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Evaluation Report

Pyrasulfotole

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OVERVIEW

Registration Decision for Pyrasulfotole

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and in accordance with the Pest Control Products Regulations, has granted conditional registration for Pyrasulfotole Technical Herbicide, Infinity Herbicide and AE 0317309 02 SE06 Herbicide containing the technical grade active ingredient pyrasulfotole to control a range of broadleaf weeds in wheat (spring, durum and winter), barley, oats, triticale, and timothy (grown for seed production).

Current scientific data from the applicant and information from other regulatory agencies were evaluated to determine if, under the proposed conditions of use, these products have value and do not present an unacceptable risk to human health or the environment.

This report summarizes the information evaluated and provides the results of the evaluation as well as the reasons for the conditional registration decision, with an outline of the additional scientific information required from the applicant. It also describes the conditions of registration that the applicant must meet to ensure that the health and environmental risks as well as the value of these pest control products are acceptable for their intended use.

This Overview describes the key points of the evaluation, while the Science Evaluation section provides detailed technical information on the human health, environmental and value assessments of Pyrasulfotole Technical Herbicide, Infinity Herbicide and AE 0317309 02 SE06 Herbicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks[1] to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions or proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act.*

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

What Is Pyrasulfotole?

Pyrasulfotole is a postemergence herbicide, i.e. a herbicide applied after the crop has emerged above the ground. It belongs to the chemical class of pyrazolones and is a pigment inhibitor or bleacher. Pyrasulfotole inhibits an enzyme in susceptible plants, which in turn disrupts the synthesis of essential pigments found in the leaves of all plants.

AE 0317309 02 SE 06 Herbicide contains the active ingredient pyrasulfatole only, while Infinity Herbicide (AE 0317309 03 EC23 Herbicide) is a coformulation of the active ingredients pyrasulfatole and bromoxynil.

Health Considerations

Can Approved Uses of Pyrasulfotole Affect Human Health?

Pyrasulfotole is unlikely to affect your health when used according to the label directions.

People could be exposed to pyrasulfotole through diet (food and water) or when handling and applying the product. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when using pyrasulfotole products according to the label directions.

Pyrasulfotole end-use products AE 0317309 02 SE 06 Herbicide and Infinity Herbicide caused eye and skin irritation in rabbits. Infinity Herbicide was moderately acutely toxic when tested in rats.

When tested in laboratory animals, technical pyrasulfotole was not genotoxic[3], but, at very high dose levels, induced urinary bladder tumours in male and female mice and a very low incidence of eye tumours in male rats. A risk assessment was conducted to ensure that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

At high dose levels, pyrasulfotole retarded the development of rat and rabbit fetuses. However, it did not affect reproductive performance in the rat. The rabbit teratology data demonstrated higher sensitivity of offspring when compared to the maternal animals. Studies did not provide evidence of teratogenicity in rats and rabbits or neurotoxicity in rats. There was no indication that pyrasulfotole affects the immune and endocrine systems.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and children, the subpopulation which would ingest the most pyrasulfotole relative to body weight, are expected to be exposed to less than 59.7% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from pyrasulfotole is not of concern for all population subgroups.

A single dose of pyrasulfotole is not likely to cause acute health effects in the general population (including infants and children). An aggregate (food and water) dietary intake estimate for females 13–49 used less than 3.8% of the acute reference dose, which is not a health concern.

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using products containing pyrasulfotole on wheat, barley, oat, triticale and timothy (grown for seed production only) were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this report.

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[3] Genotoxic chemicals are those capable of causing damage to DNA. Such damage can potentially lead to the formation of a malignant tumor, but DNA damage does not lead inevitably to the creation of cancerous cells.

Occupational Risks From Handling Pyrasulfotole

Occupational risks are not of concern when AE 0317309 02 SE 06 Herbicide or Infinity Herbicide are used according to the label directions, which include protective measures.

Farmers and pesticide applicators mixing, loading or applying AE 0317309 02 SE06 Herbicide or Infinity Herbicide as well as field workers re-entering freshly treated fields can come in direct contact with AE 0317309 02 SE06 Herbicide or Infinity Herbicide on the skin or through inhalation of spray mists. Therefore, the labels specify that a long-sleeved shirt, long pants, shoes and socks must be worn during application as well as chemical-resistant gloves and goggles or face shield must be worn during mixing/loading, clean-up and repair activities for both end-use products. The label also requires that workers do not enter treated fields for up to 12 hours after application. Taking into consideration these label statements and that occupational exposure is expected to be brief, as this herbicide is applied only once per year, risk to farmers, custom applicators or workers is not a concern.

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Pyrasulfotole Is Introduced Into the Environment?

Pyrasulfotole enters the environment when used as a herbicide on cereal crops. Pyrasulfotole is moderately persistent and mobile in soil and persistent in water. The major breakdown product AE B197555 (pyrasulfotole-benzoic acid) is moderately persistent in soil, and was only found in minor amounts in water. Pyrasulfotole and AE B197555 are expected to leach through the soil profile beyond 30 cm; therefore, they may be expected to enter groundwater. In surface waters, pyrasulfotole will partition to sediments and may be expected to accumulate in aquatic systems. Canadian field studies demonstrated that up to approximately 19% of applied pyrasulfotole is expected to carry over to the following growing season. Based on its low volatility, pyrasulfotole residues are not expected in the air.

Pyrasulfotole and its major breakdown product present a low risk to wild mammals, birds, earthworms, bees and other arthropods, aquatic invertebrates, fish, algae and aquatic plants. However, given that pyrasulfotole is a herbicide, it is expected to adversely affect terrestrial plants in adjacent areas. Therefore, buffer zones of 2 to 375 metres (depending on end-use product formulation and application equipment) are required to protect nearby plants from the effects of spray drift. The end-use product Infinity Herbicide also requires a 10-m aquatic buffer zone due to toxicity from bromoxynil in the formulation.

Value Considerations

What Is the Value of Pyrasulfotole?

> **Pyrasulfotole is a postemergence herbicide, i.e. a herbicide applied after the crop has emerged above the ground, to control lamb's quarters, redroot pigweed, wild buckwheat and volunteer canola (including herbicide tolerant varieties) in wheat (spring, durum and winter), barley, tame oats, triticale and timothy (grown for seed production)**.
>
> A single application of pyrasulfotole provides effective control of lamb's quarters, redroot pigweed, wild buckwheat as well as volunteer canola in wheat (spring, durum and winter), barley, oats, triticale and timothy (grown for seed production). Pyrasulfotole is compatible with integrated weed management practices, conservation tillage, and conventional crop production systems. Pyrasulfotole is applied after weed emergence; therefore, growers are able to assess whether the herbicide is suitable for the particular weed species present. Pyrasulfotole also provides control of both conventional and herbicide tolerant canola types including glyphosate, glufosinate-ammonium and aceto-lactate synthase (ALS) tolerant canola types.

Measures to Minimize Risk

Labels or registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. The PMRA is requiring key risk-reduction measures on the labels of AE 0317309 02 SE06 Herbicide and Infinity Herbicide.

Human Health

Because there is a concern with users coming into direct contact with AE 0317309 02 SE06 Herbicide or Infinity Herbicide via the skin or through inhalation of spray mists, a long-sleeved shirt, long pants, shoes and socks must be worn during application. In addition, chemical-resistant gloves and goggles or face shield must be worn during mixing/loading, clean-up and repair activities.

Environment

- **Environmental Label Statements for Pyrasulfatole Technical Herbicide Label**

  Add to **ENVIRONMENTAL HAZARDS:**

  > TOXIC to aquatic organisms.

Add to **DIRECTIONS FOR USE:**

DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.

- **Environmental Label Statements for AE 0317309 02 SE 06 Herbicide and Infinity Herbicide Labels:**

Add to **ENVIRONMENTAL HAZARDS:**

TOXIC to aquatic organisms and non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE.

This product contains aromatic petroleum distillates that are toxic to aquatic organisms.

The use of this chemical 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.

To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil or clay.

Avoid application 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.

Add to **DIRECTIONS FOR USE:**

DO NOT apply this product directly to freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands), or estuarine/ marine habitats.

DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

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 American Society of Agricultural and Biological Engineers (ASABE) medium classification. Boom height must be 60 cm or less above the crop or ground.

<u>Aerial application</u>: **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 American Society of Agricultural and Biological Engineers (ASABE) medium classification. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length **MUST NOT** exceed 65% of the wing- or rotorspan.

- **Buffer zones:**

For AE 0317309 02 SE06 Herbicide:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: handheld or backpack sprayer, inter-row hooded sprayer, spot treatment, soil drench and soil incorporation.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands).

Method of Application	Crop		Buffer Zones (metres) Required for the Protection of Terrestrial Habitat:
Field sprayer*	Wheat (spring, durum, winter), barley, oats, triticale, timothy (seed production only)		2
Aerial	Wheat (spring, durum, winter), barley, oats, triticale, timothy (seed production only)	Fixed wing	85
		Rotary wing	70

* For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the canopy or ground, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the canopy or ground, the labelled buffer zone can be reduced by 30%.

For Infinity Herbicide:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: handheld or backpack sprayer, inter-row hooded sprayer, spot treatment, soil drench and soil incorporation.

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

Method of Application	Crop		Buffer Zones (metres) Required for the Protection of:		
			Freshwater Habitat of Depths:		Terrestrial Habitat
			Less than 1 m	Greater than 1 m	
Field sprayer*	Wheat (spring, durum, winter), barley, triticale, timothy (seed production only)		1	1	5
Aerial	Wheat (spring, durum, winter), barley, triticale, timothy (seed production only)	Fixed wing	10	1	375
		Rotary wing	10	1	225

* For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the canopy or ground, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the canopy or ground, the labelled buffer zone can be reduced by 30%.

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture.

What Additional Scientific Information Is Required?

Although the risks and value have been found acceptable when all risk-reduction measures are followed, the applicant must submit additional scientific information as a condition of registration. More details are presented in the Science Evaluation section of this report or in the Section 12 Notice associated with these conditional registrations. The applicant must submit the following information within the time frames indicated.

- **Human Health**
    - An enforcement method that quantifies the parent pyrasulfotole and the metabolite pyrasulfotole-desmethyl in animal matrices. The applicant must submit this information no later than 1 September 2009.

- **Environment**

    - Provide the log K_{ow} for AE B197555 to demonstrate that this transformation product is not bioaccumulative according to Toxic Substances Management Policy Track1 criteria.

    - Due to the pyrasulfotole's persistence in water and ability to partition to sediments, a chronic toxicity study with a benthic invertebrate species, such as chironomids (DACO 9.3.4—Laboratory Studies with Other Species) is required. The study must conform to standard international guidelines (e.g. United States Environmenal Protection Agency, Organisation for Economic Co-operation and Development, ASTM International, Environment Canada) and be conducted under good laboratory practice. The applicant must submit this information no later than 1 September 2009.

Other Information

As these conditional registrations relate to a decision on which the public must be consulted[4], the PMRA will publish a consultation document when there is a proposed decision on the applications to convert the conditional registrations to full registrations or on the applications to renew the conditional registrations, whichever occurs first.

The test data cited in this Evaluation Report (i.e. the test data relevant in supporting the registration decision) will be made available for public inspection when the decision is made to convert the conditional registrations to full registrations or to renew the conditional registrations (following public consultation). If more information is required, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

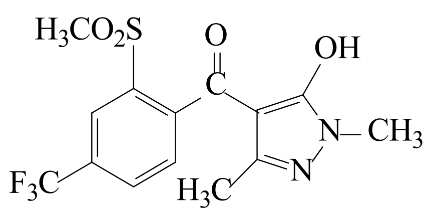
[4] As per subsection 28(1) of the *Pest Control Products Act*.

SCIENCE EVALUATION

Pyrasulfotole

1.0 The Technical Grade Active Ingredient, its Properties and Uses

1.1 Identity of the Technical Grade Active Ingredient

Active substance	Pyrasulfotole
Function	Herbicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	(5-Hydroxy-1,3-dimethylpyrazol-4-yl)(α,α,α-trifluoro-2-mesyl-*p*-tolyl)methanone
2. Chemical Abstracts Service (CAS)	(5-Hydroxy-1,3-dimethyl-1*H*-pyrazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl]methanone
CAS number	365400-11-9
Molecular formula	$C_{14}H_{13}F_3N_2O_4S$
Molecular weight	362.32 g/mol
Structural formula	
Purity of the technical grade active ingredient	98.6% nominal (limits: 96.0–100%)

1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Products

Technical Product—Pyrasulfotole Technical Herbicide

Property	Result
Colour and physical state	Light beige powder
Odour	No characteristic odour
Melting point	201 °C

Property	Result
Boiling point or range	Not applicable
Specific gravity	1.5 at 20°C
Vapour pressure	2.7×10^{-7} Pa at 20°C 6.8×10^{-7} Pa at 25°C
Henry's law constant at 20°C	pH — Value ($Pa \cdot m^3 mol^{-1}$) 4 — 2.33×10^{-8} 7 — 1.42×10^{-9} 9 — 2.00×10^{-9} doubly distilled water — 4.25×10^{-8}
Ultraviolet (UV)—visible spectrum	λ_{max} = 306 nm
Solubility in water at 20°C	pH — Solubility g/L 4 — 4.2 7 — 69.1 9 — 49.0 doubly distilled water — 2.3
Solubility in organic solvents at 20°C	Solvent — Solubility (g/L) ethanol — 21.6 n-hexane — 0.038 toluene — 6.86 dichloromethane — 120 - 150 acetone — 89.2 ethyl acetate — 37.2 dimethylsulfoxide — > 600
n-Octanol–water partition coefficient (K_{ow})	pH — log K_{ow} 4 — 0.276 7 — -1.362 9 — -1.580
Dissociation constant (pK_a)	4.2 ± 0.15
Stability (temperature, metal)	No signifiant degradation over 12 months at ambient temperatures and over 2 weeks at 54°C. Iron, aluminum ions and ferric ions do not increase the degradation.

End-Use Products: AE 0317309 02 SE06 Herbicide and Infinity Herbicide (AE 0317309 03 EC23 Herbicide)

Property	AE 0317309 02 SE06 Herbicide	Infinity Herbicide
Colour	Opaque light brown	Dark amber
Odour	Aromatic solvent odour	Aromatic solvent odour.
Physical state	Viscous liquid	Liquid
Formulation type	Suspension	Emulsifiable concentrate
Guarantee	Pyrasulfotole: 50 g/L nominal (limits: 47.5 g/L - 52.5 g/L)	Pyrasulfotole: 37.5 g/L (limits: 35.8 g/L - 39.5 g/L) Bromoxynil: 210 g/L (limits: 204 g/L - 216 g/L)
Container material and description	Fluorinated (barrier) high density polyethylene (HDPE) or HDPE/nylon coextruded bottles/jars, 1 L	Plastic 1 L - Bulk
Density	1.1441 g/cm^3 at 20°C	1.1447 g/cm^3 at 20°C
pH of 10% dispersion in water	4	3.9
Oxidizing or reducing action	The product does not contain any oxidizing or reducing agents.	The product does not contain any oxidizing or reducing agents.
Storage stability	The product was shown to be stable for one year when stored under warehouse conditions in the commercial packaging.	The product was shown to be stable for one year when stored under warehouse conditions in the commercial packaging.
Explodability	The product is not explosive.	The product is not explosive.

1.3 Directions for Use

1.3.1 AE 0317309 02 SE 06 Herbicide

AE 0317309 02 SE 06 Herbicide is a selective herbicide for use as a post-emergence treatment on wheat (spring, durum and winter), barley, tame oats, triticale, and timothy (grown for seed production), for the control of lamb's quarters, redroot pigweed, wild buckwheat and volunteer canola (including herbicide tolerant varieties). The product is applied once per growing season at a rate of 50 g a.i./ha (Table 1.3.1.1) as a broadcast treatment with either ground or aerial application equipment.

Table 1.3.1.1 Weed Control Claims for AE 0317309 02 SE 06 Herbicide

Herbicide Rate	Weeds Controlled
50 g a.i./ha or 1 L product/ha	lamb's quarters, redroot pigweed, wild buckwheat, volunteer canola (conventional and herbicide tolerant)

1.3.2 Infinity Herbicide

Infinity Herbicide is a selective herbicide for use as a post-emergence treatment on wheat (spring, durum and winter), barley, triticale, and timothy (grown for seed production), for the control of a wide range of broadleaved weeds. The product is to be applied once per growing season at a rate of 205.5 g a.i./ha (31.125 g a.i./ha pyrasulfatole and 174.3 g a.i./ha bromoxynil) (Table 1.3.2.1) as a broadcast treatment with either ground or aerial application equipment.

Table 1.3.2.1 Weed Control Claims for Infinity Herbicide

Herbicide Rate	Weeds Controlled	Weeds Suppressed
205.5 g a.i./ha or 0.83 L product/ha (174.3 g/ha bromoxynil + 31.125 g/ha pyrasulfotole)	annual sow-thistle, chickweed, cleavers, flixweed, hemp-nettle, kochia, lamb's-quarters, pale smartweed, redroot pigweed, Russian thistle, shepherd's-purse, stinkweed, volunteer canola (includes conventional and herbicide tolerant), wild buckwheat, wild mustard	Canada thistle, dandelion, perennial sow-thistle

1.4 Mode of Action of Pyrasulfotole

Pyrasulfotole is classified as a Group 27 Herbicide (refer to Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*). The primary mode of action of pyrasulfotole is as an inhibitor of the enzyme 4-hydroxyphenylpyruvate dioxygenase (4-HPPD) in susceptible plants, thereby disrupting the synthesis of carotenoids that are produced by plants to protect against oxidative and photolytic damage. Visible effects may not be observed for several days and appear as white splotches on the leaves of susceptible plants, as pyrasulfotole is a pigment inhibiting or bleaching herbicide.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Pyrasulfotole Technical Herbicide have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The methods provided for the analysis of the active ingredient in the formulations have been validated and assessed to be acceptable for use as enforcement analytical methods.

2.3 Methods for Residue Analysis

2.3.1 Multi-residue methods for residue analysis

Pyrasulfotole and pyrasulfotol-desmethyl were tested according to Protocols A, B and C of the FDA PAM I testing procedures. Protocol A of the PAM I testing procedures is not suitable for the detection of pyrasulfotole or pyrasulfotole-desmethyl because neither compound is an *N*-methyl carbamate or is naturally fluorescent. Protocol B of the PAM I testing procedures is not suitable for the detection of pyrasulfotole-desmethyl although pyrasulfotole is partially recovered through Protocol B. Protocol C module DG-17 could be used for the detection of pyrasulfotole. No other module in Protocol C can be used reliably for the detection of either pyrasulfotole or pyrasulfotole-desmethyl.

2.3.2 Methods for Residue Analysis of Plant and Plant Products

A high-performance liquid chromatography–electrospray ionization with tandem mass spectrometry (LC-MS/MS) method was developed for the analysis of pyrasulfotole, pyrasulfotole-desmethyl and pyrasulfotole-benzoic acid in food of plant origin. This method fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. The limit of quantitation for each analyte in plant products was reported to be 0.01 ppm. Acceptable recoveries (70–120%) of pyrasulfotole residues were obtained in plant matrices. Extraction efficiency data demonstrated that the enforcement method can account for incurred residues of pyrasulfotole, pyrasulfotole-desmethyl, and pyrasulfotole-benzoic acid in wheat grain, forage and hay.

2.3.3 Methods for Residue Analysis of Food of Animal Origin - Ruminant

A high-performance liquid chromatography–electrospray ionization with tandem mass spectrometry (LC-MS/MS) method was developed for the analysis of pyrasulfotole in ruminant matrices. This method fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. The limit of quantitation of 0.01 ppm was demonstrated for bovine meat, kidney, liver, fat and 0.005 ppm for whole milk, skim milk and whipping cream. Acceptable recoveries (70–120%) of pyrasulfotole residues were obtained in ruminant matrices. Extraction efficiency data demonstrated that the enforcement method can account for incurred residues of pyrasulfotole in kidney, liver and whole milk. However, the residues of pyrasulfotole-desmethyl were not determined in livestock commodities.

2.3.3.1 Methods for Residue Analysis of Food of Animal Origin - Poultry

A high-performance liquid chromatography–electrospray ionization with tandem mass spectrometry (LC-MS/MS) method was developed for the analysis of pyrasulfotole-benzoic acid in poultry matrices. This method fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. The limit of quantitation of 0.01 ppm was demonstrated for chicken muscle, liver, skin and eggs. Acceptable recoveries (70–120%) of pyrasulfotole-benzoic acid residues were obtained in poultry matrices.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

The PMRA conducted a detailed review of the toxicological database for pyrasulfotole. The database consists of an array of laboratory animal (*in vivo*) and cell culture (*in vitro*) toxicity studies currently required for health hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is acceptable, and the database is considered adequate to characterize the toxicity of this pest control product.

Technical pyrasulfotole is of low acute toxicity by the oral, dermal, and inhalation routes in rats. It was not irritating when applied to the skin of rabbits, but was mildly irritating to the rabbit eye. The skin sensitization testing in guinea pigs using the maximization method was deficient because of inadequate topical induction and challenge applications. Thus, technical pyrasulfotole is considered a potential dermal sensitizer in the absence of adequate data.

The formulations of pyrasulfotole, namely, AE 0317309 02 SE 06 Herbicide and Infinity Herbicide, are of low acute toxicity by the dermal, and inhalation routes in rats. AE 0317309 02 SE 06 Herbicide also has low acute oral toxicity potential in rats, but Infinity Herbicide is moderately acutely toxic by the oral route in rats. They are moderately irritating to the rabbit eye and are mildly irritating to the rabbit skin. The formulations are not dermal sensitizers when tested in guinea pigs based on the Buehler protocol.

The absorption, distribution, elimination, and metabolism of pyrasulfotole were studied in male Wistar rats following single oral and i.v. administration. The results indicated that pyrasulfotole was rapidly absorbed and excreted. Over 96% of the administered dose was excreted within 24 h, mostly in the urine. Fecal excretion represented 8-10% of the administered dose. No volatile residues were detected. Residue levels in tissues were low. Metabolite identification indicated that 87-95% of the administered dose was excreted unchanged as pyrasulfotole. Hydroxymethyl pyrasulfotole, desmethyl-pyrasulfotole, and AE B197555 were observed as minor metabolites in the urine and feces. Based on the metabolite profiles, the major metabolic pathway occurred via N-demethylation of pyrasulfotole.

A 4-week dermal toxicity study in rats showed no skin reaction following daily application of pyrasulfotole at ≤ 1000 mg/kg bw/d. However, repeat dermal application of pyrasulfotole resulted in pathology of the pancreas (focal degeneration) at ≥100 mg/kg bw/d in males and at 1000 mg/kg bw/d in females. In the male, thyroid pathology (colloid alteration) as well as increase in plasma levels of cholesterol and triglycerides were also induced at 1000 mg/kg bw/d.

In short- and long-term dietary toxicity studies in mice, rats, and dogs, pyrasulfotole induced systemic toxicity at high dose levels. Systemic toxicity invariably involved reduced food consumption and lowered body weight and body-weight gains. Increased levels of cholesterol and/or triglycerides were also observed. Organ toxicity involved the kidneys (♂♀ rat: pelvic dilatation, mottled, gritty content, dilated renal pelvis, urothelial hyperplasia, interstitial fibrosis, pelvic urolithiasis; ♂♀ dog: gritty content, tubular eosinophilic globular intracytoplasmic inclusions, sub-/intra-urothelial infiltrate, pelvic mineralization and/or urothelial erosion), urinary bladder and/or urinary tract (♂♀ rat: urolitheasis and/or urothelial hyperplasia; ♂ mouse: gritty content, diffuse urothelial hyperplasia, diffuse submucosal granulation, diffuse suburothelial mixed-cell infiltrate, stones; ♂♀ dog: urolithiasis and/or tubular eosinophilic globular intracytoplasmic inclusions). In the rat, pyrasulfotole induced corneal opacity and associated neovascularization, as well as thyroid pathology (colloidal alteration). It was postulated that the eye effect observed in the rat was associated with increased accumulation of plasma and cellular tyrosine. There was evidence that pyrasulfotole inhibited the tyrosine catabolic enzyme HPPDase. In the mouse and dog, apparently there was an effective alternate pathway for the catabolism of tyrosine. Thus, there was no apparent increase in tyrosine levels in these species. In the rat, however, the alternate pathway was deficient resulting in the increase in tyrosine levels.

