsin; 1 trial), Region 7 (Montana; 1 trial), Region 8 (Texas; 1 trial), Region 9 (Montana; 1 trial) and Region 11 (Idaho and Washington; 2 trials).

Canadian Trials

Commodity	Total Rate (g a.e./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	SD
Grass Forage	116–125	0	18	7.452	14.033	12.832	10.783	10.801	1.838
		6–8	18	1.276	6.108	5.901	3.746	3.716	1.214
		13–15	18	1.009	3.326	3.201	2.11	2.124	0.608
Grass Straw		0	18	12.91	51.496	49.167	21.857	24.472	10.62
		13–15	18	1.837	9.531	9.215	3.547	4.173	2.325
		20–22	18	2.119	8.708	7.957	3.466	3.976	1.825

American Trials

Commodity	Total Rate g a.i./ha	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	SD
Grass forage	115–125	0	30	3.516	15.551	13.801	7.389	7.264	2.869
		6–8	30	0.232	6.514	5.793	2.361	2.652	1.556
		13–15	30	0.535	8.009	5.464	1.785	1.998	1.315
Grass hay		0	28	9.407	29.962	29.443	17.416	18.269	6.046
		13–15	30	1.762	13.152	10.573	5.148	5.83	3.317
		20–22	30	0.784	17.15	15.623	3.662	4.63	3.593

RESIDUE DECLINE—Grass
Residues declined with time in all grass samples.

MAXIMUM RESIDUE LIMITS	
Wheat, grain	0.04 ppm
Wheat, bran	0.1 ppm
Milk	0.03 ppm
Meat and meat by-products, excluding kidney	0.02 ppm
Kidney	0.3 ppm

PROCESSED FOOD AND FEED		
Processed Commodity (wheat)	Mean Residue Levels (ppm)	Concentration Factor
Raw agricultural commodity	0.054, 0.055	—
Bran	0.143	2.6×
Flour	0.008	~0.2×
Shorts	0.067	1.2×
Middlings	0.032	0.62×
Germ	0.019, 0.021	0.4×, 0.4×
Aspirated grain fractions	0.338	6.1×

LIVESTOCK FEEDING—Cow			
The estimated MTDB for cattle is 58 ppm.			
Tissues/Matrices	Feeding level (ppm)	Mean residue levels (ppm)	Anticipated residues (ppm)
Whole Milk Cream Skimmed Milk Fat Kidney Liver Muscle	64.5	0.024 0.012 0.015 0.013 0.202 0.014 <0.01	0.024 0.012 0.015 0.013 0.202 0.014 <0.01
The MTDB for poultry is 0.18 ppm. A poultry feeding study was not submitted and is not required on the basis of the laying hen metabolism study where it was found (12 ppm aminopyralid in feed or ~66× MTDB) that all residues in poultry commodities were < 0.01 ppm.			

Storage Stability
Wheat Residues of aminopyralid were shown to be stable in/on wheat grain for 168 days and wheat straw for 175 days at -20°C. **Grass** Residues of aminopyralid were shown to be stable in grass forage and hay for 187 days at -20°C. Freezer storage stability data for residues of aminopyralid in/on grass that covers a period of at least 14.5 months are required to support the conditions under which samples were stored in the crop field trials. **Animal Matrices** No freezer storage stability data were submitted for animal matrices.

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

PLANT STUDIES			
ROC FOR ENFORCEMENT **Primary Crops** **Rotational Crops**		Aminopyralid, free and conjugated	
ROC FOR RISK ASSESSMENT **Primary Crops** **Rotational Crops**		Aminopyralid, free and conjugated	
METABOLIC PROFILE IN DIVERSE CROPS		Understood in wheat and grass	
ANIMAL STUDIES			
ANIMALS		**Poultry**	**Ruminant**
ROC FOR ENFORCEMENT		Aminopyralid *per se*	Aminopyralid *per se*
ROC FOR RISK ASSESSMENT		Aminopyralid *per se*	Aminopyralid *per se*
METABOLIC PROFILE IN ANIMALS		Similar in ruminants, poultry and the rat	
FAT SOLUBLE RESIDUE		No.	
DIETARY RISK from food and water			
Chronic Non-Cancer Dietary Risk **ADI = 0.5 mg/kg bw** **EEC = 67 µg/L**	**POPULATION**	**ESTIMATED RISK (% of ADI)**	
		Food (MRL)	**Food (MRL) + EEC**
	All infants < 1 yr old	0.1	1
	Children 1 to 2 yrs	0.3	0.7
	Children 3 to 5 yrs	0.2	0.6
	Children 6 to 12 yrs	0.2	0.4
	Youth 13 to 19 yrs	0.1	0.3
	Adults 20 to 49 yrs	0.1	0.3
	Adults 50+ yrs	0.1	0.3
	Total Population	0.1	0.4

Appendix III Environmental Assessment

Table 1 Physical and Chemical Properties of Aminopyralid Relevant to the Environment

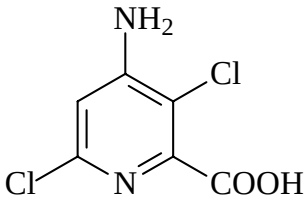
Property	Value	Comments
Chemical Structure Aminopyralid (XDE-750)		Molecular Weight: 206.8 g/mol
Water solubility	2.48 g/L, 18°C	Very soluble
Vapour Pressure	7.14×10^{-11} mm Hg, 20°C	Non-volatile
Henry's Law constant	7.842×10^{-15} (atm.m^3/mol), $1/H = 3.065 \times 10^{12}$	Not expected to be volatile from water and moist soil surfaces
log K_{ow}	0.201, unbuffered water	Not expected to bioconcentrate
pKa	2.56	Dissociates in water, conjugate base will predominate at neutral pH
UV–visible absorption	217 nm max. in neutral solution	Phototransformation in water can occur based on laboratory study

Table 2 Fate and Behaviour in the Terrestrial Environment

Property	Test Substance	Value	Comments
Abiotic transformation			
Hydrolysis	Aminopyralid	Stable	Does not hydrolyze in water and is expected to be similarly stable to hydrolysis in soil
Phototransformation on soil	Aminopyralid	72.2 days	Phototransformation on soil is not expected to be a important dissipation route in the environment
Biotransformation			
Biotransformation in aerobic soil	Aminopyralid	Half-life = 6–330 days	Biotransformation in soil was generally rapid (DT_{50} < 40 days) in four soils while one soil had a much longer transformation half-life of 330 days.
Biotransformation in anaerobic soil	—	N/A	Conducted as part of anaerobic aquatic study with flooded soil.
Mobility			

Property	Test Substance	Value	Comments
Adsorption/ desorption in soil	Aminopyralid	K_{oc} = 1–24	K_{oc} indicates very low adsorption to soil and high mobility
Field studies			
Field dissipation	Aminopyralid Liquid Concentrate Herbicide	DT_{50} = 9–54 days	Non-persistent to moderately persistent in soil, expected to leach in some soils and under conditions of high precipitation; maximum depth detected was 90 cm.

Table 3 Transformation Products in the Terrestrial Environment

Fate Process	Test Material	Major Transformation Products	Minor Transformation Products
Hydrolysis	Aminopyralid	None	
Phototransformation on soil	Aminopyralid	None	CO_2, other
Biotransformation in aerobic soil	Aminopyralid	CO_2 and bound residues	None
Biotransformation in anaerobic soil (flooded soil)	Aminopyralid	None	CO_2
Field dissipation	Aminopyralid Liquid Concentrate Herbicide	Transformation products were not analyzed due to lack of formation under laboratory studies (with exception of photolysis in water).	