Long-term dietary toxicity studies in mice and rats demonstrated systemic toxicity similar to that seen in shorter term studies. In the mouse, dietary exposure to pyrasulfotole resulted in gallstones and urinary bladder transitional cell carcinoma/papilloma in both sexes. There was evidence that the observed tumours in the urinary bladder were due to the irritation effects of stones, and were not induced via a genotoxic process. Also, these tumours were observed at dose levels that were considered excessive due to increased mortality. In the male rat, a squamous cell papilloma and a squamous cell carcinoma of the eye were observed.

No evidence of mutagenic potential of pyrasulfotole was observed in a battery of *in vitro* and *in vivo* genotoxicity assays assessing gene mutation and chromosome aberration.

When tested in the rat, pyrasulfotole did not affect the reproductive performance. However, there was evidence of reproductive toxicity based on the reduced rearing indices and increased pup mortality at dose levels that also induced maternal toxicity. Developmental studies in rats and rabbits did not demonstrate teratogenic potential of pyrasulfotole. However, increased sensitivity of the offspring (at a maternally non-toxic dose) was observed in the rabbit study. The potential developmental toxicity in rabbits indicated an increased susceptibility of offspring compared to parental animals. In addition, there was no NOAEL established on a severe toxicity end-point (increased mortality of the F_2 pups) observed in the rat reproductive toxicity study.

Pyrasulfotole was not neurotoxic as demonstrated in acute and 90-day neurotoxicity studies in rats.

In conclusion, the toxicological database for pyrasulfotole was considered adequate for human risk assessment.

3.2 Determination of Acceptable Daily Intake

The lowest NOAEL of 1 mg/kg bw/d was established in the combined 2-year dietary toxicity and oncogenicity study in the rat.

Based on the lowest NOAEL of 1 mg/kg bw/d and the standard safety/uncertainty factor of 100 (margin of exposure) to account for the inter- and intra-species variations, and the additional 10x factor for offspring sensitivity and the lack of a NOAEL for a severe toxicity end-point, an ADI of 0.001 mg/kg bw/d is determined.

The ADI proposed is calculated according to the following formula:

$$\text{ADI} = \frac{1 \text{ mg/kg bw/d}}{100 \times 10} = 0.001 \text{ mg/kg bw/d}$$

3.3 Determination of Acute Reference Dose

No acute reference dose (ARfD) for pyrasulfotole is required for the general population because of its low acute toxicity potential.

For females age 13+, an ARfD of 0.013 mg/kg bw is determined based on the NOAEL of 3.8 mg/kg bw/d from the developmental neurotoxicity study in the rat (based on decreased food consumption and ocular opacity), the standard SF/UF of 100, and an additional SF/UF of 3x accounting for the increased sensitivity of offspring demonstrated in the rabbit teratology study.

The ARfD proposed is calculated according to the following formula:

$$\text{ARfD} = \frac{3.8 \text{ mg/kg bw/d}}{100 \times 3} = 0.013 \text{ mg/kg bw}$$

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Occupational exposure to AE 0317309 02 SE06 Herbicide or Infinity Herbicide is characterized as short-term duration via the dermal or inhalation route. For dermal occupational risk assessment, the NOAEL from the 4-week rat dermal study is recommended. The NOAEL derived from the 4-week dermal study is 10 mg/kg bw/day. For inhalation occupational risk assessment, the NOAEL from the rat oral developmental neurotoxicity study of 3.8 mg/kg bw/day is recommended. The target MOEs for dermal and inhalation risk assessment are 300, which is based on a 100-fold uncertainty factor to account for expected differences in toxicological response within and between species and an additional factor of 3-fold to account for sensitivity of offspring in developmental studies.

With the lack of a dermal absorption study, a default of 100% dermal absorption was assumed.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

In addition to containing the new active, pyrasulfotole, Infinity Herbicide also contains the currently registered active ingredient, bromoxynil. As a result of the proposed rate and uses for bromoxynil fitting within the currently registered rates, a new occupational risk assessment was not required.

Individuals have potential for exposure to pyrasulfotole during mixing, loading and application. Exposure is expected to be short term in duration for both products. The products are intended for application by ground with groundboom equipment, and by air using fixed-wing or rotary aircraft equipment. For groundboom application, mixing/loading may be accomplished with either an open pour system or a liquid closed mixing/loading system and the same person may be involved in mixing/loading, application and clean-up activities. For aerial application, mixing/loading can be accomplished with a liquid closed mixing/loading system. The product label advises that the pilot must not mix chemicals to be loaded onto the aircraft, although loading of premixed chemicals with a closed system is permitted. Application equipment is typically cleaned when moving from one crop to another.

Exposure estimates for mixers, loaders, applicators (M/L/A) 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 which facilitates the generation of scenario-specific exposure estimates. To estimate exposure for each use scenario, appropriate subsets of A and B (and C grade for Groundboom, closed cab) were created from the database files of PHED for liquid open mixing and loading and closed mixing and loading , groundboom application open cab and closed cab, and aerial (fixed wing & rotary- wing)/ liquid application. All data were normalized for kg of active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e., summing the measure of central tendency for each body part which is most appropriate to the distribution of data for that body part. The confidence level is high.

The estimated worker exposure was based on worker's body weight of 70 kg and dermal absorption of 100%, for males and females. All mixer/loaders wear a single layer of protective clothing consisting of long-sleeved shirt and long pants and chemical-resistant gloves, while applicators wear a single layer of protective clothing (a long-sleeved shirt and long pants) and gloves (open cab) or no gloves (closed cab or aerial).

Table 3.4.2.1.1 : Mixer/Loader/Applicator Exposure Estimates and Risk Assessment for AE 0317309 02 SE06 Herbicide

Occupational Scenario		ATPD (ha/ day)[d]	Exposure (µg ai/ kg bw/day)[b]		Margin of Exposure		
			Dermal	**Inhalation**	**Dermal [a]**	**Inhalation [b]**	**Combined [c]**
Ground	**PHED Farmer-** Open M/L + open cab (single layer, gloves)	150	8.96	0.27	1116	14074	1034
	PHED Custom- Open M/L + open cab (single layer, gloves)	300	17.92	0.55	558	6909	516
Aerial	**PHED Custom** Open M/L	490	17.9	0.56	559	6786	516
	PHED Custom-Pilot (single layer, NO gloves)	490	3.38	0.0245	2959	155102	2904
	PHED Custom- Closed M/L (single layer, NO gloves) + Application	490	10.01	0.063	999	60317	983

a A NOAEL of 10 mg/kg bw/d from the 4-week rat dermal study is recommended. Target MOE of 300. Application rate of 0.05 kg pyrasulfotole/ha, 100% dermal absorption default

$$\text{MOE} = \frac{\text{NOAEL (10000 µg/kg bw/d)}}{\text{Exposure (µg ai/ kg bw/d)}}$$

b A NOAEL of 3.8 mg/kg bw/d from the developmental neurotoxicity study is recommended. Target MOE of 300.

$$\text{MOE} = \frac{\text{NOAEL (3800 µg/kg bw/d)}}{\text{Exposure (µg ai/ kg bw/d)}}$$

c $$\text{MOE (combined)} = \frac{1}{1/\text{MOE (dermal)} + 1/\text{MOE (inhalation)}}$$

d Area Treated Per Day

Target MOEs were achieved for farmers and custom applicators applying AE 0317309 02 SE06 Herbicide by groundboom or aerially and are considered acceptable.

Table 3.4.2.1.2: Mixer/Loader/Applicator Exposure Estimates and Risk Assessment for Infinity Herbicide (AE 0317309 03 EC23 Herbicide)

	Occupational Scenario	ATPD (ha/ day) [d]	Exposure (µg ai/ kg bw/day)		Margin of Exposure		
			dermal	inhalation	dermal [a]	inhalation[b]	combined[c]
Ground	**PHED Farmer-** Open M/L+ open cab (single layer, gloves)	150	5.61	0.17	1782	22353	1650
Ground	**PHED Custom-** Open M/L+ open cab (single layer, gloves)	300	11.22	0.34	891	11066	824
Aerial	**PHED Custom-** Open M/L	490	11.2	0.35	893	10857	825
Aerial	**PHED Custom-Pilot** (single layer, NO gloves)	490	2.12	0.015	4717	25333	3976
Aerial	**PHED Custom-** Closed M/L,(single layer, NO gloves) + Application	490	6.27	0.039	1595	97436	1569

a A NOAEL of 10 mg/kg bw/d from the 4-week rat dermal study is recommended. Target MOE of 300. Application rate of 0.0313 kg pyrasulfotole/ha, 100% dermal absorption default

$$\text{MOE} = \frac{\text{NOAEL (10000 µg/kg bw/d)}}{\text{Exposure (µg ai/ kg bw/d)}}$$

b A NOAEL of 3.8 mg/kg bw/d from the developmental neurotoxicity study is recommended. Target MOE of 300.

$$\text{MOE} = \frac{\text{NOAEL (3800 µg/kg bw/d)}}{\text{Exposure (µg ai/ kg bw/d)}}$$

c $$\text{MOE (combined)} = \frac{1}{1/\text{MOE (dermal)} + 1/\text{MOE (inhalation)}}$$

d Area Treated Per Day

Target MOEs are achieved for farmers and custom applicators applying Infinity Herbicide by groundboom or aerially and are considered acceptable.

3.4.2.2 Postapplication Worker Exposure and Risk

AE 0317309 02 SE06 Herbicide and Infinity Herbicide are post-emergent herbicides that may be applied to the crops when at the 1 leaf stage of growth to the early flag leaf stage. The majority of applications are expected to be made when the crop is at the 1-to 2-tiller growth stage, at which time the crops would be approximately 20 to 25 cm in height. Cereal and grass crops are not cultivated after post-emergent herbicide applications. Re-entry activity would consist of scouting which would typically occur within the first week of application. Duration of scouting activities is dependant upon several factors including field size and treated area.

A tier one risk assessment was performed for workers (scouting) entering field crops treated with one application of AE 0317309 02 SE 06 Herbicide and Infinity Herbicide based on a default value of 20% dislodgeable foliar residues. With the lack of a dermal absorption study, a default of 100% dermal absorption was assumed. A 12 hour REI was proposed.

Table 3.4.2.2.1: Post Applicator Exposure Estimate and Risk Assessment for AE 0317309 02 SE06 Herbicide

Scenario	Transfer Coefficient (cm^2/hr) [a]	Exposure (µg/kg bw/day) [b]	MOE [c]
Scouting	1500	17.14	583

[a] Transfer coefficient from Science Advisory Council for Exposure (revised 7 August 2000)- field/row crop low/medium spring wheat-scouting (full foliage development)

[b] Application rate of 0.5 µg pyrasulfotole/cm^2, 100% dermal absorption default

$$\textbf{Exposure} = \frac{\text{Application rate } (\mu g/cm^2) * 20\% * TC\ (cm^2/hr) * 8\ hr/d * \text{dermal absorption}}{70\ kg\ bw}$$

[c] A NOAEL of 10 mg/kg bw/d from the 4-week rat dermal study is recommended. Target MOE of 300.

$$\textbf{MOE} = \frac{\text{NOAEL } (10000\ \mu g/kg\ bw/d)}{\text{Exposure } (\mu g\ ai/\ kg\ bw/d)}$$

The target MOEs was achieved for workers (scouting) entering crops treated with one application of AE 0317309 02 SE06 Herbicide.

Table 3.4.2.2.2: Post Applicator Exposure Estimate and Risk Assessment for Infinity Herbicide (AE 0317309 03 EC23 Herbicide)

Scenario	Transfer Coefficient (cm^2/hr) [a]	Exposure (µg/kg bw/day) [b]	MOE [c]
Scouting	1500	10.73	932

[a] Transfer coefficient from Science Advisory Council for Exposure (revised 7 August 2000)- field/row crop low/medium spring wheat-scouting (full foliage development)

[b] Application rate of 0.313 µg pyrasulfotole/cm^2, 100% dermal absorption default

Exposure= Application rate (µg/cm^2)* 20% dislodgeable* TC (cm^2/hr)* 8 hrs/d * dermal absorption / 70 kg bw

[c] A NOAEL of 10 mg/kg bw/d from the 4-week rat dermal study is recommended. Target MOE of 300

MOE= NOAEL (10000 µg/kg bw/d) / Exposure (µg ai/ kg bw/d)

The target MOE was achieved for workers (scouting) entering crops treated with one application of Infinity Herbicide.

3.4.3 Residential Exposure and Risk Assessment

3.4.3.1 Handler Exposure and Risk

There are no domestic products, therefore a residential handler assessment was not required.

3.4.3.2 Post-Application Exposure and Risk

There are no domestic products, therefore a residential post-application assessment was not required.

3.4.3.3 Bystander Exposure and Risk

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for enforcement and risk assessment purposes in plant and animal commodities is pyrasulfotole and the metabolite pyrasulfotole-desmethyl. The data gathering/enforcement analytical methodologies, high-performance liquid chromatography with tandem mass spectrometry (LC-MS/MS), are valid for the quantitation of the analytes of interest in plant commodities, beef and poultry matrices. The residues of pyrasulfotole are stable in soybean grain and wheat matrices when stored in a freezer at -10ºC for up to 11 months (336 days). However, residues of pyrasulfotole-desmethyl decline by 0.12% per day in wheat forage and hay. Wheat was processed into bran, flour, middling, shorts, germ and aspirated grain fraction using simulated commercial procedures. There was concentration of the residues in aspirated grain fractions (32.8-fold) and in wheat bran (1.6-fold). Quantifiable residues of pyrasulfotole and pyrasulfotole-desmethyl are expected at or above the limit of quantitation in meat by-products as a result of feeding livestock with crops treated with pyrasulfotole. Supervised residue trials conducted across the United States and Canada using end-use products containing pyrasulfotole in or on wheat, triticale, rye, barley, oats and timothy (grown for seed production only) are sufficient to support the proposed maximum residue limits. Residue data for wheat was extended to rye in support of an import maximum residue limit.

3.5.2 Dietary Risk Assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.03).

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The refined chronic analysis took into account the following: residues in cereal grains based on median values, anticipated residue values for all animal commodities, and experimental processing factors as available. The refined chronic dietary exposure from all supported pyrasulfotole food uses (alone) for the total population, including infants and children, and all representative population subgroups are up to 3.2% (0.000032 mg/kg bw/day) of the acceptable daily intake (ADI). Aggregate exposure from food and water is considered acceptable. The PMRA estimates that the refined chronic dietary exposure to pyrasulfotole from food and water is 59.7% (0.000597 mg/kg bw/day) of the ADI for all population subgroups.

3.5.2.2 Acute Dietary Exposure Results and Characterization

The following considerations were made in a refined acute analysis: 100% crop treated, experimental processing factors, residues of cereal grains based on median values and anticipated residue values for all animal commodities. The subgroup of females 13-49 years old had no acute dietary exposure values that exceed the PMRA's level of concern. The refined acute dietary exposure (food alone) for all supported pyrasulfotole registered commodities is estimated to be 0.2% (0.000029 mg/kg/day) of the ARfD for females 13-49 years old at the 95th percentile (deterministic). The refined aggregate exposure from food and water is considered acceptable: 3.8% of the ARfD (0.000495 mg/kg/day) for females 13-49 years old.

3.5.3 Aggregate Exposure and Risk

There are at present no residential uses for pyrasulfotole. The aggregate risk from pyrasulfotole consists of exposure from food and drinking water sources only. Aggregate risks were calculated based on acute (females 13-49 years old) and chronic endpoints.

3.5.4 Proposed Maximum Residue Limits

Table 3.5.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Milk	0.01
Wheat, barley, rye, triticale; eggs, meat, meat by-product of poultry; fat, meat of cattle, goats, hogs, sheep, horses; meat by-product of hogs	0.02
Meat by-product of cattle, goats, sheep, horses	0.06
Oats	0.08
Liver of cattle, goats, sheep, horses	0.35

The nature of the residues in animal and plant matrices, analytical methodology, field trial data, and the acute and chronic dietary risk estimates are summarized in Tables 1, 5 and 6 in Appendix I.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Pyrasulfotole enters the soil when used as a herbicide on cereal crops. Under field conditions relevant to Canada, half-lives (as estimated by taking 1/3 of the 90% dissipation time) range from 15 to 177 days. The benzoic acid metabolite AE B197555 is a major transformation product in soil only, with half-lives in the field ranging from 27 to 122 days. The route of dissipation of pyrasulfotole is primarily through transformation by soil organisms and by binding to soils. Pyrasulfotole mobility is dependent on soil pH. Mobility increases with soil pH, with the greatest mobility occurring at neutral pH levels (e.g., around pH 7). Field data indicate that both pyrasulfotole and its major transformation product are expected to leach through the soil profile beyond 30 cm and therefore, may be expected to enter groundwater.

Pyrasulfotole could reach water systems by spray drift or runoff. It is very soluble in water, and the solubility is greatest at neutral pH. Pyrasulfotole is considered to be stable and persistent in aerobic water-sediment systems. Under acidic conditions, pyrasulfotole will partition to sediments, but is not lost from the system. Under neutral conditions, pyrasulfotole remains more evenly distributed between water and sediment, but is very persistent (a half-life could not be determined). The transformation product AE B197555 is produced only in minor amounts in aerobic aquatic systems. Pyrasulfotole is stable in anaerobic aquatic systems, with no identifiable transformation products being produced. The major route of dissipation is through binding to sediments.

The low vapour pressure and Henry's law constant indicate that pyrasulfotole is non-volatile in the environment. Therefore, pyrasulfotole residues are not expected in the atmosphere, and long-range transport is not expected.

Data on the fate and behaviour of pyrasulfotole and its major transformation product are summarized in Table 7 of Appendix I. The transformation pathway for pyrasulfotole is summarized in Figure 4.1 of Appendix I.

4.2 Effects on Non-Target Species

The toxicity of pyrasulfotole and its transformation product AE B197555 to terrestrial and aquatic organisms is summarized in Table 8. To estimate risk of potential adverse effects on non-target species, a quotient method is used. The risk quotient is calculated by dividing the exposure estimate by a value representing the most sensitive toxic endpoint. Risk quotients are initially calculated for a screening-level assessment in order to obtain higher estimates of risk. The screening-level assessment is a realistic worst-case scenario. Low risk is predicted if the risk quotient is less than the trigger value of one. If the trigger values are exceeded under the realistic worst-case scenario, then a refinement of the assessment is necessary to evaluate how frequently impacts might be expected in the range of conditions that occur in the field. A refined assessment takes into consideration more realistic exposure scenarios (e.g., drift to non-target habitats and runoff to water bodies) and may consider different toxicity endpoints.

4.2.1 Effects on Terrestrial Organisms

Risk of pyrasulfotole to terrestrial organisms was based upon evaluation of toxicity data for three mammal and two bird species representing vertebrates (acute gavage, short- and long-term dietary exposure); one bee species, two other arthropods and one earthworm species representing invertebrates (acute or short-term exposure); and ten crop species representing plants (short-term exposure) (Table 9, Appendix I). Risk of the transformation product AE B197555 was based upon evaluation of toxicity data for one mammal and one bird species (short term dietary exposure), one earthworm species (acute and short-term exposure), and ten crop species (short-term exposure) (Table 9, Appendix 1).

For terrestrial vertebrates, pyrasulfotole did not cause mortality or clinical signs of toxicity in an acute (gavage) limit test. A short-term dietary dose-response test showed corneal damage in female rats at 1000 mg a.i./kg diet. Observable effects on pup mortality and parental systemic toxicity in mammals was reported following long-term dietary exposure at 30 mg a.i./kg diet. The transformation product AE B197555 was not toxic to mammals on an acute oral or short-term dietary basis. The end-use product Infinity Herbicide was acutely toxic at 2000 mg/kg bw, while AE 0317309 02 SE06 did not show any mortality at the same rate. For birds, long-term dietary exposure resulted in reproductive effects (reduced hatchability for bobwhite quail) at 594 mg a.i./kg dw diet, and in reduced weight gain in adult mallard ducks at 557 mg a.i./kg dw diet. However, risk quotients calculated under a realistic worst-case scenario indicate that pyrasulfotole presents a low risk to wild mammals and birds following acute, short-term or long-term exposure; all risk quotients are less than one (Table 9, Appendix I).

For terrestrial invertebrates, pyrasulfotole was not toxic to earthworms or bees in acute dose-response studies, with LC_{50} values exceeding the highest dose (limit) tested. The transformation product AE B197555 was also non-toxic to earthworms on an acute or chronic basis. The formulated product AE 0317309 02 SE06 A103, however, was toxic to beneficial predatory and parasitic arthropods, resulting in adult mortality and reduced reproductive rates. The median lethality rate (LR_{50}) for parasitic arthropods was 80 g a.i./ha and reproduction was significantly affected at the lowest tested rate of 18 g a.i./ha. Risk quotients calculated under realistic worst-case scenarios indicate that pyrasulfotole presents a low risk to terrestrial invertebrates following acute or short-term exposure; all risk quotients are less than one (Table 9, Appendix I).

For terrestrial plants, seedling emergence and vegetative vigour were examined. Ten species of plants were exposed to the end-use products AE 0317309 02 SE06 A102 and AE 0317309 03 EC23 A8, and to the transformation product AE B197555. Exposure to the transformation product AE B197555 did not result in significant phytotoxic effects (i.e, greater than 25% reduction in health of the plant population) for any of the plant species tested. For the two formulated products, plant toxicity was expressed relative to the amount of pyrasulfotole applied. With one exception, no monocotyledons showed significant phytototoxic effects. However, both formulated products had significant effects on seedling emergence and vegetative vigour for all dicotyledonous species tested. It was noted that vegetative vigour was more sensitive than seedling emergence with plant dry weight being the most sensitive endpoint. There was differential toxicity between the two formulated products, with plants being more sensitive to AE 0317309 03 EC23 A8 (which also contains the active ingredient bromoxynil) with an ER_{25} (effective rate for 25% of the population) of 0.19 g a.i./ha as pyrasulfotole, compared to AE 0317309 02 SE06 A102, with an ER_{25} of 0.91g a.i./ha as pyrasulfotole. Risk quotients for both end-use products calculated under a realistic worst-case scenario exceeded the trigger value of one for dicotyledonous species tested (Table 9, Appendix I).

A refined assessment considered that the most likely scenario of exposure to non-target plants is through drift (Table 11, Appendix I). Under this scenario, exposure to off-field (non-target) plants was refined using empirical spray drift curves to more accurately determine the amount of drift reaching plants 1 m downwind from the edge of the application swath. Using a standard field sprayer with a boom height of 60 cm above the crop, and an assumed ASAE spray quality of medium (i.e., a volume median diameter [VMD] of 250 - 350 µm) for this herbicide application, only 6% of the on-target rate is expected to drift 1 m downwind from the edge of the application site. The revised expected environmental concentrations and resulting Tier I risk quotients from drift (see Table 11, Appendix 1) still indicate a risk to off-site non-target dicot plants 1 m downwind from the edge of the field. The proposed end-use products AE 0317309 02 SE 06 Herbicide and Infinity Herbicide will therefore require buffer zones to reduce the risk of adverse effects in non-target plants (see section "Measures to Minimize Risk" in Overview, for full buffer zone requirements).

4.2.2 Effects on Aquatic Organisms

Risk of pyrasulfotole to aquatic organisms was based upon evaluation of toxicity data for eight freshwater species (one invertebrate, three fish, three algae and one vascular plant), and four estuarine/marine species (two invertebrates, one fish and one alga) (Table 9, Appendix I). Risk of the transformation product AE B197555 was based upon evaluation of toxicity data for three freshwater species (one invertebrate, one fish, and one alga) and one estuarine/marine invertebrate species (Table 9, Appendix I).