Table 4 Fate and Behaviour in the Aquatic Environment

Property	Value	Comments
Abiotic Transformation		
Hydrolysis	Stable	Does not hydrolyze at pH 5–9
Phototransformation in water	$t_{1/2}$ = 0.6 days	Rapid transformation under laboratory conditions. Photolysis may be an important route of transformation in aquatic systems
Biotransformation		
Biotransformation in aerobic water systems	$t_{1/2}$ = 462–990 days	Does not transform to any extent, expected to accumulate, mostly in water and to a lesser extent in sediment.
Biotransformation in anaerobic water systems	Stable	
Partitioning		
Adsorption/desorption in sediment	—	Active ingredient generally partitions to water phase (52–79%), low bound residues (0.7–14%)

Table 5 Expected Environmental Concentrations in Soil

Use/Crop	Application Rate (g a.i./ha)	Number of Applications	Cumulative Application Rate (kg a.i./ha)	EEC 15 cm (mg a.i./kg)
Wheat	10	1	10	0.0044
Range and pasture	120	1	120	0.0533

Table 6 Expected Environmental Concentrations in Water

Use/Crop	Application Rate (g a.i./ha)	Number of Applications	Cumulative Application Rate (kg a.i./ha)	EEC 15 cm (mg a.i./kg)
Wheat	10	1	10	0.0033
Range and pasture	120	1	120	0.04

Table 7 Major Groundwater and Surface Water Model Inputs for Level 1 Assessment of Aminopyralid

Type of Input	Parameter	Value
Application Information	Crop(s) to be treated	Wheat (durum and spring); rangeland and pasture grasses, industrial and non-crop areas
	Maximum allowable application rate per year (kg a.i./ha)	0.12
	Maximum rate each application (kg a.i./ha)	0.12
	Maximum number of applications per year	1
	Minimum interval between applications (days)	N/A
	Method of application	Groundboom
Environmental Fate Characteristics	Hydrolysis half-life at pH 7 (days)	Stable
	Photolysis half-life in water (days)	0.6
	Adsorption K_{oc} (mL/g)	1.05
	Aerobic soil biotransformation half-life (days)	533
	Aerobic aquatic biotransformation half-life (days)	866.4
	Anaerobic aquatic biotransformation half-life (days)	No data; assume stable

Table 8 Level 1 Estimated Environmental Concentrations of Aminopyralid in Potential Drinking Water Sources

Compound	Groundwater EEC (µg a.i./L)		Surface Water EEC (µg a.i./L)			
			Reservoir		Dugout	
	Acute[1]	Chronic[2]	Acute[3]	Chronic[4]	Acute[3]	Chronic[4]
Aminopyralid	66.7	66.7	10.3	1.5	9.5	5.3

Notes:
1 90th percentile of daily average concentrations
2 90th percentile of yearly average concentrations
3 90th percentile of yearly peak concentrations
4 90th percentile of yearly average concentrations

Table 9 Maximum Expected Environmental Concentrations of Aminopyralid in Vegetation and Insects After a Direct Over-spray

Matrix	EEC (mg a.i./kg fw)[a]	Fresh to dry weight ratios	EEC (mg a.i./kg dw)
Short range grass	25.7	3.3[b]	85
Leaves and leafy crops	13.4	11[b]	148
Long grass	11.8	4.4[b]	52
Forage crops	14.4	5.4[b]	78
Small insects	6.2	3.8[c]	24
Pods with seeds	1.3	3.9[c]	5
Large insects	1.1	3.8[c]	4
Grain and seeds	1.1	3.8[c]	4
Fruit	1.6	7.6[c]	12

Note: Pasture and rangeland use and other non-crop uses (120 g a.i./ha × 1 application).
[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973).
[b] Fresh weight/dry weight ratios from Harris (1975) and Fletcher et al. (1974).
[c] Fresh weight/dry weight ratios from Spector (1956).