In the freshwater environment, pyrasulfotole and its transformation product AE B197555 were not acutely toxic to fish or invertebrate species; median lethal concentrations (LC_{50}s) were all greater than the test limits, with the exception of AE B197555 exposure to rainbow trout (96-hr LC_{50} of 160 mg/L) (Table 9, Appendix I). Long-term exposure to pyrasulfotole resulted in reduced survival for pelagic invertebrates at 25 mg a.i./L (LOEC), and reduced length for larval fish at 1.1 mg a.i./L (LOEC). The toxicity of pyrasulfotole to algae was variable (EC_{50} values ranged from 11 to 53 mg a.i./L), and was high for aquatic plants (EC_{50} of 0.028 mg a.i./L). The EC_{50} for the transformation product AE B197555 for green algae was greater than 9.4 mg/L (beyond the limit of the test).

In the marine environment, pyrasulfotole was acutely toxic to pelagic invertebrates (LC_{50} of 1.1 mg a.i./L) and algae (EC_{50} of 8.3 mg a.i./L), however, it was not acutely toxic to fish (LC_{50} was greater than 100 mg a.i./L) (Table 9, Appendix I). The transformation product AE B197555 was not acutely toxic to pelagic invertebrates (LC_{50} of 145 mg/L).

Risk quotients calculated under a realistic worst-case scenario indicate that pyrasulfotole presents a low risk to freshwater and marine invertebrates, fish and algae following short-term or long-term exposure; risk quotients are all less than one (Table 9, Appendix I).

The risk to aquatic organisms was also assessed for Infinity Herbicide, which is a mixture of bromoxynil (210 g a.i./L) and pyrasulfotole (37.5 g a.i./L). The following endpoints were used to assess bromoxynil risk to aquatic organisms - amphibians: NOEC = 9.0 µg a.i./L for early life stage exposure to fathead minnow (*Pimephales promelas*); freshwater organisms: 1/10th LC_{50} = 2.9 µg a.i./L for bluegill sunfish (*Lepomis macrochirus*); marine organisms: 1/10th LC_{50} = 17.0 µg a.i./L for sheepshead minnow (*Cyprinidon variegatus*). These data were obtained from the current PMRA re-evaluation for bromoxynil, which is based on the 1998 US EPA Re-Evaluation Decision document. Risk quotients were determined based on the proposed Canadian use rate for Infinity Herbicide. For the proposed single application rate of 1 L/ha Infinity Herbicide, buffer zones are required adjacent to sensitive freshwater habitats (see section "Measures to Minimize Risk" in Overview, for full buffer zone requirements).

The proposed end-use products AE 0317309 02 SE 06 and Infinity Herbicides contain a List 2 petroleum distillate, which is toxic to aquatic organisms. The risk to aquatic organisms was determined for the use pattern with the highest use rate for the List 2 formulant . The PMRA level of concern (i.e., a risk quotient greater than one) was not exceeded for either invertebrates, fish or amphibians (Table 10, Appendix I).

5.0 Value

5.1.1 AE 0317309 02 SE 06 Herbicide

Efficacy data were submitted from 37 replicated field trials conducted over a 2-year period at several locations in Alberta, Saskatchewan, Manitoba, Ontario and Québec. Treatments were included at various rates to determine the lowest effective rate. The herbicide treatments were applied using small plot application equipment, and were within the growth stage range indicated on the label.

The efficacy of AE 0317309 02 SE 06 Herbicide was visually assessed as percent weed control and compared to an untreated weedy check. Observations were made up to four times throughout the growing season.

5.1.2 Acceptable Efficacy Claims for AE 0317309 02 SE 06 Herbicide Applied as a Stand-Alone Herbicide Treatment

The submitted efficacy data established the lowest effective rate for AE 0317309 02 SE 06 Herbicide applied alone, and support the weed control claims summarized in Table 5.1.1.1.

Table 5.1.1.1 Weed Control Claims for AE 0317309 02 SE 06 Herbicide

Herbicide Rate	Weeds Controlled
50 g a.i./ha or 1 L product/ha	lamb's quarters, redroot pigweed, wild buckwheat, volunteer canola (conventional and herbicide tolerant)

5.1.3 Herbicide Tank Mix Combinations

No tank mixtures with AE 0317309 02 SE06 were proposed.

5.1.4 Infinity Herbicide

Efficacy data were submitted from 184 replicated field trials conducted over a 2-year period at several locations in Alberta, Saskatchewan, Manitoba, Ontario and Québec. The herbicide treatments were applied using small plot application equipment, and were within the growth stage range indicated on the proposed label.

The efficacy of Infinity Herbicide was visually assessed as percent weed control and compared to an untreated weedy check. Observations were made up to four times throughout the growing season.

5.1.5 Acceptable Efficacy Claims for Infinity Herbicide as a Stand-Alone Herbicide Treatment

The submitted efficacy data support the weed control claims summarized in Table 5.1.5.1 for Infinity Herbicide applied alone.

Table 5.1.5.1 Weed Control and Suppression Claims for Infinity Herbicide

Herbicide Rate	Weeds Controlled	Weeds Suppressed
205.5 g a.i./ha or 0.83 L product/ha (174.3 g bromoxynil/ha + 31.125 g pyrosulfotole/ha)	annual sow-thistle, chickweed, cleavers, flixweed, hemp-nettle, kochia, lamb's-quarters, pale smartweed, redroot pigweed, Russian thistle, shepherd's-purse, stinkweed, volunteer canola (includes conventional and herbicide tolerant), wild buckwheat, wild mustard	Canada thistle, dandelion, perennial sow-thistle

5.1.6 Rainfastness

The data from three simulated rainfall trials, using overhead irrigation, were submitted in support of a one hour rainfast interval. Treatments of AE 0317309 02 SE 06 were applied at 30, 60, 120 and 240 minutes prior to a simulated rainfall event of 25 mm of water across the entire trial area. Efficacy was visually assessed up to three times during the growing season, and was reported as percent control on a species-specific basis.

5.1.6.1 Supported Rainfastness Claim

Similar efficacy was demonstrated for AE 0317309 02 SE 06 Herbicide with both a one and four hour interval between application and a simulated rainfall. The data support a rainfastness claim of one hour for AE 0317309 02 SE 06 Herbicide.

5.1.7 Water Volumes Including Aerial Application

The data from ground and simulated aerial application (low water volume) trials were submitted in support of a minimum spray volume of 46.8 L/ha (ground and air) for AE 0317309 02 SE 06 Herbicide and 28.1 L/ha (air) and 46.8 L/ha (ground) for Infinity Herbicide. Applications of AE 0317309 02 SE 06 Herbicide and Infinity Herbicide were made in 28.1 or 46.8 L/ha of water and compared to treatments made in higher water volumes. All applications were made by ground boom. In addition, the trials included a tank mixture of Puma[120] Super and Buctril M applied in 28.1 L/ha to demonstrate the weed control provided by a relevant registered commercial herbicide that is labelled for aerial application.

The data support the application of AE 0317309 02 SE 06 Herbicide in a minimum water volume of 46.8 L/ha for application with ground or aerial equipment.

The data support the application of Infinity Herbicide in a minimum water volume of 46.8 L/ha for application with ground equipment and 28.1 L/ha for application with aerial equipment.

5.2 Phytotoxicity to Host Plants

5.2.1 AE 0317309 02 SE 06 Herbicide

Data from 107 trials (26 trials on spring wheat, 22 trials on durum wheat, 15 trials on winter wheat, 22 trials on spring barley, 19 trials on tame oats, nine trials on triticale, and seven trials on timothy) conducted at multiple locations over a 2-year period in Alberta, Saskatchewan, Manitoba, Ontario and Québec, were submitted in support of the host crop tolerance claims. Some trials included multiple crops, and all trials included treatments of AE 0317309 02 SE06 Herbicide applied at the 2X rate.

Crop injury (%) was visually assessed up to three times during the growing season. Crop yield, expressed as a percentage of a weed-free check, was reported in 67 dedicated crop tolerance trials.

5.2.2 Acceptable Claims for Host Plants for AE 0317309 02 SE 06 Herbicide

Crop injury to wheat (spring, durum and winter), barley, oats, triticale, and timothy (grown for seed production) treated with AE 0317309 02 SE 06 Herbicide applied alone was always less than 5%. Crop yield was also comparable to registered commercial treatments.

5.2.3 Infinity Herbicide

Data from 222 trials (101 trials on spring wheat, 50 trials on durum wheat, 18 trials on winter wheat, 52 trials on spring barley, six trials on triticale, and six trials on timothy) conducted at multiple locations over a 2-year period in Alberta, Saskatchewan, Manitoba, Ontario and Québec, were submitted in support of the host crop tolerance claims. Some trials included multiple crops, and all trials included treatments of Infinity Herbicide applied at the 2X rate.

Crop injury (%) was visually assessed up to three times during the growing season. Crop yield, expressed as a percentage of a weed-free check, was reported in 67 dedicated crop tolerance trials.

5.2.4 Acceptable Claims for Host Plants for Infinity Herbicide

Crop injury to wheat (spring, durum and winter), barley, triticale, and timothy (grown for seed production) treated with Infinity Herbicide applied alone was always less than 10%. Crop yield was also comparable to registered commercial treatments.

5.3 Impact on Succeeding Crops

Rotational crop tolerance data were submitted from 37 trials that were initiated within one to two years following an application of pyrasulfotole. The number of trials in which tolerance was evaluated varied by rotational crop. Trials were conducted in Alberta, Saskatchewan, Manitoba or Ontario.

5.3.1 Acceptable Claims for Rotational Crops for pyrasulfotole

The crop injury and yield data support a rotational crop tolerance claim for the following crops planted in the year (10 months) after application of pyrasulfotole: alfalfa, barley, canaryseed, canola, field corn, durum and spring wheat, field pea, flax, soybeans and tame oats. The data also support lentils as a rotational crop planted 22 months after an application of pyrasulfotole.

5.4 Economics

Wheat is Canada's largest agri-food export. In 2005, wheat was grown on nearly 10.1 million hectares and produced about 25.6 million tonnes of grain. In 2003 and 2004, Canada exported $CAD 2.826 and $CAD 3.479 billion dollars worth of wheat, respectively.

In 2004, barley was grown on nearly 4.8 million hectares and produced about 13.2 million tonnes of grain. In terms of total farm cash receipts, barley was worth about $CAD 434 million in 2004, and ranked sixth after wheat, canola, potatoes, corn, durum and soybeans.

In 2005, tame oats were grown on nearly 2 million hectares and produced about 3 million tonnes of grain. In 2004, the Canadian farm cash receipts for tame oat production totalled $CAD 231 million.

In Canada, the total triticale production for 2004 was 80,000 tonnes. This total has increased over two and a half times since 2001, when triticale production totaled 31,200 tonnes.

Timothy production in Canada is directed towards the hay and seed markets. In the 2002-03 August to July crop year, about 180 thousand tonnes of compressed timothy were produced in Canada. In 2003, preliminary estimates suggest that approximately 5543 tonnes of timothy seed were exported.

Pyrasulfotole is the first Group 27 herbicide for use in cereal crops in Canada, providing growers with a weed control alternative, important from a herbicide resistance management standpoint. A coformulation of pyrasulfotole and bromoxynil (WSSA Group 6 herbicide) provides growers with a useful resistance management herbicide option for small grain cereals and timothy.

5.5 Sustainability

5.5.1 Survey of Alternatives

According to the applicant, wild buckwheat and volunteer canola (including herbicide tolerant varieties) are the key weeds controlled by pyrasulfotole applied alone. The key herbicide options currently available for post-emergence control of wild buckwheat and volunteer canola in spring wheat are summarized in Table 5.5.1.1.

Table 5.5.1.1 Alternative Herbicides for Wild Buckwheat and Volunteer Canola Control in Spring Wheat

Technical Grade Active Ingredient	End-use Products	Weed Claims	Herbicide Classification	
			Group	Mode of Action
florasulam + clopyralid/MCPA	Spectrum Herbicide Tank Mix	**controls:** wild buckwheat, volunteer canola (including Roundup Ready, Liberty Link and Smart herbicide tolerant varieties), lamb's quarters, redroot pigweed, plus other broadleaved weeds.	2, 4	Acetolactate synthase (ALS) inhibitor. Synthetic auxin.
florasulam + MCPA	Frontline Herbicide Tank Mix	**controls:** wild buckwheat, volunteer canola (including all herbicide tolerant varieties), lamb's quarters, redroot pigweed, plus other broadleaved weeds.	2, 4	Acetolactate synthase (ALS) inhibitor. Synthetic auxin.
fluroxypyr + clopyralid/MCPA	Prestige Herbicide Tank Mix	**controls:** wild buckwheat, volunteer canola, lamb's quarters, redroot pigweed, plus other broadleaved weeds.	4, 4	Synthetic auxin.
bromoxynil/MCPA	Badge, Bromox 450M, Brominal M, Bromox 560, Buctril M, Buctril M, Mextrol 400M, Platinum 560 EC,	**controls**:wild buckwheat, volunteer rapeseed (including canola), lamb's quarters, redroot pigweed, plus other broadleaved weeds.	6, 4	Photosynthetic inhibitor (PSII). Synthetic auxin.

5.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

Pyrasulfotole offers broad-spectrum weed control when used as a post-emergence herbicide in wheat (spring, durum and winter), barley, tame oats, triticale and timothy (grown for seed production). It is compatible with integrated weed management practices because it controls a range of broadleaf weeds with a single application and because its post-emergence application timing permits an assessment of whether this herbicide is suitable for the particular weed species present in the field. It is compatible with both conservation tillage and conventional production systems.

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

Repeated use of herbicides having the same mode of action in a weed control program increases the probability of selecting naturally resistant biotypes. Therefore, pyrasulfotole should be used in rotation with herbicides having different modes of action.

Both AE 0317309 02 SE 06 and Infinity Herbicides provide an alternative for growers to Group 2 and Group 4 chemistries.

Both the AE 0317309 02 SE 06 Herbicide label and the Infinity Herbicide label include the resistance management statements, as per Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

6.0 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's Toxic Substances Management Policy, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, pyrasulfotole was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of pyrasulfotole were also considered, including major transformation products formed in the environment, microcontaminants in the technical product and formulants in the two proposed end-use products, Infinity Herbicide (AE 0317309 03 EC23) and AE 0317309 02 SE06 Herbicides. The PMRA has reached the following conclusions:

- Pyrasulfotole does meet the Track 1 criteria for CEPA-toxic equivalence and for persistence in water and in sediment, however, it does not meet the criteria for persistence in soil or bioaccumulation. Based on a refined risk assessment, pyrasulfotole is entering the environment at levels that pose a risk to terrestrial plants and therefore would be considered "CEPA-toxic Equivalent" under the Canadian Environmental Protection Act. Pyrasulfotole was stable in water/sediment systems, and half-life values in water and sediment are expected to be above the criterion of ≥182, and ≥365 days, respectively. However, its half-life values in soil (as estimated by taking 1/3 of its 90% dissipation time) ranged from 15 to 177 days under field conditions, which are below the criterion of ≥182 days. Its log *n*-octanol–water partition coefficient of ≤ 0.276 is below the criterion of ≥5. Pyrasulfotole does not meet all four Track 1 criteria; therefore, it is not classified as a Track 1 substance.

- Limited data were available to assess the TSMP Track-1 criteria for the only major pyrasulfotole transformation product, AE B197555. There were no laboratory studies supplied on transformation rates for AE B197555, and environmental toxicity data were supplied for a limited number of organisms. The log *n*-octanol–water partition coefficient (log K_{ow}) for AE B197555 was also not provided. **The applicant will be required to provide the log K_{ow} for AE B197555 to demonstrate that this transformation product is not bioaccumulative according to TSMP Track-1 criteria.**

- Technical grade pyrasulfotole does not contain any contaminants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

- The end-use product AE 0317309 02 SE06 Herbicide does not contain any formulants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*. However, it contains a petroleum distillate, which is a List 2 formulant, at a total of 30%.

- The end-use product AE 0317309 03 EC23 Herbicide does not contain any formulants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*. However, it contains a petroleum distillate, which is a List 2 formulant, at a total of 40%.

Therefore, the use of pyrasulfotole in the proposed end-use products AE 0317309 02 SE06 Herbicide and Infinity Herbicide is not expected to result in the entry of Track 1 substances into the environment.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for pyrasulfotole is adequate to define the majority of toxic effects that may result from human exposure to pyrasulfotole. In short- and long-term toxicity studies on laboratory animals, target organs included the eye, kidneys, urinary bladder, thyroid, and pancreas. At dose levels that were considered excessive, there was evidence of carcinogenicity based on an increased incidence of urinary bladder tumours in mice and eye tumours in male rats. There was evidence of increased susceptibility of the offspring in the rabbit teratology study.

Mixer, loader, applicators and workers entering treated cereals fields are not expected to be exposed to levels of AE 0317309 02 SE06 Herbicide or Infinity Herbicide that will result in unacceptable risk when used according to label directions. The personal protective equipment on the product label is adequate to protect workers and no additional personal protective equipment is required.

The nature of the residue in plants and ruminants is adequately understood. The residue definition for risk and enforcement purposes is pyrasulfotole and pyrasulfotole-desmethyl in plant and animal commodities. The proposed use of pyrasulfotole on timothy, wheat, barley, oats, rye and triticale does not constitute an unacceptable chronic or acute dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits to protect human health. The PMRA recommends that the following maximum residue limits be specified for:

residues of pyrasulfotole and pyrasulfotole-desmethyl in and on wheat (0.02 ppm), barley (0.02 ppm), rye (0.02 ppm), triticale (0.02 ppm),oats (0.08 ppm);
fat of cattle, sheep, goats, horses, poultry and hogs (0.02 ppm);
meat of cattle, sheep, goats, horses, poultry and hogs (0.02 ppm);
meat by-product of cattle, sheep, goats, horses (0.06 ppm);
meat by-product of hogs, and poultry (0.02 ppm);
liver of cattle, sheep, goats, horses (0.35 ppm);
milk (0.01 ppm); eggs (0.02 ppm)

7.2 Environmental Risk

Pyrasulfotole and its major transformation product AE B197555 are of low risk to pelagic aquatic organisms at the proposed maximum Canadian use rate of 50 g a.i./ha (maximum RQ of 0.45 for pyrasulfotole exposure to the floating macrophyte *Lemna gibba*). However, the risk to benthic organisms was not assessed as no toxicity studies with benthic organisms were provided by the registrant. Given pyrasulfotole's ability to partition to sediments, and its persistence in aquatic systems, pyrasulfotole accumulation in sediments is likely to result in exposure to sediment-dwelling organisms.

Pyrasulfotole does pose a risk to non-target dicot plants, however, this may be mitigated by the observance of buffer zones for sensitive terrestrial habitats. The difference in aerial buffer zones between the two EP products (i.e., up to 85 m for AE 0317309 02 SE06 Herbicide vs. 375 m for Infinity Herbicide) is due to the higher toxicity seen with the Infinity formulation which also contains bromoxynil. The bromoxynil content in the Infinity formulation also poses a risk to freshwater organisms and therefore a 10 m buffer zone is required for Infinity Herbicide when sprayed upwind of sensitive freshwater habitats.

Of primary concern is pyrasulfotole's potential for persistence and mobility in the environment. Pyrasulfotole is transformed to AE B197555, a low risk transformation product, and mineralized to CO_2 through microbial activity in aerobic soil. Transformation is initially rapid. However, it soon slows down, leaving significant residues in the soil which persist for longer than one year. In terrestrial field studies in Canadian locations (or equivalent US Ecozones), up to 19% of applied pyrasulfotole remained in soils at the beginning of the following growing season. Laboratory studies showed that a significant portion of the applied pyrasulfotole may physically bind to the soil matrix (i.e., 35 – 62% bound residues), however, the field studies also showed that it has the potential to move vertically in the soil column up to 1 m, which suggests that it can reach groundwater.

Once it reaches the aquatic environment, pyrasulfotole is expected to be persistent. It does not undergo hydrolysis or photolysis and was shown to be stable in aerobic and anaerobic water-sediment systems. In aerobic surface waters, pyrasulfotole may partition to sediments, particularly if water / soil pH is <5, however, it is not readily transformed and therefore is not lost from the system. Ground water modelling with LEACHM and surface water modelling with PRZM/EXAMS predicts that concentrations will continue to accumulate in water bodies with no outflow. Predicted annual concentrations in groundwater (38 µg a.i./L) and closed prairie dugouts (> 53 µg a.i./L) after a 50 year modelling scenario are greater than the EEC used to predict risk to aquatic organisms in this review (i.e., 6.3 µg a.i./L in an 80 cm deep water body). Therefore, it is possible that continuous use of this pesticide at the same site for an extended number of years could result in surface water concentrations in closed systems that may pose a risk to some aquatic plants.

7.3 Value

7.3.1 AE 0317309 02 SE 06 Herbicide

The data submitted to register AE 0317309 02 SE 06 Herbicide are adequate to describe its efficacy for use in wheat (spring, durum and winter), barley, tame oats, triticale, and timothy (grown for seed production). A single post-emergence application of AE 0317309 02 SE 06 Herbicide provides control of wild buckwheat and volunteer canola (including herbicide tolerant varieties), as well as lamb's quarters and redroot pigweed, in wheat (spring, durum, winter), barley, tame oats, triticale, and timothy (grown for seed production). The submitted phytotoxicity and yield data demonstrate an adequate margin of safety of labelled host crops to AE 0317309 02 SE 06 Herbicide. AE 0317309 02 SE 06 Herbicide (Group 27) provides an alternative mode of action to commonly used Group 2 and Group 4 herbicides.

7.3.2 Infinity Herbicide

The data submitted to register Infinity Herbicide are adequate to describe its efficacy for use in wheat (spring, durum and winter), barley, triticale, and timothy (grown for seed production). A single post-emergence application of Infinity Herbicide provides control of wild buckwheat and volunteer canola (including herbicide tolerant varieties) as well as lamb's quarters and redroot pigweed, in wheat (spring, durum, winter), barley, triticale, and timothy (grown for seed production). The submitted phytotoxicity and yield data demonstrate an adequate margin of safety of labelled host crops to Infinity Herbicide. Infinity Herbicide (Group 27) provides an alternative mode of action to commonly used Group 2 and Group 4 herbicides.

8.0 Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and in accordance with the Pest Control Products Regulations, has granted conditional registration for the sale and use of the technical grade active ingredient pyrasulfotole and the end-use products Infinity Herbicide and AE 0317309 02 SE06 Herbicide to control a range of broadleaved weeds in wheat (spring, durum and winter), barley, triticale, and timothy (grown for seed production).

An evaluation of current scientific data from the applicant, scientific reports and information from other regulatory agencies has resulted in the determination that, under the approved conditions of use, the end-use products have value and do not present an unacceptable risk to human health or the environment.

Although the risks and value have been determined to be acceptable when all risk reduction measures are followed, as a condition of these registrations, additional scientific information is being requested from the applicant as a result of this evaluation

- **Human Health**
    - An enforcement method that quantifies the parent pyrasulfotole and the metabolite pyrasulfotole-desmethyl in animal matrices, including extraction efficiency and ILV data.
    - Two ion transitions should be monitored during the MS/MS analysis (Method AI-001-P04-01) for each analyte; pyrasulfotole and pyrasulfotole-desmethyl.
- **Environment**
    - Provide the log K_{ow} for AE B197555 to demonstrate that this transformation product is not bioaccumulative according to TSMP Track-1 criteria.
    - Due to the pyrasulfotole's persistence in water and ability to partition to sediments, a chronic toxicity study with a benthic invertebrate species, such as chironomids (DACO 9.3.4 - Laboratory Studies with Other Species) is required. The study must conform to standard international guidelines (e.g. US EPA, OECD, ASTM, Environment Canada) and be conducted under GLP.