Table 10 Maximum Expected Environmental Concentrations in the Diet of Birds and Mammals After a Direct Over-spray

Organism	Matrix	EEC (mg a.i./kg dw diet)
Bobwhite quail	30% small insects 15% forage crops 55% grain **Total**	7.11 11.66 2.23 **21.02**
Mallard duck	30% large insects 70% grain **Total**	1.22 2.84 **4.06**
Rat	70% short grass 20% grain/seeds 10% large insects **Total**	59.32 0.81 0.41 **60.54**
Mouse	25% short grass 50% grain/seeds 25% leaves and leafy crops **Total**	21.19 2.03 36.96 **60.18**
Rabbit	25% short grass 25% leaves and leafy crops 25% long grass 25% forage crops **Total**	21.19 36.96 12.94 19.44 **90.52**

Note: Pasture and rangeland use and other non-crop uses (120 g a.i./ha × 1 application).

Table 11 Effects on Terrestrial Organisms

Organism	Exposure	Test Substance	Endpoint Value	Degree of Toxicity[a]
Invertebrates				
Earthworm	Acute	Aminopyralid (TGAI)	LC_{50} > 1000 mg a.i./kg	Non-toxic
Bee	Oral	Aminopyralid (TGAI)	NOEC = 100 µg a.i./bee LD_{50} > 100 µg a.i./bee	Relatively non-toxic
	Contact	Aminopyralid (TGAI)	NOEC = 117 µg a.i./bee LD_{50} > 117 µg a. i./bee	Relatively non-toxic
Birds				
Bobwhite quail	Acute	Aminopyralid (TGAI)	LD_{50} > 2250 mg a.i./kg bw NOAEL = 14 mg a.i./kg bw (sublethal effects)	Practically non-toxic
	Dietary	Aminopyralid (TGAI)	LC_{50} > 5556 mg a.i./kg dw NOAEL 5556 mg a.i./kg dw	Practically non-toxic
	Reproduction	Aminopyralid (TGAI)	NOAEL = 2610 mg a.i./kg dw LOAEL > 2610 mg a.i./kg dw	—

Organism	Exposure	Test Substance	Endpoint Value	Degree of Toxicity[a]
Mallard duck	Dietary	Aminopyralid (TGAI)	LC_{50} > 5496 mg a.i./kg dw NOAEL = 5496 mg a.i./kg dw	Practically non-toxic
	Reproduction	Aminopyralid (TGAI)	NOAEL = 2623 mg a.i./kg dw LOAEL > 2623 mg a.i./kg dw	—
Mammals				
Rat	Acute-oral	Aminopyralid (TGAI)	LD_{50} greater than 5,000 mg/kg bw for both sexes	Practically non-toxic
	Acute-oral	Aminopyralid (EP)	LD_{50} greater than 5000 mg/kg bw for both sexes	Practically non-toxic
	Dietary (90-day)	Aminopyralid (TGAI)	NOAEL: Males: 6750 mg a.i./kg diet (500 mg/kg bw/day). Females: 14 100 mg a.i./kg diet (1000 mg/kg bw/day). LOAEL: Males: 13 100 mg a.i./kg diet (1000 mg/kg bw/day). Females: not determined	—
	Reproduction (2-generation)	Aminopyralid (TGAI)	**Parental//Offspring/ Reproductive:** NOAEL: 10 000 mg a.i./kg dw diet (1000 mg a.i./kg bw) LOAEL: not reported	—
Mouse	Dietary (90 day)	Aminopyralid (TGAI)	NOAEL: Males and females: 6520 mg a.i./kg diet (1000 mg/kg bw/day) LOAEL: not reported	—
Vascular Plants				
Vascular plant	Seedling emergence	Aminopyralid Liquid Concentrate Herbicide	EC_{25} = 1.4 g aminopyralid/ha[b]	
	Vegetative vigour	Aminopyralid Liquid Concentrate Herbicide	EC_{25} = 0.39 g aminopyralid/ha	

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

[b] aminopyralid = acid equivalent = active ingredient.