List of Abbreviations

µg	micrograms
µm	micrometer
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
ARfD	acute reference dose
atm	atmosphere
bw	body weight
CAS	chemical abstracts service
cm	centimetres
d	day(s)
DF	dry flowable
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in the test population)
DT_{75}	dissipation time 75% (the dose required to observe a 75% decline in the test population)
dw	dry weight
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
EEC	estimated environmental concentration
ER_{25}	effective rate for 25% of the population
FDA	Food and Drugs Act
g	gram
h	hour(s)
ha	hectare(s)
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC-MS/MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOD	level of detection
LOEC	low observed effect concentration

LOQ	limit of quantitation
LR_{50}	lethal rate 50%
m/z	mass to charge ratio
mg	milligram
mL	millilitre
MAS	maximum average score
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
MS/MS	mass tandem spectrometry
MTDB	maximum theoretical dietary burden
N/A	not applicable
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
PCPA	Pest Control Products Act
PBI	plantback interval
PHI	preharvest interval
PHED	Pesticide Handlers Exposure Database
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
REI	reentry interval
RSD	relative standard deviation
SC	soluble concentrate
SF	safety factor
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
VMD	volume median diameter
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Plant	AI-004-A05-01	Pyrasulfotole, Pyrasulfotole-desmethyl, Pyrasulfotole-benzoic acid	LC-MS/MS	0.010 ppm for each analyte in each matrix	1.1899e+20
Beef Matrices	AI-004-A05-01	Pyrasulfotole	LC-MS/MS	0.010 ppm bovine muscle, liver, kidney, and fat; 0.005 ppm for bovine milk	1.1899e+20
Poultry Matrices	AI-005-A05-01	Pyrasulfotole-benzoic acid (AE B197555)	LC-MS/MS	0.010 ppm for tissues, including eggs	1.1899e+13

Table 2 Acute Toxicity of Pyrasulfotole and Its Associated End-use Products (AE 0317309 02 SE 06 Herbicide and AE 0317309 03 EC23 Herbicide)

ACUTE STUDIES - TECHNICAL (pyrasulfotole; AE0317309)				
Study type	**Species, strain**	**Results**	**Comments**	**PMRA #**
Oral	rat, Wistar (HsdCpb:Wu)	LD_{50} >2000	Low toxicity	1189970
Dermal	rat, Wistar (HsdCpb:Wu)	LD_{50} >2000	Low toxicity	1189974
Inhalation	rat, Wistar (HsdCpb:Wu)	LC_{50} >5.03 mg/L	Low toxicity	1189978
Eye irritation	rabbit, New Zealand (NZ) albino	MIS at 1h = 16.3/110	mildly irritating CAUTION - EYE IRRITANT	1189984
Skin irritation	rabbit, (Crl:KBL(NZW)BR)	MAS = 0/8	Non-irritating	1189981
Skin sensitization (maximization)	guinea pig (Crl:HA)	study deficient due to inadequate induction and challenge	POTENTIAL SKIN SENSITIZER	1189987
ACUTE STUDIES - FORMULATION [AE 0317309 02 SE 06 Herbicide]				
Oral	rat, Wistar (HsdCpb:Wu)	LD_{50} >2000	Low toxicity	1309311
Dermal	rat, Wistar (HsdCpb:Wu)	LD_{50} >4000	Low toxicity	1309312
Inhalation	rat, Wistar (HsdCpb:Wu)	LC_{50} >2.9 mg/L	Low toxicity	1309313
Eye irritation	rabbit, (Crl:KBL(NZW)BR)	MIS at 24h = 49/110 MAS = 35/110	moderately irritating WARNING - EYE IRRITANT	1309314
Skin irritation	rabbit, (Crl:KBL(NZW)BR)	MIS at 72 h = 2.33/8 MAS = 2/8	mildly irritating CAUTION - SKIN IRRITANT	1309315
Skin sensitization (Buehlar)	guinea pig (Crl:HA)	negative	Not a dermal sensitizer	1309316

Study type	Species, strain	Results	Comments	PMRA #
ACUTE STUDIES - FORMULATION [AE 0317309 03 EC23 Herbicide]				
Oral	rat, Wistar (HsdCpb:Wu)	LD_{50} >300 <2000	moderately toxic WARNING POISON	1270163
Dermal	rat, Wistar (HsdCpb:Wu)	LD_{50} >4000	Low toxicity	1270164
Inhalation	rat, Wistar (HsdCpb:Wu)	LC_{50} >2 mg/L	Low toxicity	1270165
Eye irritation	rabbit, (Crl:KBL(NZW)BR)	MIS at 24h = 44.7/110 MAS = 28.2/110	moderately irritating WARNING - EYE IRRITANT	1270166
Skin irritation	rabbit, (Crl:KBL(NZW)BR)	MIS at 24/48 h = 2.34/8 MAS = 2.33/8	mildly irritating CAUTION - SKIN IRRITANT	1270167
Skin sensitization (Buehlar)	guinea pig (Crl:HA)	negative	Not a dermal sensitizer (challenge dose of 25 % was too low)	1270168

Table 3 Toxicity Profile of Technical Pyrasulfotole

SHORT-TERM TOXICITY			
Study type	**Species, strain**	**Results and comments**	**PMRA#**
14-day dietary	dog, beagle; ♂ 0, 18000 (dry diet), 18000 (moist diet) ppm = 0, 399, 330 mg/kg bw/d	study not designed for NOAEL determination similar treatment-induced effects after administration of pyrasulfotole in dry or wet diet: - red-coloured urine, slight ↓ bw, ↓ food intake, ↑ BUN, ↑ urinary ketones - plasma and urinary level of pyrasulfotole peaked at 2 h - elimination essentially complete at 24 h dry-feed group (2/5 dogs): urinary tract calculi with evidence of thickening of bladder	1189890
28-day dietary	mouse; C57BL/6J 0, 200, 1000, 5000 ppm ♂ = 0, 35.8, 192, 961; ♀ = 0, 45, 233, 1082 mg/kg bw/d	NOAEL: ♂ = 1000 ppm (192 mg/kg bw/d) ♀ = 5000 ppm (1082 mg/kg bw/d) LOAEL: ♂ = 5000 ppm (961 mg/kg bw/d) based on pathology of urinary bladder (gritty content, diffuse urothelial hyperplasia, diffuse submucosal granulation, diffuse suburothelial mixed-cell infiltrate) ♀ >5000 ppm, HDT	1189990
28-day dietary	dog, beagle 0, 5000, 13000, 26000 ppm ♂ = 0, 174, 469, 860 ♀ = 0, 171, 440, 782 mg/kg bw/d	NOAEL not established (a range-finding study) treatment effects: ↑ triglycerides, kidney and urinary bladder pathology	1189991
90 (28)-day dietary	dog, beagle 0, 1500, 9000, 18000 ppm dose in mg/kg bw/d not determined	NOAEL not appropriate due to incomplete study excessive toxic effects; study terminated on day 28.	1189998

Study type	Species, strain	Results and comments	PMRA#
90-day dietary	mouse; C57BL/6J@Ico 0, 100, 750, 1500, 3000 ppm ♂ = 0, 17, 124, 259, 500; ♀ = 0, 20, 152, 326, 617 mg/kg bw/d	NOAEL: 3000 ppm ♂ = 500, ♀ = 617 mg/kg bw/d, HDT (hematology not investigated)	1189999
90-day dietary	rat, Wistar 0, 2, 30, 1000, 7000, 12000 ppm ♂= 0, 0.13, 1.96, 66, 454, 830; ♀ = 0, 0.15, 2.32, 77, 537, 956 mg/kg bw/d	NOAEL = 30 ppm; ♂ = 1.96, ♀ = 2.32 mg/kg bw/d LOAEL = 1000 ppm; ♂ = 66, ♀ = 77 mg/kg bw/d (↑ plasma cholesterol and triglycerides, ↑ urinary ketones, thyroid histopathology) notable findings at 7000 ppm: ♂♀ - corneal opacity and/or neovascularisation	1190000
90-day dietary	dog, beagle 0, 100, 500, 1000 ppm; ♂ = 0, 3, 17, 40 ♀ = 0, 3, 17, 33 mg/kg bw/d	NOAEL = 1000 ppm; ♂ = 40, ♀ = 33 mg/kg bw/d, HDT. MTD was not reached. Repeat study unnecessary because availability of 1-year dog study tested at a higher dose.	1190009
1-year dietary	dog, beagle 0, 250, 1000, 3000 ppm ♂ = 0, 7, 34, 101 ♀ = 0, 9, 33, 93 mg/kg bw/d	NOAEL: ♂ = 250 ppm or 7mg/kg bw/d; ♀ = 1000 ppm or 33 mg/kg bw/d LOAEL: ♂ = 250 ppm or 34 mg/kg bw/d (kidney histopathology) ♀ = 3000 ppm or 93 mg/kg bw/d (liver hepatocytomegaly, ↑ liver and thyroid wt)	1190010
4-week dermal	rat, Wistar 0, 10, 100, 1000 mg/kg bw/d	NOAEL: localized toxicity = 1000 mg/kg bw/d, HDT systemic toxicity: ♂ = 10 mg/kg bw/d; ♀ = 100 mg/kg bw/d LOAEL: systemic ♂ = 100 mg/kg bw/d (pancreas pathology) ♀ = 1000 mg/kg bw/d (pathology of pancreas and liver)	1190013
CHRONIC TOXICITY AND ONCOGENICITY			
78-week dietary oncogenicity	mouse 0, 100, 1000, 4000 ppm ♂ = 0, 13.6, 137, 560 ♀ = 0, 16.7, 168, 713 mg/kg bw/d	NOAEL = not established; gallstones at all test groups oncogenicity NOAEL : ♂♀ = 1000 ppm (♂ = 137, ♀ = 168 mg/kg bw/d) oncogenicity LOAEL: 4000 ppm (♂ = 560, ♀ = 713 mg/kg bw/d) based on urinary bladder tumours notable findings: gallstones	1190031
2-year dietary/ oncogenicity	rat, Wistar 0, 25, 250, 1000, 2500 ppm ♂ = 0, 0.97, 9.92, 40.5, 104.3 ♀ = 0, 1.39, 13.8, 56.9, 140.1 mg/kg bw/d	NOAEL = 25 ppm; ♂ = 1, ♀ = 1.4 mg/kg bw/d LOAEL = 250 ppm; ♂ = 9.9, ♀ = 13.8 mg/kg bw/d based on bw, bwg, pathology of the eye, liver, thyroid, kidneys oncogenicity NOAEL: ♂ = 1000 ppm or 41 mg/kg bw/d ♀ = 2500 ppm or 140 mg/kg bw/d 2500 ppm: tumour: eye (squamous cell papilloma (1♂) and squamous cell carcinoma (1♂) notable findings: pathology of liver, thyroid, kidneys, pancreas, and eye	1190028

Study type	Species, strain	Results and comments	PMRA#
REPRODUCTION AND DEVELOPMENTAL TOXICITY			
2-generation reproductive toxicity	rat, Wistar 0, 30, 300, 3000 ppm ♂ = 0, 2.5, 26.3, 272.4 ♀ = 0, 3.1, 32.6, 345.7 mg/kg bw/d	NOAELs: parental systemic toxicity <30 ppm; ♂ <2.5, ♀ <3.1 mg/kg bw/d offspring toxicity <30 ppm; ♂ <2.5, ♀ <3.1 mg/kg bw/d reproductive toxicity = 30 ppm; ♂ = 2.5, ♀ = 3.1 mg/kg bw/d LOAELs: parental systemic toxicity = 30 ppm; ♂ = 2.5, ♀ = 3.1 mg/kgbw/d (thyroid pathology - colloid alteration) offspring toxicity = 30 ppm; ♂ = 2.5, ♀ = 3.1 mg/kg bw/d (↑ F_2 pup mortality) reproductive toxicity = 300 ppm; ♂ = 26.3, ♀ = 32.6 mg/kg bw/d (F_2 generation: ↓ rearing indices) notable findings: parental: cornial opacity; pathology of liver, kidneys, thyroid) offspring: ↓ viability; corneal effects	1190038
Developmental toxicity	rat, Sprague Dawley 0, 10, 100, 300 mg/kg bw/d	NOAELs: maternal and developmental toxicity = 10 mg/kg bw/d LOAELs: maternal and developmental toxicity = 100 mg/kg bw/d (maternal: clinical signs, ↓ bwg developmental: ↓ fetal wt, skeletal variation) Note: the eyes were not examined	1190044
Developmental toxicity	rabbit, NZ white 0, 10, 75, 250 mg/kg bw/d	NOAELs: maternal toxicity = 75 mg/kg bw/d developmental toxicity = 10 mg/kg bw/d LOAELs: maternal toxicity = 250 mg/kg bw/d (↓ bw, ↓ food intake, liver pathology) developmental toxicity = 75 mg/kg bw/d (↑ skeletal variation) Fetotoxicity at maternal non-toxic dose	1190044

GENOTOXICITY			
Study	**Species and strain or cell type and concentrations or doses**	**Results**	**PMRA#**
Gene mutations in bacteria	*Salmonella typhimurium* strains TA 98, TA 100, TA 102, TA 1535 and TA 1537	negative	1190016
Gene mutations in mammalian cells *in vitro*	Chinese hamster V79 cells (HGPRT locus)	negative	1190022
Chromosome aberrations *in vitro*	Chinese hamster V79 cells	negative	1190019
Micronucleus assay (*in vivo*)	mouse, HsdNVin: NMR ♂ = 0, 125, 250, 500; ♀ = 0, 250, 500, 1000 mg/kg bw	similar toxic effects between ♂ & ♀; consequently, only ♂ used to assess micronucleus induction negative	1190025
SPECIAL STUDIES			
Study type	**Species/strain/dose levels**	**Results and Comments**	**PMRA#**
acute neurotoxicity	rat, Wistar 0, 200, 500, 2000 mg/kg bw	NOAELs: acute neurotoxicity = 2000 mg/kg bw, HDT systemic toxicity = 500 mg/kg bw 2000 mg/kg bw: marginal ↓ motor activity at day 0 insufficient evidence of neurotoxicity	1190047
90-day dietary neurotoxicity	rat, Wistar 0, 45, 2500, 5000 ppm ♂ = 0, 32.3, 166, 345 ♀ = 0, 41.9, 206, 416 mg/kg bw/d	neurotoxicity NOAEL = 5000 ppm; ♂ = 345, ♀ = 416 mg/kg bw/d, HDT notable findings: a few ♀ had corneal opacity, but no dose relationship	1190050
developmental neurotoxicity	rat, Wistar 0, 45, 450, 4500 ppm ♀ = 0, 3.8, 37, 354 mg/kg bw/d	NOAELs: maternal systemic = 45 ppm; 3.8 mg/kg bw/d offspring toxicity = 45 ppm; 3.8 mg/kg bw/d developmental neurotoxicity = 45 ppm; 3.8 mg/kg bw/d LOAELs: maternal systemic = 450 ppm; 37 mg/kg bw/d (↓ food intake and ocular opacity) offspring toxicity = 450 ppm; 37 mg/kg bw/d (↓ bw & bwg, delayed preputial separation, & retinal degeneration) developmental neurotoxicity = 450 ppm; 37 mg/kg bw/d (↓ passive avoidance test performance)	1190053

Study type	Species/strain/dose levels	Results and Comments	PMRA#
Mechanistic study: dietary tyrosine and ocular toxicity	mouse, CD-1; rat, CD,; rat, Brown Norway tyrosine at 0, 2%, 5% daily administration for 14 d	Purpose of study: to determine 1. relationship of plasma tyrosine level and ocular toxicity 2. species/strain susceptibility of tyrosine-induced ocular lesions ocular toxicity: CD-1 mice: no effects CD rats: ♂ at 5% - severe Brown Norway rats: 1♂ at 5%, slight positive relationship between plasma tyrosine level and corneal lesions Conclusions: Corneal opacity found in ♂ CD rats (and 1 ♂ Brown Norway rats, only slight effect) that received tyrosine at 5% level; some correlation of increased plasma tyrosine level and corneal opacity in ♂ CD rats	1189895
Mechanistic study: NTBC on cellular level of tyrosine and HPLA, *in vitro*	Liverbeads™ from rat, mouse, rabbit, dog, and human incubation of Liverbeads™ with NTBC (30 µM), L-tyrosine (100 mg/L), or combination of NTBC and L-tyrosine	Purpose of study: to determine 1. inhibition of metabolism of tyrosine 2. the presence of an alternate tyrosine metabolic pathway rat, dog, rabbit Liverbeads™: minimal HPLA detected after incubation with NTBC; deficient alternate tyrosine metabolic pathway mouse and human Liverbeads™: HPLA detected, level increased with time of incubation with NTBC; efficient alternate tyrosine metabolic pathway Conclusions: - No clear evidence of increased tyrosine levels due to inhibition of HPPDase by NTBC - demonstration of an efficient alternate tyrosine metabolic pathway in mouse and human hepatocytes but not in rat, dog, or rabbit hepatocytes	1189897
Mechanistic study: tyrosemia on pregnancy, embryo-feto development	rat, Sprague Dawley 0, tyrosine (dietary 20000 ppm), NTBC (10 µg/kg bw/d), tyrosine (dietary 20000 ppm) + NTBC (10 µg/kg bw/d)	Purpose of study: to determine an association of fetal skeletal effects and increased plasma tyrosine levels maternal toxicity: NTBC groups - slight ↓ bw (GD 6-8) combined tyrosine/NTBC group - slight ↓ food intake; corneal opacity fetotoxicity: NTBC groups - slight ↓ bw; ↑ minor skeletal anomalies (mostly delayed/incomplete ossification) plasma tyrosine levels: NTBC groups - ↑; more pronounced in combined tyrosine/NTBC group Conclusions: Minor skeletal anomalies (developmental delays) associated with fetotoxicity, secondary to maternal toxicity; association of skeletal effects and increased plasma tyrosine levels a possibility but not definitive	1189892

STUDIES ON A METABOLITE (RPA 203328) also a metabolite of isoxaflutole			
Study type	**Species/strain/dose levels**	**Results and comments**	**PMRA#**
Oral	rat, Sprague Dawley	LD_{50} >5000 mg/kg bw Low toxicity	1189961
28-day dietary	rat, Sprague Dawley 0, 150, 500, 5000, 15000 ppm ♂= 0, 11.1, 37.6, 377, 1118; ♀ = 0, 12.7, 42.7, 421, 1269 mg/kg bw/d	NOAEL = 15000 ppm; ♂ = 1118, ♀ = 1269 mg/kg bw/d, HDT	1189900
90-day dietary	rat, Sprague Dawley; 0, 1200, 4800, 12000 ppm ♂= 0, 73.2, 306, 769; ♀ = 0, 93.1, 371, 952 mg/kg bw/d	NOAEL = 12000 ppm; ♂ = 769, ♀ = 952 mg/kg bw/d, HDT	1189966
Developmental toxicity	rat, Sprague Dawley 0, 75, 250, 750 mg/kg bw/d	NOAELs: maternal toxicity = 75 mg/kg bw/d developmental toxicity = 750 mg/kg bw/d, HDT LOAELS: maternal toxicity = 250 mg/kg bw/d (↓ food intake, transient ↓ bw)	1189948
Gene mutations in bacteria	*Salmonella typhimurium* strains TA 98, TA 100,TA 1535 and TA 1537	negative	1189963
Gene mutations in mammalian cells *in vitro*	Chinese hamster ovary cells (HGPRT locus)	negative	1189958
Chromosome aberrations *in vitro*	Chinese hamster ovary cells	negative	1189955
Micronucleus assay (*in vivo*) mouse	mice, Crl:CD-l®(ICR) BR	negative	1189952

Compound-induced mortality:
90-day rat dietary: ≥7000 ppm (≥454 mg/kg bw/d) - ♂; 12000 ppm (956 mg/kg bw/d) - ♀
78-week mouse dietary oncogenicity: 4000 ppm (♂ = 560, ♀ = 713 mg/kg bw/d)
2-year rat dietary / oncogenicity: 2500 ppm (♂ = 104 mg/kg bw/d)

Recommended ARfD:
Because of the increased sensitivity of offspring at maternal non-toxic dose demonstrated in the rabbit teratology study, an additonal safety factor (SF) of 3x was applied to the standard SF of 100 in the determination of the acute reference dose (ARD) for the subpopulation females (13+ years). The recommended ARD is 0.013 mg/kg bw based on the NOAEL of 3.8 mg/kg bw/d established in the rat DNT study.

An ARfD for the general population was not required, since pyrasulfotole was not considered to present an acute hazard. There were no significant treatment-related findings in the acute or short-term toxicity studies or in the acute or subchronic neurotoxicity studies to indicate a concern in acute dietary risk assessment for the general population.

Recommended ADI: 0.001 mg/kg bw/d based the NOAEL of 1 mg/kg bw/d established in the combined 2-year rat dietary toxicity and oncogenicity; the standard safety factor of 100 is applied and an additional 10x factor accounting for higher sensitivity of offspring in the absence of maternal toxicity observed in the rabbit teratology study and the lack of an established NOAEL for a severe toxicity end-point (F_2 pup mortality) observed in the rat reproductive toxicity study.

Tox endpoints for occupational risk assessment:
MOE = 300
short-term dietary and dermal exposure: 28-d rat dermal NOAEL of 10 mg/kg bw/d
short-term occupational inhalation exposure: NOAEL of 3.8 mg/kg bw/d from the rat DNT study

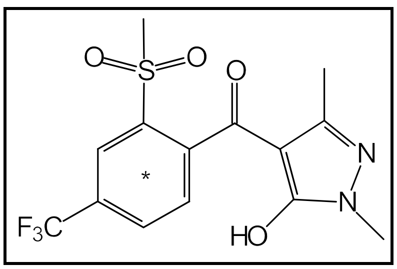
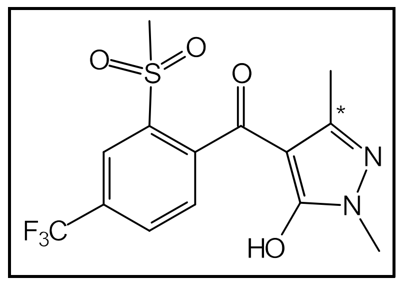
Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Pyrasulfotole

Exposure scenario	NOAEL used (mg/kg bw/d)	UF/SF	ARfD / ADI (mg/kg bw/d)	MOS / Remarks
Acute dietary risk - General population	-	-	-	Not required because of low acute toxicity
Acute dietary risk - Females 13-49 years of age	3.8 from rat DNT study	10x interspecies variation 10x intraspecies variation 3x increased offspring sensitivity at maternal non-toxic dose	3.8/10x10x3 = 0.013	
Chronic dietary - All population	1 from 2-year rat dietary/oncogenicity	10x interspecies variation 10x intraspecies variation 10x increased offspring sensitivity at maternal non-toxic dose and the absence of an established NOAEL for a severe toxicity end-point (F_2 pup mortality) observed in rat reproductive toxicity study	1/10x10x10 = 0.001	MOS for systemic toxicity = 1/0.001 = 1000 MOS for eye tumour in ♂ rat = 104.3/0.001 = 1430 MOS for rat F_2 pup mortality = 4.2/0.001 = 4200
short-term occupational dietary/dermal	10 from 28-day rat dermal toxicity study	10x interspecies variation 10x intraspecies variation 3x increased offspring sensitivity at maternal non-toxic dose		MOS = 300
short-term occupational inhalation	3.8 from rat DNT study	10x interspecies variation 10x intraspecies variation 3x increased offspring sensitivity at maternal non-toxic dose		300

Table 5 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN WHEAT With and Without Safener (mefenpyr-diethyl)			PMRA # 1190095
Radiolabel Position	**[14C-Phenyl]**		
Test Site	Outdoor, vegetation hall, surrounded by wire-mesh fencing, covered with a glass roof		
Treatment	Wheat plants treated at growth stage 21-22 (early tillering)		
Rate	96 g a.i./ha (without safener); 98 g a.i./ha + 68 g a.i./ha mefenpyr-diethyl		
End-use product	[14C-Phenyl]-pyrasulfotole formulated as an oil suspension (OD 5)		
Preharvest interval	79 days		
Matrix	**PHI (days)**	**[14C-Phenyl]-pyrasulfotole with mefenpyr-diethyl (ppm)**	**[14C-Phenyl]-pyrasulfotole without mefenpyr-diethyl (ppm)**
Forage	21	2.40	2.44
Hay	44	3.14	3.12
Straw	79	2.90	2.8
Grain	79	0.16	0.24
Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**
Radiolabel Position	**[14C-Phenyl]**		**[14C-Phenyl]**
Without Mefenpyr-diethyl			
Wheat forage	Pyrasulfotole, Pyrasulfotole-benzoic acid, Pyrasulfotole-desmethyl-*O*-glucoside		Pyrasulfotole-sulfinyl-lactate
Wheat hay	Pyrasulfotole, Pyrasulfotole-benzoic acid, Pyrasulfotole-desmethyl-*O*-glucoside		Pyrasulfotole-sulfinyl-lactate
Wheat straw	Pyrasulfotole-benzoic acid, Pyrasulfotole-desmethyl-*O*-glucoside		Pyrasulfotole, Pyrasulfotole-sulfinyl-lactate
Wheat grain	Pyrasulfotole-benzoic acid		-

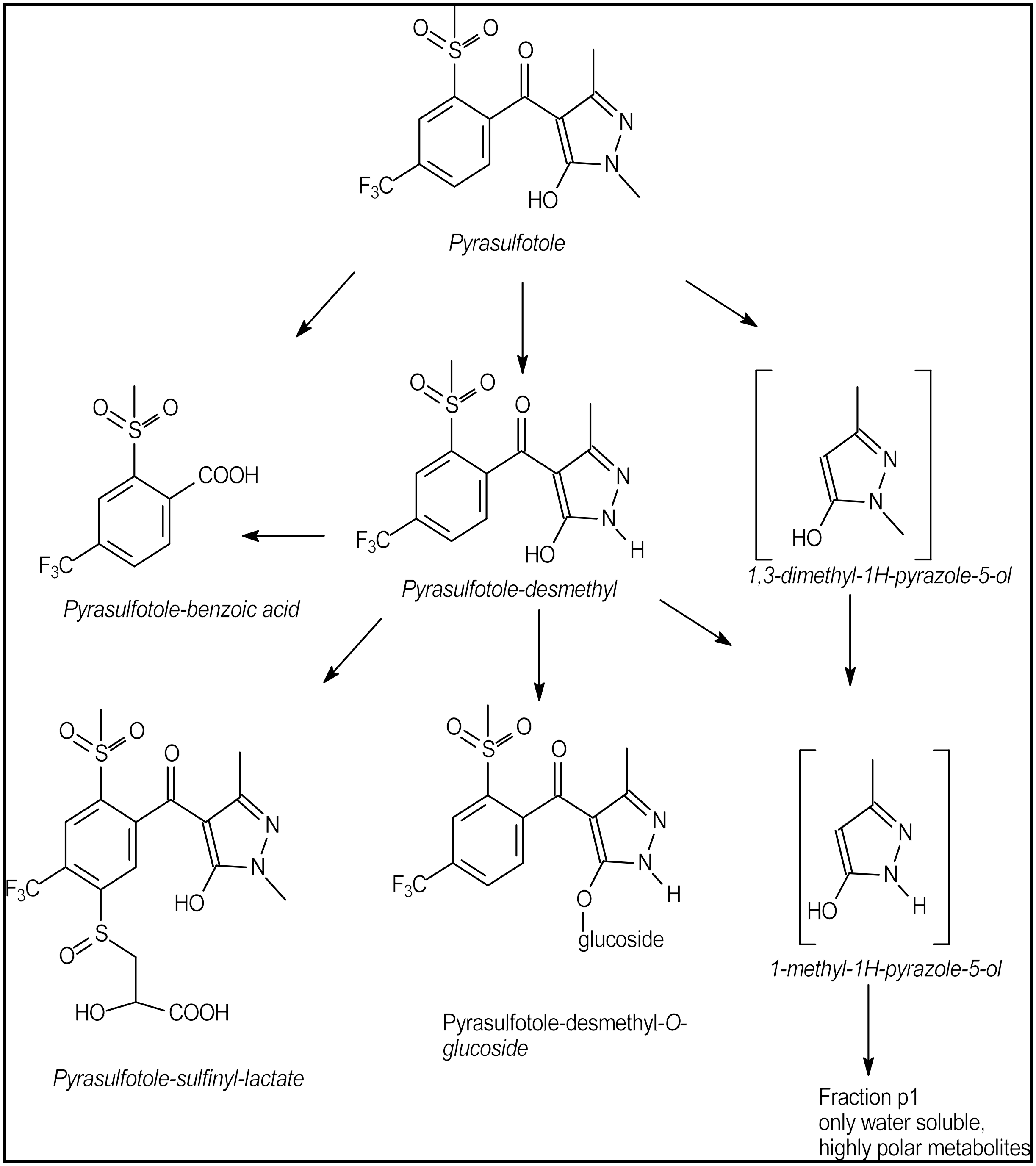
NATURE OF THE RESIDUE IN WHEAT With and Without Safener (mefenpyr-diethyl)		PMRA # 1190095
With Mefenpyr-diethyl		
Wheat forage	Pyrasulfotole-benzoic acid, Pyrasulfotole-desmethyl-*O*-glucoside	Pyrasulfotole, Pyrasulfotole-sulfinyl-lactate
Wheat hay	Pyrasulfotole-benzoic acid, Pyrasulfotole-desmethyl-*O*-glucoside	Pyrasulfotole, Pyrasulfotole-sulfinyl-lactate
Wheat straw	Pyrasulfotole-benzoic acid, Pyrasulfotole-desmethyl-*O*-glucoside	Pyrasulfotole, Pyrasulfotole-sulfinyl-lactate
Wheat grain	Pyrasulfotole-benzoic acid	-
Based on the predominant residues and toxicological significance, the residue definition is pyrasulfotole and pyrasulfotole-desmethyl for enforcement and risk assessment purposes.		

NATURE OF THE RESIDUE IN WHEAT Without Mefenpyr-diethyl			PMRA # 1190094/1190096	
Radiolabel Position	**[^{14}C-Phenyl]**		**[^{14}C-Pyrazole**	
Structure				
Test Site	Outdoor conditions			
Treatment	Wheat plants treated at growth stage 21-22 (early tillering)			
Rate	100 g a.i./ha; 200 g a.i./ha (to isolate metabolites)			
End-use product	[^{14}C-Phenyl] and [^{14}C-Pyrazole]-pyrasulfotole formulated as an oil suspension (OD 5)			
Preharvest interval	90 days		89 days	
Matrix	**PHI (days)**	**TRR (ppm)**	**PHI (days)**	**TRR (ppm)**
Whole plant	0	10.96	0	11.49
Forage	28	0.44	27	0.47
Hay	50	0.18	49	0.06
Straw	90	0.55	89	0.38
Grain	90	0.30	89	0.03

Metabolites Identified		Major Metabolites (> 10% TRR)		Minor Metabolites (< 10% TRR)	
Radiolabel Position		**[^{14}C-Phenyl]**	**[^{14}C-Pyrazole]**	**[^{14}C-Phenyl]**	**[^{14}C-Pyrazole]**
Wheat forage		Pyrasulfotole-benzoic acid, Pyrasulfotole-desmethyl-*O*-glucoside	Pyrasulfotole-desmethyl-*O*-glucoside	-	-
Wheat hay		Pyrasulfotole-benzoic acid, Pyrasulfotole-desmethyl-*O*-glucoside	Pyrasulfotole-desmethyl-*O*-glucoside	-	-
Wheat straw		Pyrasulfotole-benzoic acid	Pyrasulfotole-desmethyl-*O*-glucoside	Pyrasulfotole-desmethyl-*O*-glucoside	-
Wheat grain		Pyrasulfotole-benzoic acid	-	-	Pyrasulfotole-desmethyl-*O*-glucoside
CONFINED ACCUMULATION IN ROTATIONAL CROPS – Wheat, Swiss Chard and Turnips				**PMRA # 1190083**	
Radiolabel Position		[^{14}C-Phenyl]		[^{14}C-Pyrazole]	
Test site		Oval tub moved between greenhouse and patio as needed.			
Formulation used for trial		Suspension concentrate (SC) formulation blank with added [^{14}C-Phenyl] or [^{14}C-Pyrazole].			
Application rate and timing		82 g a.i./ha applied to soil in large troughs.			
Metabolites Identified		**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Matrix	**PBI (days)**	**[^{14}C-Phenyl]**	**[^{14}C-Pyrazole]**	**[^{14}C-Phenyl]**	**[^{14}C-Pyrazole]**
Wheat Forage	120	Pyrasulfotole-benzoic acid	-	-	-
Wheat Hay	120	Pyrasulfotole-benzoic acid	-	-	Pyrasulfotole
Wheat Straw	120	Pyrasulfotole-benzoic acid	-	-	Pyrasulfotole
Wheat Grain	120	Pyrasulfotole-benzoic acid	-	Pyrasulfotole	
Wheat Forage	301	Pyrasulfotole-benzoic acid			
Wheat Hay	301	Pyrasulfotole-benzoic acid		Pyrasulfotole	
Wheat Straw	301	Pyrasulfotole-benzoic acid			
Wheat Grain	301	Pyrasulfotole-benzoic acid			

Based on the predominant residues and toxicological significance, the residue definition for rotational crops is pyrasulfotole. Although pyrasulfotole-benzoic acid was a major metabolite found in wheat metabolism, confined rotational crops, wheat, barley and oat crop field trial studies, based on available toxicology studies of pyrasulfotole-benzoic acid, it was not considered to be of toxicological concern. Therefore, it was not included in the residue definition for enforcement or risk assessment purposes for cereal grains.

Proposed metabolic scheme in wheat



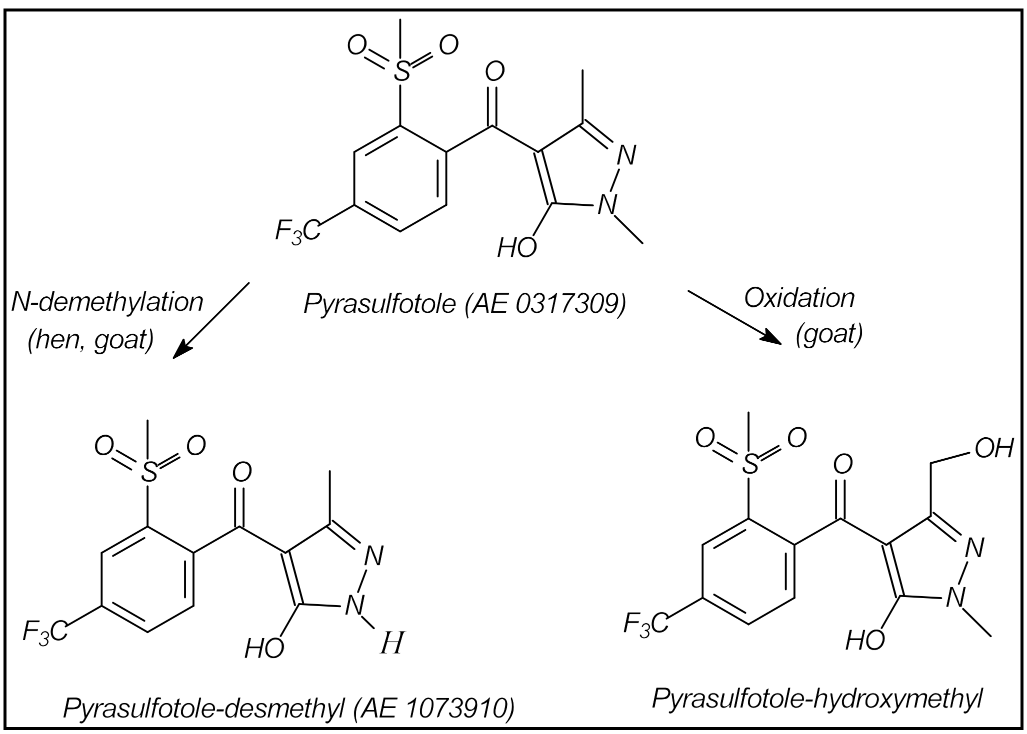
NATURE OF THE RESIDUE IN LAYING HEN			PMRA # 1190101/1190102	
Six laying hens were each dosed orally once daily for 14 consecutive days with 8.6 ppm [phenyl-U-^{14}C]-pyrasulfotole equivalents (0.82 mg/kg body weight/day), and 10.5 ppm [pyrazole-3-^{14}C]-pyrasulfotole equivalents (0.81 mg/kg body weight/day). Hens were sacrificed approximately 30 minutes after the last dose. For the phenyl-label study, more than 97% of the administered dose was recovered in the excreta as pyrasulfotole, with less than 0.4% in tissues and eggs. For the pyrazole-label study, most of the radioactivity (> 85%) was recovered in excreta as pyrasulfotole, with less than 0.2% remaining in the tissues and eggs.				
Matrices			**% of Administered Dose**	
			[^{14}C-Phenyl]	**[^{14}C-Pyrazole]**
Excreta			97.158	85.234
Muscle			0.050	0.048
Fat			0.005	0.016
Liver			0.307	0.108
Eggs			0.006	0.005
Metabolites identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**[^{14}C-Phenyl]**	**[^{14}C-Pyrazole]**	**[^{14}C-Phenyl]**	**[^{14}C-Pyrazole]**
Muscle	Pyrasulfotole	Pyrasulfotole	Pyrasulfotole-desmethyl	Pyrasulfotole-desmethyl
Fat	Pyrasulfotole	Pyrasulfotole	Pyrasulfotole-desmethyl	Pyrasulfotole-desmethyl
Liver	Pyrasulfotole	Pyrasulfotole	Pyrasulfotole-desmethyl	Pyrasulfotole-desmethyl
Eggs	-	-	-	-
Based on the predominant residues and toxicological significance, the residue definition is pyrasulfotole and the metabolite pyrasulfotole-desmethyl.				

NATURE OF THE RESIDUE IN LACTATING GOAT	PMRA # 1190103/1190108	
Two lactating goats were dosed orally once daily for 3 consecutive days at a dose level equal to 51.2 ppm [phenyl-U-^{14}C]-pyrasulfotole equivalents (0.93 mg /kg body weight per day). Also, two lactating goats were dosed orally once daily for 3 consecutive days at a dose level equal to 28.1 ppm [pyrazole-3-^{14}C]-pyrasulfotole equivalents (1.24 mg /kg body weight per day). Goats were sacrificed 23 hours after the last dose. More than 67% of the administered dose was recovered as pyrasulfotole in urine and feces, with less than 1.2% in tissues, and 0.012% in milk for the phenyl-label study. In the pyrazole-radiolabel study, most of the radioactivity (>92%) was recovered as pyrasulfotole in urine and feces, with less than 0.1% in milk, and 0.9% in tissues.		
Matrices	**% of Administered Dose**	
	[^{14}C-Phenyl]	**[^{14}C-Pyrazole]**
Urine and feces	67.3	92.3
Muscle	0.004	0.003
Fat	0.004	0.003

NATURE OF THE RESIDUE IN LACTATING GOAT			**PMRA # 1190103/1190108**	
Kidney			0.064	0.027
Liver			1.074	0.892
Milk			0.012	0.1
Metabolites identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**[^{14}C-Phenyl]**	**[^{14}C-Pyrazole]**	**[^{14}C-Phenyl]**	**[^{14}C-Pyrazole]**
Muscle	Pyrasulfotole	-	Pyrasulfotole-hydroxymethyl	-
Fat	-	-	-	-
Kidney	Pyrasulfotole	Pyrasulfotole	-	-
Liver	Pyrasulfotole	Pyrasulfotole	-	Pyrasulfotole-desmethyl
Milk	Pyrasulfotole	Pyrasulfotole, Pyrasulfotole-desmethyl	Pyrasulfotole-hydroxymethyl	-
Based on the predominant residues and toxicological significance, the residue definition is pyrasulfotole and the metabolite pyrasulfotole-desmethyl for enforcement and risk assessment purposes.				

Proposed Metabolic Scheme in Livestock

The metabolic profile involved *N*-demethylation of the parent pyrasulfotole to afford the pyrasulfotole-desmethyl metabolite (AE 1073910), or oxidation resulting in the pyrasulfotole-hydroxymethyl metabolite.



STORAGE STABILITY					PMRA # 1190082
Soybean grain, wheat grain, wheat forage, and wheat hay were spiked individually at 0.250 ppm with each pyrasulfotole, pyrasulfotole-desmethyl and pyrasulfotole-benzoic acid. Samples were analyzed at 1, 3, 6, and 11 months (336 days). Residues of pyrasulfotole-desmethyl declined by 0.12% per day in wheat hay and forage.					
		Percent decline			
Analyte	**Storage interval (days)**	**Soybean grain**	**Wheat grain**	**Wheat forage**	**Wheat hay**
Pyrasulfotole	336	1.0	1.4	6.2	7.5
Pyrasulfotole-desmethyl	336	0	1.5	46.3	46.5
Pyrasulfotole-benzoic acid	336	0	0	0	0

CROP FIELD TRIALS ON WHEAT	PMRA # 1190060

During the 2004 and 2005 wheat growing seasons, field trials were conducted at 44 locations to evaluate the magnitude of residues in/on wheat forage, hay, grain, and straw following application of either end-use product, AE 0317309 02 SE06 A1 (SE06) or AE 0317309 03 EC23 A8 (EC23). Trials for both formulations were carried out in zones 2(GA; 2 trials), 4(MS; 1 trial), 5(KS, IL, NE, MN, ON; 6 trials), 6(TX; 1 trial), 7(ND, NE, SD, ND, SA; 10 trials), 7A(AB; 1 trial), 8(KS, TX; 6 trials), 11(ID; 1 trial) and 14(SA, AB, MB; 15 trials).

Wheat trials conducted with the end-use product AE 0317309 02 SE06 A1.
Residues reported as < LOD were assumed to be half the LOQ for purposes of computation.

Commodity	Total Applic. Rate (kg a.i./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Pyrasulfotole-benzoic acid (AE B197555)									
Forage	0.046–0.055	18-25	68	0.003	0.447	0.437	0.030	0.081	0.1
		41-46	68	0.002	0.296	0.273	0.024	0.058	0.071
Grain		40-56	72	0.028	0.873	0.502	0.121	0.149	0.117
Hay		21-25	70	0.015	1.149	1.100	0.176	0.236	0.202
Straw		40-56	72	0.022	0.420	0.388	0.083	0.104	0.085
Pyrasulfotole-desmethyl (AE 1073910)									
Forage	0.046–0.055	18-25	68	<LOD	0.165	0.169	0.009	0.032	0.047
		41-46	68	<LOD	0.072	0.064	0.007	0.013	0.018
Grain		40-56	72	0.001	0.009	0.008	0.005	0.004	0.002
Hay		21-25	70	0.016	0.567	0.492	0.150	0.165	0.115
Straw		40-56	72	0.005	0.154	0.149	0.049	0.055	0.038

Pyrasulfotole									
Forage	0.046–0.055	18-25	68	<LOD	0.061	0.058	0.005	0.008	0.011
		41-46	68	<LOD	0.026	0.026	0.005	0.006	0.004
Grain		40-56	72	0.001	0.009	0.008	0.005	0.005	0.001
Hay		21-25	70	<LOD	0.625	0.563	0.009	0.042	0.108
Straw		40-56	72	0.001	0.030	0.025	0.003	0.005	0.005

Wheat trials conducted with the end-use product AE 0317309 03 EC23 A8.
Residues reported as < LOD were assumed to be half the LOQ for purposes of computation.

Commodity	Total Applic. Rate (kg a.i./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Pyrasulfotole-benzoic acid (AE B197555)									
Forage	0.035–0.042	18-25	64	0.005	0.362	0.350	0.029	0.076	0.091
		41-46	64	0.003	0.214	0.208	0.022	0.049	0.059
Grain		40-56	72	0.022	0.386	0.354	0.110	0.127	0.081
Hay		21-25	62	0.036	0.795	0.727	0.174	0.207	0.14
Straw		40-56	72	0.019	0.281	0.246	0.065	0.088	0.059
Pyrasulfotole-desmethyl (AE 1073910)									
Forage	0.035–0.042	18-25	64	<LOD	0.138	0.135	0.010	0.029	0.035
		41-46	64	<LOD	0.050	0.044	0.005	0.010	0.013
Grain		40-56	72	0.001	0.006	0.006	0.005	0.004	0.002
Hay		21-25	62	0.014	0.601	0.594	0.142	0.165	0.118
Straw		40-56	72	0.004	0.151	0.146	0.043	0.051	0.037
Pyrasulfotole									
Forage	0.035–0.042	18-25	64	<LOD	0.060	0.060	0.005	0.009	0.012
		41-46	64	<LOD	0.026	0.024	0.005	0.006	0.004
Grain		40-56	72	0.001	0.005	0.005	0.005	0.005	0.001
Hay		21-25	62	<LOD	0.361	0.294	0.008	0.031	0.062
Straw		40-56	72	0.001	0.016	0.016	0.004	0.005	0.004

CROP FIELD TRIALS ON BARLEY										PMRA # 1190058
A total of 35 field trials (33 harvest and 2 decline) were conducted to measure the magnitude of the residue for the herbicide pyrasulfotole in/on barley hay, grain, and straw following application of the end-use products AE 0317309 02 SE06 A1 (SE06) or AE 0317309 03 EC23 A8 (EC23) on barley. Trials for both formulations were carried out in zones 2(GA; 1 trial), 5(NE, MN, ON, WI; 4 trials), 5B(ON, QC; 1 trial), 7(ND, NE, SK; 4 trials), 9(ID; 1 trials), 10(CA; 1 trial), 11(OR, WA; 2 trials), and 14(SK, AB, MB; 10 trials).										
Barley trials conducted with the end-use product AE 0317309 02 SE06 A1. Residues reported as < LOD were assumed to be half the LOQ for purposes of computation.										
Commodity	Total Applic. Rate (kg a.i./ha)	PHI (days)	Residue Levels (ppm)							
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.	
Pyrasulfotole-benzoic acid (AE B197555)										
Grain	0.046–0.055	35-45	50	0.004	0.116	0.110	0.031	0.034	0.025	
Hay		21-25	56	0.027	0.631	0.614	0.133	0.184	0.14	
Straw		34-45	48	0.008	0.451	0.380	0.054	0.084	0.092	
Pyrasulfotole-desmethyl (AE 1073910)										
Grain	0.046–0.055	35-45	50	<LOD	0.008	0.008	0.002	0.003	0.002	
Hay		21-25	56	0.01	0.185	0.171	0.067	0.082	0.045	
Straw		34-45	48	0.004	0.220	0.156	0.027	0.043	0.04	
Pyrasulfotole										
Grain	0.046–0.055	35-45	50	<LOD	0.005	0.005	0.005	0.004	0.001	
Hay		21-25	56	<LOD	0.050	0.044	0.008	0.013	0.012	
Straw		34-45	48	<LOD	0.031	0.022	0.003	0.006	0.006	

Barley trials conducted with the end-use product AE 0317309 03 EC23 A8. Residues reported as < LOD were assumed to be half the LOQ for purposes of computation.										
Commodity	Total Applic. Rate (kg a.i./ha)	PHI (days)	Residue Levels (ppm)							
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Pyrasulfotole-benzoic acid (AE B197555)									
Grain	0.035–0.042	35-45	50	0.003	0.080	0.077	0.026	0.031	0.022
Hay		21-25	48	0.024	0.401	0.391	0.116	0.155	0.104
Straw		35-45	50	0.007	0.326	0.289	0.050	0.062	0.054
Pyrasulfotole-desmethyl (AE 1073910)									
Grain	0.035–0.042	35-45	50	<LOD	0.005	0.005	0.005	0.004	0.002
Hay		21-25	48	0.007	0.168	0.161	0.059	0.062	0.039
Straw		35-45	50	0.003	0.070	0.066	0.024	0.026	0.017
Pyrasulfotole									
Grain	0.035–0.042	35-45	50	<LOD	0	0.005	0.005	0	0.001
Hay		21-25	48	0.001	0.027	0.024	0.007	0.009	0.007
Straw		35-45	50	<LOD	0.011	0.010	0.004	0.004	0.003

CROP FIELD TRIALS ON OATS Residues reported as < LOD were assumed to be half the LOQ for purposes of computation.	PMRA # 1190059

During the 2004 and 2005 growing seasons, field trials were conducted at 39 locations to evaluate the magnitude of residues in/on oat forage, hay, grain, and straw following application of either AE 0317309 02 SE06 A1 (SE06) or AE 0317309 03 EC23 A8 (EC23). In total, 38 field trials (36 harvest and 2 decline) for both formulations were carried out in zones 1(PA; 1 trials), 2(FL; 1 trial), 5(KS, IL, NE, MN, OH, ON, ND; 9 trials), 5A(ON; 1 trial), 5B(ON; 1 trial), 6(TX; 1 trial), 7(ND, SK; 6 trials), 8(KS; 1 trial) and 14(SK, AB, MB; 17 trials).