Table 12 Effects on Aquatic Organisms

Organism	Exposure	Endpoint Value	Degree of Toxicity[a]
Freshwater Species			
Daphnia magna	Acute	48-hour EC_{50} > 98.6 mg a.i./L 48-hour NOEC = 98.6 mg a.i./L	Practically non-toxic
	Chronic	21-day NOEC = 102 mg a.i./L (reproduction and growth)	—
Chironomus riparius	Chronic	28-day NOEC = 33 mg a.i./kg (123 mg a.i./L) (% emergence)	—
Rainbow trout	Acute	The 96-hour LC_{50} > 100 mg a.i./L NOEC = 100 mg a.i./L. (mortality; note 2/30 fish showed partial loss of equilibrium)	Practically non-toxic
Bluegill sunfish	Acute	96-hour LC_{50} > 100 mg a.i./L NOEC = 100 mg a.i./L. (mortality and sublethal effects)	Practically non-toxic
Fathead minnow	Early life-stage	**NOEC = 1.36 mg a.i./L** (growth, larval survival and sublethal effects) LOEC = 2.44 mg a.i./L (growth, larval survival and sublethal effects)	—
Freshwater alga	Acute	*Pseudokirchneriella* NOEC = 23 mg a.i./L (all endpoints). EC_{50} = 30 mg a.i./L (growth rate) *Navicula pelliculosa* 96-hour NOEC = 6 mg a.i./L (cell density and biomass) LOEC = 12 mg a.i./L (cell density and biomass)	—
Vascular plant (Lemna)	Dissolved	14-day NOEC = 44 mg a.i./L (frond number) EC_{50} >88 mg a.i./L (frond number)	Low acute sensitivity
	Over-spray	—	—
Leopard frog	acute	96-hour LC_{50} > 95.2 mg a.i./L NOEC = 95.2 mg a.i./L	Practically non-toxic
Marine Species			
Crustacean (Mysid)	Acute	96-hour LC_{50} > 100mg a.i./L 96-hour NOEC = 100 mg a.i./L (mortality) LOEC > 100 mg a.i./L	Practically non-toxic
Eastern oyster	Acute	96-hour EC_{50} > 89 mg a.i./L (shell deposition) NOEC = 89 mg a.i./L.	Practically non-toxic
Sheepshead minnow	Acute	96-hour LC_{50} >120 mg a.i./L 96-hour NOEC = 120 mg a.i./L	Practically non-toxic
	Salinity challenge	Not submitted	—

Organism	Exposure	Endpoint Value	Degree of Toxicity[a]
Marine alga (Skeletonema)	Acute	96-hour NOEC = 13 mg a.i./L (biomass and growth rate) EC_{50} = 70 mg a.i./L (biomass)	Low acute sensitivity

[a] USEPA classification, where applicable.

Table 13 Classification of Risk Quotients

Risk Quotient (RQ) [EEC/NOEC or EEC/EC_{25} for terrestrial plants)]	Risk Category
<0.1	Negligible risk
0.1 to <1.0	Low risk
1.0 to <10	Moderate risk
10 to <100	High risk
100 to <1000	Very high risk
≥1000	Extremely high risk