Commodity	Total Applic. Rate (kg a.i./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Pyrasulfotole-benzoic acid (AE B197555)									
Forage	0.046–0.055	21-26	60	0.001	0.133	0.124	0.014	0.026	0.031
		41-46	60	<LOD	0.156	0.146	0.008	0.019	0.035
Grain		35-50	54	0.002	0.085	0.080	0.006	0.016	0.021
Hay		21-26	60	0.026	0.509	0.431	0.142	0.168	0.115
Straw		35-50	54	0.007	0.107	0.097	0.033	0.041	0.029
Pyrasulfotole-desmethyl (AE 1073910)									
Forage	0.046–0.055	21-26	60	0.001	0.116	0.100	0.014	0.023	0.023
		41-46	60	<LOD	0.072	0.066	0.005	0.010	0.014
Grain		35-50	54	0.001	0.083	0.080	0.008	0.011	0.016
Hay		21-26	60	0.036	0.587	0.527	0.147	0.167	0.107
Straw		35-50	54	0.010	0.156	0.144	0.048	0.053	0.031
Pyrasulfotole									
Forage	0.046–0.055	21-26	60	<LOD	0.006	0.006	0.003	0.003	0.002
		41-46	60	<LOD	0.005	0.005	0.005	0.004	0.001
Grain		35-50	54	<LOD	0.022	0.020	0.005	0.004	0.004
Hay		21-26	60	0.002	0.105	0.081	0.010	0.016	0.02
Straw		35-50	54	<LOD	0.014	0.012	0.004	0.004	0.003

Summary of Residue Data from Oat Field Trials with AE 0317309 03 EC23 A8.

Commodity	Total Applic. Rate (kg a.i./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Pyrasulfotole-benzoic acid (AE B197555)									
Forage	0.035–0.042	21-26	48	0.003	0.131	0.105	0.013	0.025	0.03
		41-46	48	<LOD	0.146	0.118	0.005	0.017	0.032
Grain		35-50	52	0.003	0.128	0.116	0.007	0.019	0.029
Hay		21-26	48	<LOD	0.510	0.472	0.163	0.188	0.129
Straw		35-50	52	0.007	0.108	0.106	0.035	0.041	0.028
Pyrasulfotole-desmethyl (AE 1073910)									
Forage	0.035–0.042	21-26	48	0.001	0.107	0.105	0.018	0.026	0.027
		41-46	48	0.001	0.087	0.077	0.005	0.010	0.016
Grain		35-50	52	0.001	0.089	0.088	0.005	0.010	0.017
Hay		21-26	48	<LOD	0.623	0.606	0.167	0.209	0.143
Straw		35-50	52	0.012	0.137	0.134	0.046	0.052	0.03
Pyrasulfotole									
Forage	0.035–0.042	21-26	48	<LOD	0.005	0.005	0.003	0.003	0.002
		41-46	48	<LOD	0.005	0.005	0.005	0.005	0.001
Grain		35-50	52	<LOD	0.022	0.022	0.005	0.004	0.004
Hay		21-26	48	<LOD	0.050	0.046	0.012	0.013	0.01
Straw		35-50	52	<LOD	0.012	0.011	0.003	0.004	0.003

FIELD ACCUMULATION IN ROTATIONAL CROPS	PMRA # 1190056

AE 0317309 02 SE06 A1 was applied to wheat planted in silty loam soil at a nominal rate of 0.050 kg a.i./ha with one application at three sites (zone 4 and 5) in 2004. The wheat crop was harvested and/or destroyed to allow planting of corn and soybeans with a plant-back interval (PBI) of 114 to 123 days following the application to wheat.

Summary of Residue Data in Rotational Crops Following Primary Treatment with AE 0317309 02 SE06 A1.

Commodity	Total Applic. Rate (kg a.i./ha)	PBI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Pyrasulfotole-benzoic acid (AE B197555)									
Corn forage	0.049–0.051	114-123	6	<LOD	0.0018	0.0018	<LOD	<LOD	<LOD
Corn Grain	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Corn Stover	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Soybean Forage	0.049–0.051	114-123	6	<LOD	0.0027	0.0026	<LOD	<LOD	<LOD
Soybean Grain	0.049–0.051	114-123	4	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Soybean Hay	0.049–0.051	114-123	6	<LOD	0.0126	0.0124	<LOD	0.0053	0.0055
Pyrasulfotole-desmethyl (AE 1073910)									
Corn forage	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Corn Grain	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Corn Stover	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Soybean Forage	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Soybean Grain	0.049–0.051	114-123	4	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Soybean Hay	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Pyrasulfotole (AE 0317309)									
Corn forage	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Corn Grain	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Corn Stover	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD

Commodity	Total Applic. Rate (kg a.i./ha)	PBI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Pyrasulfotole (AE 0317309)									
Soybean Grain	0.049–0.051	114-123	4	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Soybean Hay	0.049–0.051	114-123	6	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD

PROCESSED FOOD AND FEED	**PMRA # 1190057**
Test Site	Zone 5 (Sabin, Minnesota)
Treatment	Spring wheat was treated at the flag stage of development (BBCH 39)
Rate	0.258 kg a.i./ha
End-use product	AE 0317309 02 SE6; suspo-emulsion containing pyrasulfotole and mefenpyr-diethyl
Preharvest interval	57 days
Processed Commodity	**Processing Factor**
Aspirated Grain Fractions	32.8
Wheat Bran	1.6
Wheat Flour	0.3
Wheat Middling	0.4
Wheat Shorts	0.6
Wheat Germ	0.7

LIVESTOCK FEEDING – Dairy cattle								PMRA # 1190061
Pyrasulfotole was administered orally *via* gelatin capsule to 10 lactating Holstein cows (*Bos taurus*) for 29 consecutive days. There were 3 animals per treatment group and a single control animal, which were dosed at 0 ppm (control), 3 ppm, 9 ppm or 30 ppm in the feed (dry weight basis). This corresponds to 7.7-fold, 23-fold, and 77-fold of the calculated anticipated maximum dietary burden in dairy cattle arising from the use of pyrasulfotole on the cereal grains.								
Matrix	**Feeding Level (ppm/d)**	**n**	**LOD**	**Min**	**Max**	**Median**	**Mean**	**Standard Deviation**
Milk	30[a]	30	0.0015	0.0042	0.0134	0.0103	0.0096	0.0024
Milk Fat	30	3	0.0003	0.0061	0.0085	0.0074	0.0073	0.0012
Milk Skim	30	3	0.0002	0.0086	0.0105	0.0090	0.0094	0.0010
Fat	3	3	0.0007	0.0017	0.0062	0.0040	0.0040	0.0022
	9	3		<LOD	0.0033	——	——	——
	30	3		0.0024	0.0143	0.0046	0.0071	0.0064
Kidney	3	3	0.0004	0.1748	0.2224	0.1973	0.1982	0.0238
	9	4		0.1232	0.4240	0.2420	0.2631	0.1515
	30	3		0.3778	0.4144	0.3811	0.3911	0.0202
Liver	3	3	0.0005	1.019	1.230	1.187	1.145	0.1113
	9	3		0.6922	1.594	1.577	1.288	0.5159
	30	3		1.642	1.939	1.795	1.792	0.1488
Muscle	3	3	0.0006	<LOD	0.0010	——	——	——
	9	3		<LOD	0.0007	——	——	——
	30	3		0.0013	0.0039	0.0025	0.0026	0.0013
[a] For milk samples at the 30 ppm level Day 0 were excluded from the statistical analysis because dosing was not started until Day 1 (i.e. Day 0 was predosing).								

Anticipated Residues in Beef/Dairy, and Hog Milk and Tissues						
Commodity	**Feeding level (ppm)**	**Maximum Residues (ppm)***	**MTDB (ppm)**		**Anticipated Residue (ppm)**	
			Beef/Dairy	**Hog**	**Beef/Dairy**	**Hog**
Milk	9	0.0066	0.18	0.014	0.00013	-
Fat	3	0.0124	0.39	0.014	0.00161	0.00006
Kidney	3	0.4448	0.39	0.014	0.0578	0.0021
Liver	3	2.46	0.39	0.014	0.3198	0.011
Muscle	3	0.002	0.39	0.014	0.0003	0.000009
* Maximum residues include residues of pyrasulfotole from the feeding study and the assumption that pyrasulftole-desmethyl residues would be of equivalent amount in the tissues.						

LIVESTOCK FEEDING – Laying hens	PMRA # 1190062
Forty laying hens, divided into three treatment groups with three sub-groups of four hens each and four control hens, were orally dosed once daily for 29 consecutive days with pyrasulfotole-benzoic acid (AE B197555) at target dose rates of 0 ppm (control), 0.4, 1.2, or 4.0 ppm/day in the feed. The applicant based these levels on field residue data that were approximately 6.9-fold, 20.7-fold and 67-fold the anticipated maximum dietary burden of 0.058 ppm arising from the use of pyrasulfotole (AE 0317309) on cereal grains.	

Matrix	Feeding Level	Residue Levels (ppm)						
		n	LOD	Min	Max	Median	Mean	Standard Deviation
Egg	4.0 ppm [a]	30	0.0022	<LOD	<LOD	——	——	——
Fat	0.4 ppm	3	0.0014	<LOD	<LOD	——	——	——
	1.2 ppm	3		<LOD	0.0085	——	——	——
	4.0 ppm	3		0.0025	0.0057	0.0052	0.0045	0.0018
Liver	0.4 ppm	3	0.0010	<LOD	0.0016	——	——	——
	1.2 ppm	3		0.0024	0.0035	0.0031	0.0029	0.0008
	4.0 ppm	3		0.0102	0.0209	0.0105	0.0139	0.0061
Muscle	0.4 ppm	3	0.0018	<LOD	<LOD	——	——	——
	1.2 ppm	3		<LOD	<LOD	——	——	——
	4.0 ppm	3		0.0023	0.0038	0.0036	0.0032	0.0008
Skin	0.4 ppm	3	0.0014	0.0014	0.0030	0.0017	0.0021	0.0009
	1.2 ppm	3		0.0040	0.0073	0.0042	0.0052	0.0019
	4.0 ppm	3		0.0203	0.0226	0.0207	0.0212	0.0013

[a] For egg samples at 4.0 ppm dosing level, samples from Day 0 were excluded in the statistical analysis since dosing was not started until Day 1 (i.e., Day 0 was pre-dosing day).

Anticipated Residues in Poultry Eggs and Tissues.

Commodity	Feeding level (ppm)	Maximum residues * (ppm)	MTDB (ppm)	Anticipated residue (ppm)
Muscle	8.6	0.037	0.058	0.0002
Fat	8.6	0.065	0.058	0.0004
Liver	8.6	1.557	0.058	0.0105
Eggs	8.6	-	0.058	-

* Maximum residues include residues of pyrasulfotole and pyrasufotole-desmethyl from the hen metabolism study.

Table 6 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

<table>
<tr><th colspan="2">PLANT STUDIES</th></tr>
<tr><td>RESIDUE DEFINITION FOR ENFORCEMENT AND RISK ASSESSMENT
Primary crops</td><td>Pyrasulfotole and pyrasulfotole-desmethyl</td></tr>
<tr><td>Rotational crops</td><td>Pyrasulfotole</td></tr>
<tr><td colspan="2">Based on the structural similarity between the parent and the pyrasulfotole-desmethyl metabolite, and in the absence of toxicological evidence to the contrary, pyrasulfotole-desmethyl metabolite is assumed to be of comparable toxicity to the parent.

Pyrasulfotole-desmethyl had quantifiable levels in wheat (forage, hay, and straw), barley (hay and straw), and oat (forage, grain, hay and straw) in the submitted crop field trial studies. Additionally, in the majority of the commodities pyrasulfotole-desmethyl was present at levels equal to or greater than the parent, pyrasulfotole.

Although pyrasulfotole-benzoic acid was a major metabolite found in wheat metabolism, confined rotational crops, wheat, barley and oats crop field trial studies, based on available toxicology studies and dissimilar structure from the parent pyrasulfotole, it was considered to be not of toxicological concern. Therefore, it was not included in the residue definition for enforcement or risk assessment purposes for cereal grains.</td></tr>
<tr><td>METABOLIC PROFILE IN DIVERSE CROPS</td><td>The profile in diverse crops cannot be determined because only wheat was investigated.</td></tr>
<tr><th colspan="2">ANIMAL STUDIES</th></tr>
<tr><th>ANIMALS</th><th>Ruminant</th></tr>
<tr><td>RESIDUE DEFINITION FOR ENFORCEMENT AND RISK ASSESSMENT</td><td>Pyrasulfotole, pyrasulfotole-desmethyl</td></tr>
<tr><td colspan="2">In available crop field trials, pyrasulfotole-desmethyl was one of the major residues detected in livestock feed items; therefore, the secondary residues that livestock are likely to be exposed to are pyrasulfotole-desmethyl instead of parent.</td></tr>
<tr><td>METABOLIC PROFILE IN ANIMALS
(goat, hen, rat)</td><td>The profile is similar in that all the metabolites found in ruminants were also identified in rat.</td></tr>
<tr><td>FAT SOLUBLE RESIDUE</td><td>No</td></tr>
</table>

DIETARY RISK FROM FOOD AND WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
Refined chronic non-cancer dietary risk **ADI = 0.001 mg/kg bw** **Estimated chronic drinking water concentration = 0.0085 ppm**	**All infants < 1 year**	1.0	59.7
	Children 1–2 years	3.2	29.8
	Children 3 to 5 years	3.2	28.1
	Children 6–12 years	1.9	19.1
	Youth 13–19 years	1.0	14.0
	Adults 20–49 years	1.0	17.7
	Adults 50+ years	1.1	18.7
	Total population	1.3	19.2
Refined acute dietary exposure analysis, 95th percentile **Estimated acute drinking water concentration = 0.0098 ppm**	**POPULATION**	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**	
		Food Only	**Food and Water**
ARfD = 0.013 mg/kg bw	**Females 13–49 years**	0.2	3.8

Table 7 Fate and Behaviour in the Environment

Property	Test substance	Value	Comments
Terrestrial Environment			
Abiotic transformation			
Hydrolysis	[pyrazole-3-^{14}C] AE 0317309 pH 5, pH 7, pH 9	Stable in water at pHs 5, 7 and 9.	Stable to hydrolysis at environmentally relevant pH levels (no transformation occurred over 30 day study).
Phototransformation on soil	[pyrazole-3-^{14}C] AE 0317309	Stable on silt loam soil, pH 7.4.	Stable to photolysis on soils (no difference between irradiated and dark controls).

Property	Test substance	Value	Comments
Terrestrial Environment			
Biotransformation			
Biotransformation in aerobic soil	[phenyl-U-^{14}C] and [pyrazole-3-^{14}C] AE 0317309	DT_{50}, DT_{90}, 1/3 DT_{90} of both radiolabels combined: Loamy sand soil: 5.8, 749, 249 days Silt loam soil: 63, 1424, 475 days Sandy loam soil: 23, 208, 69 days	Moderately persistent to persistent in aerobic soils based on 1/3 DT_{90} estimates.
Biotransformation in anaerobic soil	[phenyl-U-^{14}C] and [pyrazole-3-^{14}C] AE 0317309	$t_{½}$ of both radiolabels combined: whole system = stable	Stable in anaerobic soils.
Mobility			
Adsorption or desorption in soil	[pyrazole-3-^{14}C] AE 0317309	Non-Freundlich coefficients in silt loam (x2), loamy sand, clay loam and sandy loam soils, and one sandy loam sediment: $K_{d\text{-}ads}$: 0.37- 18.2 $K_{OC\text{-}ads}$: 22 - 395 $K_{d\text{-}des}$: 0.15 – 12.7 $K_{OC\text{-}des}$: 9 - 276	Moderate to very high mobility.
	AE B197555	Freundlich coefficients in clay loam, sandy loam and silt loam: $K_{F\text{-}ads}$: 0.01 - 0.03 $K_{FOC\text{-}ads}$: 1 - 2 1/n: 0.53 – 0.86 $K_{F\text{-}des}$: not determined* $K_{FOC\text{-}des}$: not determined*	Very high mobility.
Soil leaching		Not submitted.	Not required.
Volatilization		Not submitted.	Not required.
Field studies			
Field dissipation	U.S. studies: AE 0317309 02 SE06 A103 (50 g a.i./L pyrasulfotole) Canadian studies: AE 0317309 02 OD14 A102 (115 g a.i./L pyrasulfotole + 29 g a.i./L mefenpyr-diethyl)	North Dakota DT_{50}: 6 days DT_{90}: 44 days 1/3 DT_{90}: 15	Slightly persistent based on 1/3 DT_{90} estimate.
		Washington DT_{50}: 6 days DT_{90}: 213 days 1/3 DT_{90}: 71	Moderately persistent based on 1/3 DT_{90} estimate.
		Saskatchewan DT_{50}: 10 days DT_{90}: 260 days 1/3 DT_{90}: 87	Moderately persistent based on 1/3 DT_{90} estimate.
		Manitoba DT_{50}: 9 days DT_{90}: 531 days 1/3 DT_{90}: 177	Moderately persistent based on 1/3 DT_{90} estimate.

Property	Test substance	Value	Comments
Terrestrial Environment			
		Ontario DT_{50}: 18 days DT_{90}: 178 days 1/3 DT_{90}: 59	Moderately persistent based on 1/3 DT_{90} estimate.
Field leaching		Not submitted.	Not required.
Aquatic Environment			
Abiotic transformation			
Hydrolysis	[pyrazole-3-^{14}C] AE 0317309	Estimated $t_{½}$: > 1 year at pH 5, 7, 9	Stable to hydrolysis.
Phototransformation in water	[phenyl-U-^{14}C] and [pyrazole-3-^{14}C] AE 0317309	$t_{½}$ = stable	Stable to photolysis in water.
Biotransformation			
Biotransformation in aerobic water systems	[phenyl-U-^{14}C] and [pyrazole-3-^{14}C] AE 0317309	Sandy loam system $t_{½}$ whole system = could not be determined (stable)	Considered stable in aerobic whole water-sediment system due to test material partitioning to bound residues in sediment, but not being lost from the system.
		Silt clay system Observed DT_{50} > 131 days in water, sediment and whole system.	Stable in aerobic whole water-sediment system.
Biotransformation in anaerobic water systems	[phenyl-U-^{14}C] AE 0317309	Observed DT_{50} > 1 year	Stable in anaerobic whole water-sediment system.
	[pyrazole-3-^{14}C] AE 0317309	Observed DT_{50} > 1 year	Stable in anaerobic whole water-sediment system.
Partitioning			
Adsorption or desorption in sediment (results from soil adsorption / desorption study)	[pyrazole-3-^{14}C] AE 0317309	Non-Freundlich coefficients in Nidda sandy loam sediment $K_{d\text{-}ads}$: 18.2 $K_{OC\text{-}ads}$: 395 $K_{d\text{-}des}$: 12.7 $K_{OC\text{-}des}$: 276	Moderate mobility.
Field studies			
Field dissipation	Not Submitted		

Fate process	Test material	Major transformation products	Minor transformation products
Hydrolysis	[pyrazole-3-^{14}C] AE 0317309	None.	None.
Phototransformation on soil	[pyrazole-3-^{14}C] AE 0317309	None.	None.
Phototransformation in water	[phenyl-U-^{14}C] and [pyrazole-3-^{14}C] AE 0317309	None.	Unknown A (detected once at 4.1% on Day 3; [phenyl-U-^{14}C] label only).
Biotransformation in aerobic soil	[phenyl-U-^{14}C] and [pyrazole-3-^{14}C] AE 0317309	AE B197555 ([phenyl-U-^{14}C] label only, 3.8 - 12.2%; Days 7 - 30) CO_2 (16.3 - 40.5%; study termination, Days 120 - 358)	Unidentified polar compounds (2.6 - 14.1%; Days 41 - 358)
Biotransformation in anaerobic soil (flooded soil)	[phenyl-U-^{14}C] and [pyrazole-3-^{14}C] AE 0317309	None.	AE B197555 (≤ 0.6%) Unidentified polar compounds (≤ 1.5%)
Field dissipation	U.S. studies: AE 0317309 02 SE06 A103 (50 g a.i./L pyrasulfotole) Canadian studies: AE 0317309 02 OD14 A102 (115 g a.i./L pyrasulfotole + 29 g a.i./L mefenpyr-diethyl)	AE B197555 (20.8 – 67.3%; Days 7 – 29)	None.
Biotransformation in aerobic water/sediment system	[phenyl-U-^{14}C] and [pyrazole-3-^{14}C] AE 0317309	None.	Both sandy loam and silty clay systems: AE B197555 (max. 2.6-3.0% in whole systems; phenyl-U-^{14}C label only). Unidentified [^{14}C]residues (total max. 3.0% in the whole systems both labels).
Biotransformation in anaerobic water/sediment system	[phenyl-U-^{14}C] and [pyrazole-3-^{14}C] AE 0317309	None.	Unidentified polar compounds (≤ 3.4%). CO_2 (≤ 2.8%).

Table 8 Toxicity to Non-Target Species

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Invertebrates				
Earthworm	Acute (artificial soil)	AE 0317309 (95.4% purity)	NOEC = 1000 mg a.i./kg soil LC_{50} > 1000 mg a.i./kg soil	Practically non-toxic
	Acute (artificial soil)	AE B197555 (990 g/kg purity)[b]	NOEC = 556 mg/kg soil LC_{50} > 1000 mg/kg soil	Practically non-toxic
	Chronic (artificial soil)	AE B197555 (990 g/kg purity)	NOEC = 1000 mg/kg soil	
Bee	Oral	AE 0317309 (95.4% purity)	NOEC = 120 ug a.i./bee LD_{50} > 120 ug a.i./bee (i.e., LD_{50} > 134 kg a.i./ha)	Relatively non-toxic.
	Contact	AE 0317309 (95.4% purity)	NOEC = 75 ug a.i./bee LD_{50} > 75 ug a.i./bee (i.e., LD_{50} > 84 kg a.i./ha)	Relatively non-toxic.
Predatory arthropod	Contact	AE 0317309 02 SE06 A103 [4.32% w/w AE 0317309 plus 1.02% w/w AE F107892 (product safener)]	Mortality: NOEC = 18 g a.i./ha LR_{50} > 100 g a.i./ha Reproduction: NOEC = 18 g a.i./ha IR_{50} = 58.6 g a.i./ha	
Parasitic arthropod	Contact	AE 0317309 02 SE06 A103 [4.32% w/w AE 0317309 plus 1.02% w/w AE F107892 (product safener)]	Mortality: NOEC = 32 g a.i./ha LR_{50} = 80.3 g a.i./ha Reproduction: NOEC = <18 g a.i./ha IR_{50} = 31.1 g a.i./ha	
Birds				
Bobwhite quail	Acute	AE 0317309 (95.4% purity)	NOEL = 2000 mg a.i./kg bw LD_{50} > 2000 mg a.i./kg bw	Practically non-toxic.
	Dietary	AE 0317309 (95.4% purity)	NOEC = 4911 mg a.i./kg diet LC_{50} > 4911 mg a.i./kg diet	Practically non-toxic.
		AE B197555 (990 g/kg purity)	NOEC = 5620 mg a.i./kg diet LC_{50} > 5620 mg a.i./kg diet	Practically non-toxic.
	Reproduction	AE 0317309 (95.4% purity)	NOEC = 205 mg a.i./kg diet Endpoint: proportion of hatchlings to live 3-week embryos.	