Table 14 Risk to Terrestrial Organisms

Organism	Exposure	Endpoint Value	EEC	RQ	Risk
Invertebrates					
Earthworm	Acute	LC_{50} > 1000 mg a.i./kg	0.0533 mg a.i./kg	5×10^{-5}	Negligible
Bee	Oral	LD_{50} > 100 µg a.i./bee	120 g a.i./ha	N/A	Relatively non-toxic
	Contact	LD_{50} > 117 µg a. i./bee (131 kg a.i./ha)	120 g a.i./ha	N/A	Relatively non-toxic
Birds					
Bobwhite quail	Acute	NOAEL = 14 mg a.i./kg bw	21.02 mg a.i./kg dw diet	5.9 days[a]	Negligible
	Dietary	NOEC = 5556 mg a.i./kg dw	21.02 mg a.i./kg dw diet	0.0038	Negligible
	Reproduction	NOEC = 2610 mg a.i./kg dw	21.02 mg a.i./kg dw diet	0.008	Negligible
Mallard duck	Dietary	NOEC = 5496 mg a.i./kg dw	4.06 mg a.i./kg dw diet	0.00074	Negligible
	Reproduction	NOEC = 2623 mg a.i./kg dw	4.06 mg a.i./kg dw diet	0.0015	Negligible
Mammals					
Rat	Acute	Oral LD_{50} > 5000 mg/kg bw 1/10 LD_{50} = 500 mg/kg bw	60.54 mg a.i./kg dw diet	48.2 days[a]	Negligible
	Dietary (90-day)	NOAEL = 6750 mg a.i./kg dw diet	60.54 mg a.i./kg dw diet	0.009	Negligible
	Reproduction	NOAEL = 15 400 mg a.i./kg dw diet	60.54 mg a.i./kg dw diet	0.0039	Negligible
Mouse	Dietary (90-day)	NOEC = 6520 mg a.i./kg dw diet	60.18 mg a.i./kg dw diet	0.009	Negligible
Vascular Plants					
Vascular plant	Seedling emergence	EC_{25} = 1.4 g aminopyralid/ha (shoot weight)	120 g aminopyralid/ha[b]	86	**High**
	Vegetative vigour	EC_{25} = 0.39 g aminopyralid/ha (shoot length)	120 g aminopyralid/ha[b]	308	**Very high**

N/A Not available for bees.

[a] The number of feeding days required to reach the toxicity endpoint was calculated as # days = $NOEL_{(individual)}$/daily intake.

[b] Vascular plants were exposed to the end-use product Aminopyralid Liquid Concentrate Herbicide containing the TIPA salt of aminopyralid, EEC is expressed based on acid equivalent (aminopyralid)/ha.

Table 15 Risk to Aquatic Organisms

Organism	Exposure	Endpoint Value	EEC	RQ	Risk
Freshwater Species					
Daphnia magna	Acute	48-hour NOEC = 98.6 mg a.i./L	0.04 mg a.i./L	0	Negligible
	Chronic	21-day NOEC = 102 mg a.i./L (reproduction and growth)	0.04 mg a.i./L	0	Negligible
Chironomus riparius	Chronic	28-day NOEC = 33 mg a.i./kg (123 mg a.i./L)	0.04 mg a.i./L	0	Negligible
Rainbow trout	Acute	NOEC = 100 mg a.i./L (mortality)	0.04 mg a.i./L	0	Negligible
Bluegill sunfish	Acute	NOEC = 100 mg a.i./L (mortality and sublethal effects)	0.04 mg a.i./L	0	Negligible
Freshwater alga	Acute	96-hour NOEC = 6 mg a.i./L (cell density and biomass)	0.04 mg a.i./L	0.007	Negligible

Organism	Exposure	Endpoint Value	EEC	RQ	Risk
Vascular plant	Dissolved	14-day NOEC = 44 mg a.i./L (frond number)	0.04 mg a.i./L	0	Negligible
Leopard frog tadpole	Acute	NOEC = 95.2 mg a.i./L	0.04 mg a.i./L	0	Negligible
Marine Species					
Crustacean (Mysid)	Acute	96-hour NOEC = 100 mg a.i./L (mortality)	0.04 mg a.i./L	0	Negligible
Mollusk	Acute	NOEC = 89 mg a.i./L	0.04 mg a.i./L	0	Negligible
Sheepshead minnow	Acute	96-hour NOEC = 120 mg a.i./L	0.04 mg a.i./L	0	Negligible
Marine alga	Acute	96-hour NOEC = 13 mg a.i./L (biomass and growth rate)	0.04 mg a.i./L	0.003	Negligible

References

Atkins, EL; Kellum D; Atkins KW. 1981. *Reducing Pesticide Hazards to Honey Bees: Mortality Prediction Techniques and Integrated Management Techniques*. University of California, Division of Agricultural Sciences, Leaflet 2883. 22 pp.