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Mallard duck	Acute	Not submitted.	Not submitted.	
	Dietary	AE 0317309 (95.4% purity)	NOEC = 5089 mg a.i./kg diet LC_{50} > 5089 mg a.i./kg diet	Practically non-toxic.
	Reproduction	AE 0317309 (95.4% purity)	NOEC = 167 mg a.i./kg diet Endpoint: adult male body weight gain	
Mammals				
Rat	Acute	AE 0317309 (95.4% purity)	NOAEL = 2000 mg a.i./kg bw LD_{50} > 2000 mg a.i./kg bw Enpoint: mortality	Practically non-toxic.
	Dietary (90-Day)	AE 0317309 (95.4% purity)	NOAEL= 30 mg a.i./kg diet ♂= 1.96 mg a.i./kg bw/d ♀= 2.32 mg a.i./kg bw/d Endpoint: decreased kidney function in ♂and corneal opacity in ♀	
	2-Generation Reproduction	AE 0317309 (95.4% purity)	NOAELs: parental systemic toxicity <30 mg a.i./kg diet ♂ <2.5, ♀ <3.1 mg/kg bw/d Endpoint: thyroid effects offspring toxicity <30 mg a.i./kg diet ♂ <2.5, ♀ <3.1 mg/kg bw/d Endpoint: pup mortality reproductive toxicity = 30 mg a.i./kg diet ♂ = 2.5, ♀ = 3.1 mg/kg bw/d Endpoint: decreased rearing indices	
	Acute	AE B197555 (990 g/kg purity)	NOAEL = 5000 mg/kg bw LD_{50} >5000 mg/kg bw Endpoint: no mortality	Practically non-toxic.
	Dietary (28-Day)	AE B197555 (990 g/kg purity)	NOAEL = 15000 mg/kg diet Endpoint: no mortality, sublethal effects	Practically non-toxic.
	Dietary (90-Day)	AE B197555 (990 g/kg purity)	NOAEL = 12000 mg/kg diet Endpoint: no mortality, sublethal effects	Practically non-toxic.
	Developmental toxicity	AE B197555 (990 g/kg purity)	NOAEL = 75 mg/kg bw/d Endpoint: maternal toxicity (decreased food intake, transient decreased bw)	

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
	Acute	AE 0317309 02 SE06 Herbicide	LD_{50} >2000 mg/kg bw	Practically non-toxic.
	Acute	AE 0317309 03 EC23 Herbicide	LD_{50} >300 <2000 mg/kg bw	Slightly toxic.
Mouse	Dietary (90-Day)	AE 0317309 (95.4% purity)	NOAEL= 3000 mg a.i./kg diet ♂ = 500 mg a.i./kg bw/d ♀ = 617 mg a.i./kg bw/d Endpoint: no mortality, sublethal effects	Practically non-toxic.
Rabbit	Developmental toxicity	AE 0317309 (95.4% purity)	NOAELs: maternal toxicity = 75 mg/kg bw/d Endpoints: kidney function, decreased bw, decreased food intake, increased liver wt developmental toxicity = 10 mg/kg bw/d Endpoints: skeletal variation, but effects not considered biologically relevant at 10 mg/kg bw/d	
Vascular plants				
Vascular plant	Seedling emergence	AE 0317309 03 EC23 (37.5 g a.i./L)	EC_{25} = 0.28 g a.i./ha Endpoint: tomato dry weight	
		AE 0317309 02 SE06 (50 g a.i./L)	EC_{25} = 1.23 g a.i./ha Endpoint: tomato dry weight	
		AE B197555 (990 g/kg purity)	EC_{25} > 157 g/ha Endpoint : none > 25%	
	Vegetative vigour	AE 0317309 03 EC23 (37.5 g a.i./L)	EC_{25} = 0.19 g a.i./ha Endpoint: cucumber dry weight	
		AE 0317309 02 SE06 (50 g a.i./L)	EC_{25} = 0.91 g a.i./ha Endpoint: tomato dry weight	
		AE B197555 (990 g/kg purity)	EC_{25} > 146 g/ha Endpoint : none > 25%	

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Aquatic Invertebrates				
Water flea (*Daphnia magna*)	Acute	AE 0317309 (97.4% purity)	NOEC = 95.8 mg a.i./L EC_{50} > 95.8 mg a.i./L	Practically non-toxic
		AE B197555 (990 g/kg purity)[b]	NOEC = 150 mg/L EC_{50} > 150 mg/L	Practically non-toxic
	Chronic	AE 0317309 (95.4% purity)	NOEC = 12.8 mg a.i./L EC_{50} > 52.9 mg a.i./L	
Aquatic Vertebrates				
Rainbow trout (*Oncorhynchus mykiss*)	Acute	AE 0317309 (97.4% purity)	NOEC = 96.0 mg a.i./L LC_{50} > 96.0 mg a.i./L	Practically non-toxic
		AE B197555 (990 g/kg purity)	NOEC = 130 mg a.i./L LC_{50} = 160 mg/L	Practically non-toxic
Fathead minnow (*Pimephales promelas*)	Chronic (Early Life Stage test)	AE 0317309 (95.4% purity)	NOEC = 0.58 mg a.i./L LOEC = 1.10 mg a.i./L Effects: length (most sensitive parameter), dry weight	
Bluegill sunfish (*Lepomis macrochirus*)	Acute	AE 0317309 (98.2% purity)	NOEC = 96.5 mg a.i./L LC_{50} > 96.5 mg a.i./L	Practically non-toxic
Freshwater algae / plants				
Green algae (*Pseudokirchneriella subcapitata*)	Acute	AE 0317309 (95.4% purity)	NOEC = 2.6 mg a.i./L EC_{50} = 11.0 mg a.i./L Endpoint: cell density, biomass	
		AE B197555 (990 g/kg purity)	NOEC = 2.4 mg a.i./L EC_{50} > 9.4 mg a.i./L Endpoint: cell density	
Diatom (*Navicula pelliculosa*)	Acute	AE 0317309 (95.4% purity)	NOEC = 25.8 mg a.i./L EC_{50} = 53.0 mg a.i./L Endpoint: biomass	
Blue-green algae (*Anabaena flos-aquae*)	Acute	AE 0317309 (95.4% purity)	NOEC = 40.1 mg a.i./L EC_{50} = 45.7 mg a.i./L Endpoint: growth rate	
Vascular plant (*Lemna gibba*)	Acute	AE 0317309 (95.4% purity)	NOEC = 0.00957 mg a.i./L EC_{50} = 0.028 mg a.i./L Endpoint: frond dry weight	

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Marine species				
Crustacean (*Mysidopsis bahia*)	Acute	AE 0317309 (95.4% purity)	NOEC = 0.37 mg a.i./L LC_{50} = 1.1 mg a.i./L	Moderately toxic
		AE B197555 (990 g/kg purity)	NOEC = 25 mg/L LC_{50} = 145 mg/L	Practically non-toxic
Mollusk (*Crassostrea virginica*)	Acute	AE 0317309 (95.4% purity)	NOEC = 104 mg a.i./L EC_{50} > 104 mg a.i./L	Practically non-toxic
Sheepshead minnow (*Cyprinidon variegatus*)	Acute	AE 0317309 (95.4% purity)	NOEC = 100 mg a.i./L LC_{50} > 100 mg a.i./L	Practically non-toxic
Marine alga (*Skeletonema costatum*)	Acute	AE 0317309 (95.4% purity)	NOEC = 2.53 mg a.i./L EC_{50} = 8.3 mg a.i./L	

Table 9 Screening Level Risk Assessment on Non-target Species

Organism	Test Substance	Exposure	End point value	EEC	RQ[a]
Terrestrial Invertebrates					
Earthworm	AE 0317309	Acute	1/2 LC_{50} > 500 mg a.i./kg soil	0.022 mg a.i./kg dw soil	0.000044
	AE B197555	Acute	1/2 LC_{50} > 500 mg/kg soil	0.016 mg/kg dw soil[f]	0.000032
		Chronic	NOEC = 500 mg/kg soil	0.016 mg/kg dw soil[b]	0.000032
Bee	AE 0317309	Oral	LD_{50} > 120 ug a.i./bee (i.e., LD_{50} > 134 kg a.i./ha)	50 g a.i./ha	0.00037
		Contact	LD_{50} > 75 ug a.i./bee (i.e., LD_{50} > 84 kg a.i./ha)	50 g a.i./ha	0.00060
Predatory arthropod	AE 0317309	Contact	LR_{50} > 100 g a.i./ha	50 g a.i./ha	0.50
Parasitic arthropod	AE 0317309	Contact	LR_{50} = 80.3 g a.i./ha	50 g a.i./ha	0.62
Terrestrial Vertebrates					
Bobwhite quail	AE 0317309	Acute	NOEL = 2000 mg a.i./kg bw	0.929 mg a.i./kg bw[c]	0.00046
		Dietary	NOEC = 4911 mg a.i./kg diet	8.75 mg a.i./kg dw diet	0.0018
		Reproduction	NOEC = 205 mg a.i./kg diet	8.75 mg a.i./kg dw diet	0.042
	AE B197555	Dietary	NOEC = 5620 mg/kg diet	6.48 mg/kg diet[b]	0.0012

Organism	Test Substance	Exposure	End point value	EEC	RQ[a]
Mallard duck	AE 0317309	Dietary	NOEC = 5089 mg a.i./kg diet	1.69 mg a.i./kg dw diet	0.00033
		Reproduction	NOEC = 167 mg a.i./kg diet	1.69 mg a.i./kg dw diet	0.010
Rat	AE 0317309	Acute	LD_{50} >2000 mg a.i./kg bw	4.32 mg a.i./kg bw[d]	0.0022
		90-d Dietary	NOAEL = 30 mg a.i./kg diet	25.22 mg a.i./kg dw diet	0.84
		2-Generation Reproduction	LOAEL = 30 mg a.i./kg diet	25.22 mg a.i./kg dw diet	0.84 (note: RQ for LOAEL; RQ for NOAEL could not be determined)
	AE B197555	Acute oral	LD_{50} >5000 mg/kg bw	3.19 mg/kg bw[e]	0.00064
		28-d Dietary	NOAEL = 15000 mg/kg diet	18.66 mg/kg dw diet[f]	0.0012
		Developmental toxicity	NOAEL = 75 mg/kg bw/d maternal toxicity (decreased food intake, transient decrease body weight)	3.19 mg/kg bw[e]	0.043
	AE 0317309 02 SE06 Herbicide	Acute	LD_{50} >2000 mg/kg bw	95.9 mg/kg bw[f]	0.048
	AE 0317309 03 EC23 Herbicide	Acute	LD_{50} >300 <2000 mg/kg bw	130.9 mg/kg bw[g]	0.44
Mouse	AE 0317309	28-d Dietary	NOAEL = 1000 mg a.i./kg diet	25.07 mg a.i./kg dw diet	0.025
Rabbit	AE 0317309	Developmental toxicity	NOAEL = 10 mg/kg bw/d developmental toxicity	1.13 mg/kg bw[h]	0.11
Terrestrial Plants					
Vascular plant	AE 0317309 03 EC 23	Seedling emergence	EC_{25} = 0.28 g a.i./ha	31.25 g a.i./ha	**112**
		Vegetative vigour	EC_{25} = 0.19 g a.i./ha	31.25 g a.i./ha	**164**
	AE 0317309 02 SE 06	Seedling emergence	EC_{25} = 1.23 g a.i./ha	50 g a.i./ha	**41**
		Vegetative vigour	EC_{25} = 0.91 g a.i./ha	50 g a.i./ha	**55**
	AE B197555	Seedling emergence	EC_{25} > 157 g/ha	37 g/ha[b]	0.24
		Vegetative vigour	EC_{25} > 146 g/ha	37 g/ha[b]	0.25

Organism	Test Substance	Exposure	End point value	EEC	RQ[a]
Freshwater Invertebrates					
Daphnia magna	AE 0317309	Acute	1/2 EC_{50} > 47.9 mg a.i./L	0.0063 mg a.i./L	0.00013
		Chronic	NOEC = 12.8 mg a.i./L	0.0063 mg a.i./L	0.00049
	AE B197555	Acute	1/2 EC_{50} > 75 mg/L	0.0047 mg/L[b]	0.000063
Freshwater Vertebrates					
Rainbow trout	AE 0317309	Acute	1/10 LC_{50} > 9.6 mg a.i./L	0.0063 mg a.i./L	0.00066
	AE B197555	Acute	1/10 LC_{50} = 16.0 mg/L	0.0047 mg/L[b]	0.00029
Bluegill sunfish	AE 0317309	Acute	1/10 LC_{50} > 9.65 mg a.i./L	0.0063 mg a.i./L	0.00065
Fathead minnow	AE 0317309	Chronic	NOEC = 0.58 mg a.i./L	0.0063 mg a.i./L	0.011
Amphibians	AE 0317309	Chronic	NOEC = 0.58 mg a.i./L[g]	0.033 mg a.i./L	0.057
Freshwater Plants					
Freshwater alga	AE 0317309	Acute	1/2 EC_{50} = 5.5 mg a.i./L	0.0063 mg a.i./L	0.0012
	AE B197555	Acute	1/2 EC_{50} > 4.7 mg a.i./L	0.0047 mg/L[b]	0.0010
Vascular plant (*Lemna gibba*)	AE 0317309	Acute	1/2 EC_{50} = 0.014 mg a.i./L	0.0063 mg a.i./L	0.45
Marine Invertebrates					
Marine crustacean (mysid)	AE 0317309	Acute	1/2 LC_{50} = 0.55 mg a.i./L	0.0063 mg a.i./L	0.012
	AE B197555	Acute	1/2 LC_{50} = 72.5 mg/L	0.0047 mg/L[b]	0.000065
Marine mollusk	AE 0317309	Acute	1/2 EC_{50} > 52 mg a.i./L	0.0063 mg a.i./L	0.00012
Marine Vertebrates					
Marine salmonid	AE 0317309	Acute	1/10 LC_{50} > 10 mg a.i./L	0.0063 mg a.i./L	0.00063
Marine Plants					
Marine alga	AE 0317309	Acute	1/2 EC_{50} = 4.2 mg a.i./L	0.0063 mg a.i./L	0.0015

[a] Risk quotient = exposure / toxicity. Bold RQ values indicate that the risk quotient exceeds the PMRA LOC of 1.
[b] EECs for AE B197555 (a.k.a RPA 203328) based on assumed 100% conversion of pyrasulfotole and a molar ratio of 0.74 (268.2 g/mol AE B197555 / 362.3 g/mol pyrasulfotole). For example, 50 g a.i./ha * 0.74 = 37 g/ha AE B197555.
[c] EEC according to body weight = 8.75 mg a.i./kg dw diet for bobwhite quail x 0.0189 kg dw diet/day for daily food intake rate (Nagy 1987) / 0.178 kg for body weight (Dunning 1993).
[d] EEC according to body weight = 25.22 mg a.i./kg dw diet for rat x 0.060 kg dw diet/day for daily food intake rate (U.S. EPA 1988) / 0.35 kg for body weight (U.S. EPA 1988).
[e] EEC according to body weight = 18.66 mg a.i./kg dw diet for rat x 0.060 kg dw diet/day for daily food intake rate (U.S. EPA 1988) / 0.35 kg for body weight (U.S. EPA 1988).
[f] Conversion of EEC in diet: 25.22 mg a.i./kg dw diet / 4.51% pyrasulfotole in SE06 formulation = 559.2 mg/kg dw diet. EEC according to body weight = 559.2 mg/kg dw diet for rat x 0.060 kg dw diet/day for daily food intake rate (U.S. EPA 1988) / 0.35 kg for body weight (U.S. EPA 1988).
[g] Conversion of EEC in diet: 25.22 mg a.i./kg dw diet / 3.30% pyrasulfotole in EC23 formulation = 763.5 mg/kg dw diet. EEC according to body weight = 763.5 mg/kg dw diet for rat x 0.060 kg dw diet/day for daily food intake rate (U.S. EPA 1988) / 0.35 kg for body weight (U.S. EPA 1988).
[h] EEC according to body weight = 37.72 mg a.i./kg dw diet for rabbit x 0.060 kg dw diet/day for daily food intake rate (U.S. EPA 1988) / 2.0 kg for body weight (U.S. EPA 1988).

Table 10 Screening Level Risk Assessment for List 2 Petroleum Distillate Formulant on Non-target Aquatic Species

Organism	Test Substance	Exposure	End point value	EEC	RQ[a]
Daphnia magna	List 2 Petroleum Distillate	Acute	1/2 EC_{50} = 0.475 mg/L	0.038 mg/L[b]	0.1
Rainbow trout	List 2 Petroleum Distillate	Acute	1/10 LC_{50} = 0.234 mg/L	0.038 mg/L[b]	0.2
Amphibians	List 2 Petroleum Distillate	Acute	1/10 LC_{50} = 0.234 mg/L[c]	0.20 mg/L	0.9

[a] Risk quotient = exposure / toxicity. Bold RQ values indicate that the risk quotient exceeds the PMRA LOC of 1.
[b] EEC for aquatic habitats based on an application rate of 300.4 g/ha List 2 petroleum distillate to a 1 ha pond 80 cm deep.
[c] 1/10 LC_{50} from acute rainbow trout study was used to determine risk to amphibians in a 15 cm deep water body.

Table 11 Refined Risk Assessment on Non-Target Terrestrial Plant Species

Organism	Test Substance	Exposure	End point value	EEC	RQ[a]
Vascular plant	AE 0317309 03 EC 23	Seedling emergence	EC_{25} = 0.28 g a.i./ha	1.9 g a.i./ha	6.7
		Vegetative vigour	EC_{25} = 0.19 g a.i./ha	1.9 g a.i./ha	9.9
	AE 0317309 02 SE 06	Seedling emergence	EC_{25} = 1.23 g a.i./ha	3.0 g a.i./ha	2.4
		Vegetative vigour	EC_{25} = 0.91 g a.i./ha	3.0 g a.i./ha	3.3

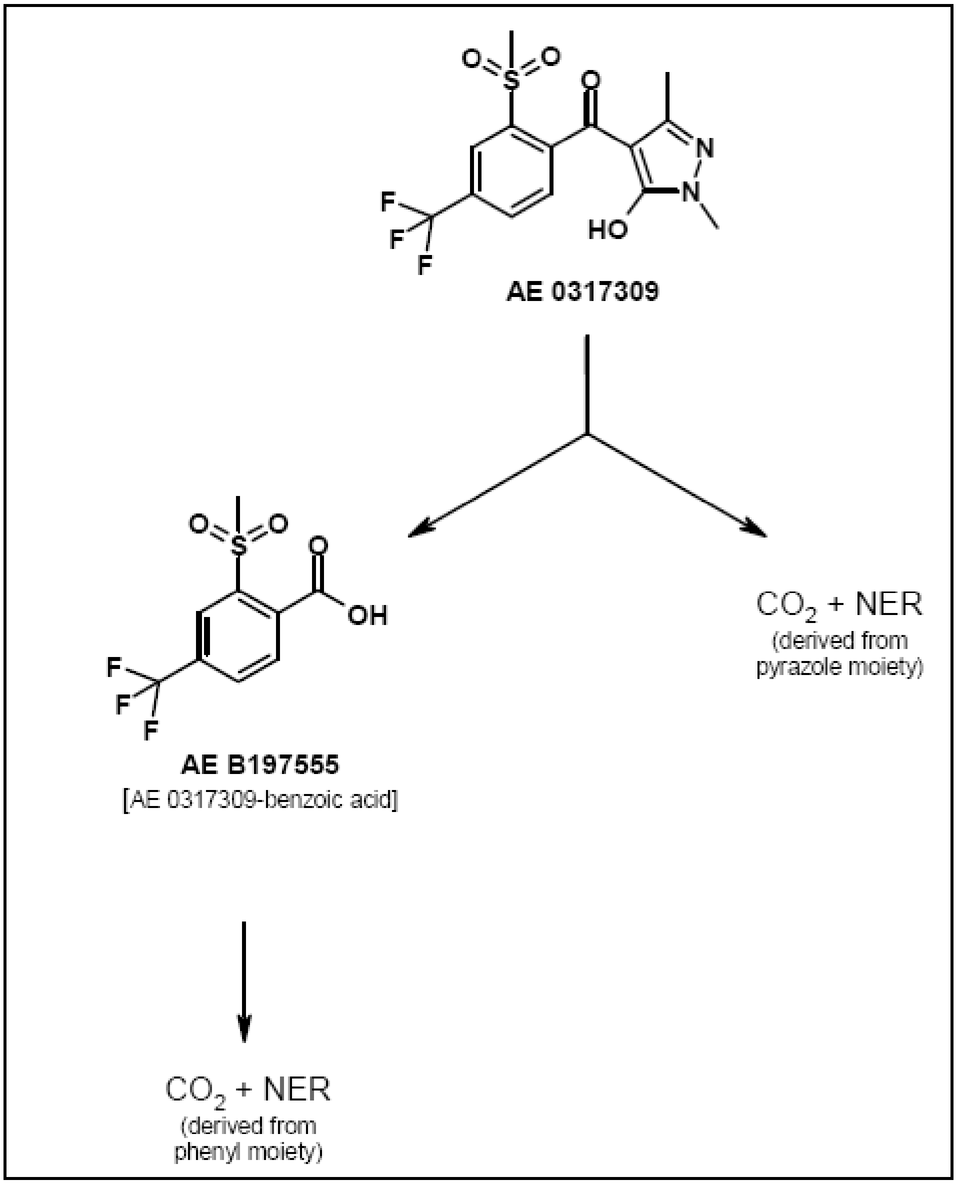


Figure 4.1 Transformation Pathway for pyrasulfotole (AE 0317309) in Aerobic Soil

References

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

1.0 Chemistry Assessment

PMRA 1189809 2006, AE 0317309 - Technical material - Discussion of the formation of impurities, M-265968-01-1, DACO: 2.12.2,2.13.4

PMRA 1189810 2006, Analytical Testing of Pyrasulfotole (AE 0317309) - Determination of Cyanide, 2006/0009/01, DACO: 2.13.3

PMRA 1189811 2006, Material accountability of Ae 0317309 (pyrasulfotole) Analytical profile of five production batches, PA05/052, DACO: 2.13.3

PMRA 1189812 2006, AE 0317309 - Technical grade active substance - Description of the manufacturing process of the technical A.S., M-265958-01-1, DACO: 2.11.1,2.11.2,2.11.3,2.11.4

PMRA 1189813 2006, External composition statement technical material - Pyrasulfotole AE 0317309, M-264794-01-1, DACO: 2.12.1,2.12.2,2.13.4

PMRA 1189814 2006, AE 0317309; substance, pure - AE 0317309 00 1B99 0001 - Melting point, boiling point, thermal stability - 1st amendment to report-No. 20040374.01, 20040374.01, DACO: 2.14.4,2.14.5,2.16

PMRA 1189815 2005, Storage stability and corrosion characteristics of AE 0317309, PA03/076, DACO: 2.14.14

PMRA 1189817 2005, Stability of AE 0317309 to normal and elevated temperature, metals and metal ions, PA04/097, DACO: 2.14.13

PMRA 1189818 2003, AE 0317309 - substance, technical - AE 0317309 00 1C96 0001 - Auto-flammability (Solids - Determination of relative self-ignition temperature), 20031005.03, DACO: 2.16

PMRA 1189819 2003, AE 0317309 - substance, technical - AE 0317309 00 1C96 0001 - Explosive properties, 20031005.02, DACO: 2.16

PMRA 1189820 2003, AE 0317309 - substance, technical - AE 0317309 00 1C96 0001 - Flammability (solids), 20031005.01, DACO: 2.16