British Columbia Ministry of Agriculture, Food and Fisheries. 1998. *Integrated Weed Management: An Introductory Manual*. Province of British Columbia. Available online at www.agf.gov.bc.ca/cropprot/weedman.htm.

Fraiser Basin Council. [N.D.] *Invasive Plant Strategy for British Columbia*. 36 pp. Available online through www.fraserbasin.bc.ca/.

Cohen SZ, Creeger SM, Carsel RF, Enfield CG. 1984. Potential for pesticide contamination of groundwater resulting from agricultural uses. In RF Krugger and JN Seiber (eds). *Treatment and Disposal of Pesticide Wastes*. ACS Symposium Series No. 259. American Chemical Society, Washington, DC. pp 297–325.

Fletcher JS; Nellessen JE; Pfleeger TG. 1994. Literature review and evaluation of the EPA food chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. *Environmental Toxicology and Chemistry*, 13:1383–1391.

Ganzelmeier H; et al. 1995. Studies on the spray drift of plant protection products: Results of a test program carried out throughout the Federal Republic of Germany. Report Number 305 from the Biologischen Bundesanstalt fur Land und Forstwirtschaft, Berlin-Dahlem. Blackwell Wissenschafts-Verlag GmbH, Berlin/Vienna.

Goring CAI; Laskowski DA; Hamaker JH; Meikle RW. 1975. Principles of pesticide degradation in soil. In R Haque and VH Freed (eds). *Environmental Dynamics of Pesticides*. Plenum Press, New York. pp 135–172 .

Harris, LE. 1975. *Guide for Estimating Toxic Residues in Animal Feeds or Diets*. Unites States Environmental Protection Agency, Washington. Document Code EPA/540/9-75-019 (NTIS reference #: PB 243 748).

Hoerger, F; Kenaga EE. 1972. Pesticide residues on plants: correlation of representative data as basis for estimation of their magnitude in the environment. In Coulston F and Korte F (eds). *Global Aspects of Chemistry, Toxicology and Technology as Applied to the Environment*, Vol. I. Thieme, Stuttgart, and Academic Press, New York. pp. 9–28.

Kenaga EE. 1973. Factors to be considered in the evaluation of the toxicity of pesticides to birds in their environment. In: Coulston F; Dote F. (eds). *Global Aspects of Chemistry, Toxicology and Technology as Applied to the Environment*, Vol. II. Thieme, Stuttgart, and Academic Press, New York. pp. 166–181.

Kennedy, J.M., and R.E. Talbert. 1977. Comparative persistence of dinitroaniline type herbicides on the soil surface. *Weed Science*. 25(5): 373–381.

McCall JP; Laskowski DA; Swann RL; Dishburger HJ. 1981. Measurement of sorption coefficients of organic chemicals and their use in environmental fate analysis. In: Proceedings of symposium, Test protocols for environmental fate and movement of toxicants, Association of Official Environmental Chemists, 94th Annual Meeting, Washington, DC, 21–22 October1980. pp 89–109.

McEwen, F.L., and G.R. Stephenson. 1979. *The Use and Significance of Pesticides in the Environment*. John Wiley and Sons Inc, Toronto, Ontario, Canada.

Spector WS. 1956. *Handbook of Biological Data*. W. B. Saunders, Philadelphia, p. 78, 187.

Urban DG; Cook NJ.1986. *Ecological Risk Assessment*. United States Environmental Protection Agency, Washington, DC. Document Code EPA 540.9-85-001. 96 pp.