PMRA 1189821 2005, AE 0317309 substance, pure - Surface tension - Code: AE 0317309 00 1B99 0001, M-255551-01-1, DACO: 2.16

PMRA 1189822 2003, Determination of the pH -value of AE 0317309 substance, pure Code: AE 0317309 00 1B99 0001, C033462, DACO: 2.16

PMRA 1189823 2005, Final report AE 0317309; substance, technical AE 0317309 001C99 0002 - Oxidizing properties A.17, 20050877.01, DACO: 2.16

PMRA 1189824 2005, Relative density of AE 0317309 substance, technical, PA05/101, DACO: 2.16

PMRA 1189825 2006, The oxidation or reduction properties of AE 0317309 - Technical substance - AE 0317309 00 1C99 0002, PA05/110, DACO: 2.16

PMRA 1189826 2003, AE 0317309 - Relative density, PA03/040, DACO: 2.14.6

PMRA 1189827 2004, Vapour pressure AE 0317309; substance, pure Code: AE 0317309 00 1B99 0001, C042368, DACO: 2.14.9

PMRA 1189828 2003, AE 0317309 - Physical characteristics color, appearance and odor, PA03/044, DACO: 2.14.1,2.14.2,2.14.3

PMRA 1189829 2005, Physical characteristics color, appearance and odor of AE 0317309 substance, technical, PA05/102, DACO: 2.14.1,2.14.2,2.14.3

PMRA 1189830 2003, AE 0317309 - Spectral data (UV/VIS, IR, 1H-NMR, 13C-NMR, MS) and molar extinction coefficient, PA03/023, DACO: 2.13.2,2.14.12

PMRA 1189831 2004, Water solubility of AE 0317309 at pH 4, pH 7, pH 9 and bidistilled water, PA03/008, DACO: 2.14.7

PMRA 1189832 2003, AE 0317309 - Solubility in organic solvents, PA03/009, DACO: 2.14.8

PMRA 1189833 2003, AE 0317309 - Partition coefficient 1-octanol/water (AE 0317309 00 1B99 0001), PA03/010, DACO: 2.14.11

PMRA 1189834 2006, AE 0317309 - Determination of the dissociation constant, PA03/045A1, DACO: 2.14.10,8.2.3.2

PMRA 1189837 2006, Material safety data sheet - Pyrasulfotole technical, M-266812-01-1, DACO: 2.11.2

PMRA 1189838	2004, Determination of AE 0317309 in technical grade and pure AE 0317309 by high performance liquid chromatographie (HPLC), C045951, DACO: 2.13.1
PMRA 1189839	2006, Validation of HPLC-method AM006904FP1 Determination of AE 0317309 in technical grade and pure AE 0317309 by high performance liquid chromatographie (HPLC), AF04/086, DACO: 2.13.1
PMRA 1189840	2006, AE 0317309 - Determination of cyanide by polarography validation of method 2201-0225603-96, VB-2201-0225603, DACO: 2.13.4
PMRA 1189841	2005, Analytical method - Determination of by-products in technical grade and pure AE 0317309 by high performance liquid chromatography (HPLC), AM007505FP1, DACO: 2.13.4
PMRA 1189842	2005, Analytical method: determination of the solvents Acetonitrile (AE 0173080), Toluene (AE F125577) and MTBE (AE F146605) in AE 0317309 technical materials by gas chromatography, AM009105FP2, DACO: 2.13.4
PMRA 1189843	1996, Cyanide; FRee and inorganicly bound cyanide - Polarography, 2201-0225603-96, DACO: 2.13.4
PMRA 1189844	2005, Laboratory method LM011306FP1 Determination of chloride in AE 0317309 by titration, Lm011306FP1, DACO: 2.13.4
PMRA 1189845	2005, Laboratory method LM011306FP1 Determination of triethyamine in AE 0317309 by titration, LM011406FP1, DACO: 2.13.4
PMRA 1189846	2000, MT 30 Water ; 30.1 Karl Fischer Method, CIPAC MT 30.1, DACO: 2.13.4
PMRA 1189847	2005, Validation of GC-method AM009105FP1: determination of Acetonitril (AE 0173080), Toluene (AE F125577) and MTBE (AE F146605) in technical grade and pure AE 0317309 by gas chromatography (GC), AF05/30, DACO: 2.13.4
PMRA 1189848	2005, Validation of HPLC-method AM00750FP1- Determination of by-products in technical grade and pure AE 0317309 by high performance liquid chromatographie (HPLC), AF05/008, DACO: 2.13.4

PMRA 1326887 — 2003, The Determination of the pKa for the Isoxaflutole Metabolite RPA203328, CX/03/016A, DACO: 2.14.11

PMRA 1188988 — 2006, Stability of AE 0317309 02 SE06 A105, 201423-1, DACO: 3.5.10,3.5.14,3.5.5

PMRA 1188996 — 2006, BCS DER for AE 0317309 02 SE06 herbicide product chemistry data review for the registration of a manufacturing concentrate (MA) or an end-use product (EP)., M-268189-01-1, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,3.2.1,3.2.2,3.2.3,3.3.1,3.3.2,3.4.1,3.4.2,3.5.1

PMRA 1188997 — 2006, BCS DER for AE 0317309 02 SE06 herbicide product chemistry data, M-268189-01-1, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,3.2.1,3.2.2,3.2.3,3.3.1,3.3.2,3.4.1,3.4.2,3.5.1,3.5.10,3.5.11,3.5.12,3.5.13,3.5.14,3.5.15,3.5.2,3.5.3,3.5.4,3.5.5,3.5.6,3.5.7,3.5.8,3.5.9

PMRA 1189096 — 2006, BCS DER for AE 0317309 03 EC23 herbicide product chemistry data, —268193- 01-1, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,3.2.1,3.2.2,3.2.3,3.3.1,3.3.2,3.4.1,3.4.2,3.5.1,3.5.10,3.5.11,3.5.12,3.5.13,3.5.14,3.5.15,3.5.2,3.5.3,3.5.4,3.5.5,3.5.6,3.5.7,3.5.8,3.5.9

PMRA 1189097 — 2006, BCS DER for AE 0317309 03 EC23 herbicide product chemistry data, M-268193-01-1, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,3.2.1,3.2.2,3.2.3,3.3.1,3.3.2,3.4.1,3.4.2,3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.4,3.5.5,3.5.6,3.5.7,3.5.9

PMRA 1189124 — 2006, Stability of AE 0317309+bromoxynil EC23, 201394-1, DACO: 3.5.10,3.5.14,3.5.5

PMRA 1224379 — 2006, Product Chemistry AE 0317309 + Bromo Herbicide, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,3.2.1,3.2.2,3.2.3,3.3.1,3.4.1,3.4.2,3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.4,3.5.5,3.5.6,3.5.7,3.5.9

2.0 Impact on Human and Animal Health

PMRA 1188970 — 2006. AE 0317309 02 SE06 A1 - Acute inhalation toxicity in rats. Lab report # AT01972, Bayer HealthCare AG. DACO: 4.6.3

PMRA 1188973 — 2006. AE 0317309 02 SE06 A1 - Acute toxicity in the rat after dermal application. Lab report # AT01987, Bayer HealthCare AG. DACO: 4.6.2

PMRA 1188975 — 2006. Acute toxicity in the rat after dermal application. Lab report # M-267974-01-1, Bayer CropScience AG. DACO: 4.6.2

PMRA 1188976 2006. AE 0317309 02 SE06 A1 - Acute toxicity in the rat after oral administration. Lab report # AT01989, Bayer HealthCare AG. DACO: 4.6.1

PMRA 1188979 2006. AE 0317309 02 SE06 A1 - Acute eye irritation on rabbits. Lab report # AT02030, Bayer HealthCare AG. DACO: 4.6.4

PMRA 1188982 2006. AE 0317309 02 SE06 A1 - Acute skin irritation/corrosion on rabbits. Lab report # AT02029, Bayer HealthCare AG. DACO: 4.6.5

PMRA 1188985 2006, AE 0317309 02 SE06 A1 (Project: AE 0317309) - Study for the skin sensitization effect in guinea pigs (Buehler Patch Test). Lab report # AT02026, Bayer HealthCare AG. DACO: 4.6.6

PMRA 1189066 2005. AE 0317309 03 EC23 A8 - Acute eye irritation on rabbits . Lab report # AT01910, Bayer HealthCare AG. DACO: 4.6.4

PMRA 1189067 2005. AE 0317309 03 EC23 A8 - Acute inhalation toxicity in rats. Lab report # AT01974, Bayer HealthCare AG. DACO: 4.6.3

PMRA 1189068 2005. AE 0317309 03 EC23 A8 - Acute skin irritation/corrosion on rabbits. Lab report # AT01911, Bayer HealthCare AG. DACO: 4.6.5

PMRA 1189069 2006. AE 0317309 03 EC23 A8 - Acute toxicity in the rat after dermal application. Lab report # AT01956, Bayer HealthCare AG. DACO: 4.6.2

PMRA 1189070 2006. AE 0317309 03 EC23 A8 - Acute toxicity in the rat after oral administration. Lab report # AT01957, Bayer HealthCare AG. DACO: 4.6.1

PMRA 1189071 2005. AE 0317309 03 EC23 A8 - Study for the skin sensitization effect in guinea pigs (Buehler patch test). Lab report # AT02006, Bayer HealthCare AG. DACO: 4.6.6

PMRA 1189888 2005. The Metabolism of (Phenyl-UL-^{14}C) and (Pyrazole-3-^{14}C) AE 0317309 in Rats. Lab report # MEAIX021, Bayer CropScience. DACO 4.5.9

PMRA 1189890 2006. A 14-day Comparative Toxicity Feeding Study in M Beagle Dogs with Technical Grade AE 0317309. Lab report # 201379, Bayer CropScience. DACO 4.2.9, 4.3.8, 4.4.5, 4.5.8, 4.8

PMRA 1189892 2006. Effect of Tyrosinaemia on Pregnancy and Embryo-fetal Development in the Rat. Lab report # SA 05192, Bayer CropScience.. DACO 4.2.9, 4.3.8, 4.4.5, 4.5.8, 4.8

PMRA 1189895 1995. Tyrosine. Exploratory 14-day (Ocular Toxicity) Study in the Rat and Mouse. Lab report # C021325, Rhone-Poulenc Agrochimie Centre de Recherche. DACO 4.2.9, 4.3.8, 4.4.5, 4.5.8, 4.8

PMRA 1189897 2006. NTBC - *In Vitro* Inhibition of HPPDase using Liverbeads™ from Different Species. Lab report # SA04276, Bayer CropScience.. DACO 4.2.9, 4.3.8, 4.4.5, 4.5.8, 4.8

PMRA 1189900 1995. 28-day Toxicity Study in the Rat by Dietary Administration - RPA203328 (a Metabolite of RPA201772). Lab report # R005242, Rhone-Poulenc Agrochimie Centre de recherche. MRID: 43904813, DACO: 4.1

PMRA 1189930 Anon. 2006. RPA203328: Developmental Toxicology Study in the Rat by Gavage. Lab report # SA 98427, Bayer CropScience. DACO: 4.1

PMRA 1189933 1999. RPA203328: Developmental Toxicity Study in the Rat by Gavage. Lab report # SA 98427, Bayer CropScience. DACO: 4.1

PMRA 1189934 1998. Mutagenicity test on RPA 203328 in the In Vivo Mouse Micronucleus Assay. Lab report # 19201-0-455OECD, B CS. DACO: 4.1

PMRA 1189935 1998. Mutagenicity Test on RPA 203328 in the In Vivo Mouse Micronucleus Assay. Lab report # M-268153-01-1, B CS. DACO: 4.1

PMRA 1189936 1998. RPA 203328 - 90-day Oral Toxicity (Dietary) - Rat. Lab report # M-267685-01-1, B CS. DACO: 4.1

PMRA 1189937 1998. RPA 203328 - 90-Day Oral Toxicity (Dietary) - Rat. Lab report # SA 98129, B CS. DACO: 4.1

PMRA 1189938 1998. Mutagenicity Test on RPA 203328 - In the CHO/HGPRT Forward Mutation Assay with Duplicate Cultures and a Confirmatory Assay. Lab report # M-267725-01-1, B CS. DACO: 4.1

PMRA 1189940 1998. Mutagenicity test on RPA 203328 - In the CHO/HGPRT Forward Mutation Assay with Duplicate Cultures and a Confirmatory Assay. Lab report # 19201-0-435-OECD, BCS. DACO: 4.1

PMRA 1189941 1998. Mutagenicity Test on RPA 203326 Measuring Chromosomal Aberrations. Lab report # 19201-0-437OECD, BCS. DACO: 4.1

PMRA 1189943 1994. RPA 203328 - Salmonella typhimurium Reverse Mutation Assay (Ames Tes). Lab report # SA 94057, BCS. DACO: 4.1

PMRA 1189945 1994. RPA 203328 - Salmonella Typhimurium Reverse Mutation Assay (Ames Test). Lab report # SA 94057, BCS. DACO: 4.1

PMRA 1189948 1999. Developmental Toxicology Study in the Rat by Gavage - RPA203328. Lab report # SA 98427, Rhone-Poulenc Agrochimie Centre de Recerche. MRID: 45655906, DACO: 4.1

PMRA 1189952 1998. Mutagenicity Test on RPA 203328 in the In Vivo Mouse Micronucleus Assay. Lab report # C026351, Covance Laboratories Inc. MRID: 44545302, DACO: 4.1

PMRA 1189955 1998. Mutagenicity Test on RPA203328 - Measuring Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells. Lab report # R000093, Covance Laboratories Inc. MRID: 44545301, DACO: 4.1

PMRA 1189958 1998. Mutagenicity test on RPA203328 in the CHO/HGPRT Forward Mutation Assay with Duplicate Cultures and a Confirmatory Assay. Lab report # 19201-0-435 OECD, Covance Laboratories Inc. MRID: 44545303, DACO: 4.1

PMRA 1189961 1995. Oral limit test in the rat RPA203328. Lab report # R005364, Rhone-Poulenc Agrochimie Centre de Recherche. MRID: 43904812, DACO: 4.1

PMRA 1189963 1994. RPA203328. Salmonella typhimurium. Reverse Mutation Assay (Ames Test). Lab report # R005218, Rhone-Poulenc Secteur Agro Centre de Recherche. MRID: 43904814, DACO: 4.1

PMRA 1189966 1998. RPA 203328: 90-Day Toxicity Study in the Rat by Dietary Administration. Lab report # B003642, Rhone-Poulenc Agrochimie Centre de Recherche. MRID: 45655903, DACO: 4.1

PMRA 1189970 2004. AE 0317309 - Acute Toxicity in Rat After Oral Administration. Lab report # AT01067, Bayer HealthCare AG. DACO 4.2.1

PMRA 1189974 2004. AE 0317309 - Acute Toxicity in Rat After Dermal Application. Lab report # AT01069, Bayer HealthCare AG. DACO 4.2.2

PMRA 1189978 2004. AE 0317309 - Study on Acute Inhalation Toxicity in Rats According to OECD no. 403. Lab report # AT00964, Bayer HealthCare AG. DACO 4.2.3

PMRA 1189981 2004. AE 0317309 - Acute Skin Irritation/Corrosion on Rabbits. Lab report # M-003613-01-3, Bayer HealthCare AG. DACO 4.2.5

PMRA 1189984 2006. AE 0317309 Technical - Primary Eye Irritation Study in Rabbits. Lab report # 18739, Product Safety Laboratories. DACO 4.2.4

PMRA 1189987 2004. AE 0317309 - Study for the Skin Sensitization Effect in Guinea Pigs (Guinea Pig Maximization Test According to Magnusson and Kligman). Lab report # AT01261, Bayer HealthCare AG. DACO 4.2.6

PMRA 1189990 2002. AE 0317309 - Preliminary 28 Day Toxicity Study in the Mouse by Dietary Administration. Lab report # M-211308-01-3, Bayer CropScience. DACO 4.3.3

PMRA 1189991 2002. AE 0317309 - Preliminary 28-Day Toxicity Study in the Dog by Dietary Administration. Lab report # SA 02053, Bayer CropScience. DACO 4.3.3

PMRA 1189998 2006. Technical Grade AE 0317309: A 90-Day Subchronic Toxicity Feeding Study in the Beagle Dog. Lab report # 201019-1, Bayer CropScience. DACO 4.3.3

PMRA 1189999 2003. AE 0317309 - 90-day Toxicity Study in the Mouse by Dietary Administration. Lab report # SA03015, Bayer CropScience. DACO 4.3.1

PMRA 1190000 2003. AE 0317309 - 90-Day Toxicity Study in the Rat by Dietary Administration. Lab report # M-102924-01-2, Bayer CropScience. DACO 4.3.1

PMRA 1190009 2005. Technical Grade AE 0317309 - A 90-Day Subchronic Toxicity Feeding Study on the Beagle Dog. Lab report # 201210, Bayer CropScience. DACO 4.3.2

PMRA 1190010 2006. A Chronic Toxicity Feeding Study in the Beagle Dog with Technical Grade AE 0317309. Lab report # 201450, Bayer Corporation LP. DACO 4.3.2

PMRA 1190013 2005. AE0317309 - Subacute Toxicity Study in the Rat (4 Weeks Dermal Administration). Lab report # AT02678, Bayer HealthCare AG. DACO 4.3.5

PMRA 1190016 2004. AE 0317309 - Salmonella/Microsome Test - Plate Incorporation and Preincubation Method. Lab report # AT01032, Bayer HealthCare AG. DACO 4.5.4

PMRA 1190019 2004. AE 0317309 - *In Vitro* Chromosome Aberration Test with Chinese Hamster V79 Cells. Lab report # AT01285, Bayer HealthCare AG. DACO 4.5.6

PMRA 1190022 2006. AE 0317309 (Project: AE 0317309) - V79/HPRT- Test *In Vitro* Detection of Induced Forward Mutations - 1. Amendment to Bayer report AT01401 of July 6, 2004. Lab report # AT01401A, Bayer HealthCare AG. DACO 4.5.5

PMRA 1190025 2005. AE 0317309 - Micronucleus-Test Using Mice. Lab report # AT00719, Bayer HealthCare AG. DACO 4.5.7

PMRA 1190028 2006. 6-Month Toxicity, Chronic Toxicity and Carcinogenicity Study of AE 0317309 in the Wistar Rat by Dietary Administration. Lab report # SA02453, Bayer CropScience SA. DACO 4.4.2, 4.4.4

PMRA 1190031 2006. Carcinogenicity Study of AE 0317309 in the C57BL/6J Mouse by Dietary Administration. Lab report # SA03172, Bayer CropScience SA. DACO 4.4.3

PMRA 1190038 2005. AE 0317309 - Two-Generation Reproduction Study in the Wistar Rat by Administration in the Diet. Lab report # AT02705, Bayer HealthCare AG. DACO 4.5.1

PMRA 1190041 2006. AE 0317309 - Developmental Toxicity Study in the Rat by Gavage. Lab report # M-267036-01-2, Bayer CropScience SA. DACO 4.5.2

PMRA 1190044	2006. AE 0317309 - Developmental Toxicity Study in the Rabbit by Gavage. Lab report # M-266702-01-2, Bayer CropScience SA. DACO 4.5.3
PMRA 1190047	2005. An Acute Oral Neurotoxicity Screening Study with Technical Grade AE 0317309 in Wistar Rats. Lab report # 201392, Bayer CropScience SA. DACO 4.5.12
PMRA 1190050	2005. A Subchronic Neurotoxicity Screening Study with Technical Grade AE 0317309 in Wistar Rats. Lab report # 201381, Bayer CropScience SA. DACO 4.5.13
PMRA 1190053	2006. A Developmental Neurotoxicity Screening Study with Technical Grade AE0317309 in Wistar Rats. Lab report # 201439, Bayer CropScience SA. DACO 4.5.14
PMRA 1388309	2007. AE 0317309 - Historiacl control data for selected findings from the mouse oncogenicity study SA 03172.
PMRA 1388310	2007. AE 0317309 - Historical control data for selected findings from the rat chronic / oncogenicity study SA 02453
PMRA 1388311	2007. AE 0317309 - Historical control data for fetal body weight in rabbit developmental toxicity study SA 03131
PMRA 1189010	Canadian Use Description Scenario for AE 0317309 02 SE06 Herbicide. Report Date 16-MAR-06. Lab Report No. BCS RA 06-03. Company Report No. —267809-01-1. DACO 5.2 Description of pest problem.
PMRA 1189013	Occupational exposure & risk assessment for mixer/loaders, applicators and reentry workers during use of AE 0317309 02 SE06. Report Date 13-MAR-06. Lab Report No. 201488. Company Report No. —267815-01-1. DACO 5.3 Pesticides handlers exposure database assessment (or other database).
PMRA 1189108	Canadian use description scenario for AE 0317309 03 EC23 herbicide. Report Date 16-MAR-06. Lab Report No. M-267813-01-1. Company Report No. M- 267813-01. DACO 5.2 Description of pest problem.
PMRA 1189870	2006, Extraction Efficiency of AE B197555, AE 1073910, and AE 0317309 by Method AI-0001-P04-01, Bayer CropScience, RAAIX011, DACO: 7.2.2,8.2.2.4

PMRA 1189871 2006, Extraction Efficiency of Bayer CropScience Method AI-004-A05-01 - Analytical Method for the Determination of Residues of AE 0317309 in Animal Tissues and Milk Using LC-MS/MS, Bayer CropScience, RAAIX010, DACO: 7.2.2,8.2.2.4

PMRA 1189872 2006, Independent Laboratory Validation of Method AI-005-A05-01 - An Analytical Method for the Determination of AE B197555 in Poultry and Eggs Using LC/MS/MS, Enviro-Test Laboratories, RAAIP011, DACO: 7.2.1,7.2.3,7.2.4,8.2.2.4

PMRA 1189873 2005, Independent Laboratory Validation of the Analytical Method Al-004-A05-01 for the Determination of Residues of AE 0317309 in Animal Tissues and Milk Using LC-MS/MS, Bayer CropScience AG, MR-122/05, DACO: 7.2.1,7.2.3,7.2.4,8.2.2.4

PMRA 1189874 2005, Independent Laboratory Validation of the Analytical Method AI-001-P04-01 for the Determination of Residues of AE 0317309, AE 1073910 and AE B197555 in Plant Material, Bayer CropScience AG, MR-097/05, DACO: 7.2.1,7.2.3,7.2.4,8.2.2.4

PMRA 1189875 2006, PAM I multiresidue protocol testing of AE 0317309 and its metabolite: AE 1073910, Pyxant Labs Inc., 1624, DACO: 7.2.1,7.2.4

PMRA 1189880 2006, Validation of Bayer CropScience Method AI-001-P04-01 an Analytical Method for the Determination of Residues of AE 0317309, AE 1073910, and AE B197555 in Wheat, Corn, and Soybean Matrices Using LC/MS/MS, Bayer CropScience, RAAIX005, DACO: 7.2.1,7.2.4

PMRA 1189882 2006, Validation of Bayer CropScience Method AI-004-A05-01 Analytical Method for the Determination of Residues of AE 0317309 in Animal Tissues and Milk Using LC-MS/MS, Bayer CropScience, RAAIX006, DACO: 7.2.2,7.2.5,8.2.2.4

PMRA 1189884 2006, Validation of Bayer CropScience method AI-005-A05-01 Analytical Method for the Determination of Residues of AE B197555 in Poultry and Eggs Using LC/MS/MS, Bayer CropScience, RAAIP012, DACO: 7.2.2,7.2.5,8.2.2.4

PMRA 1190056 2006, AE 0317309 - Magnitude of the Residue in Corn and Soybeans Planted as Rotational Crops Following Treatment of Wheat with AE 0317309 02 SE06 A1 (120-Day Plant-Back Interval), Bayer CropScience, RAAIM021, DACO: 7.4.4

PMRA 1190057 2006, AE 0317309 02 SE06 A1 - Magnitude of the Residue in/on Wheat Aspirated Grain Fractions and Wheat Processed Commodities, Bayer CropScience, RAAIM003, DACO: 7.4.1,7.4.5

PMRA 1190058 2006, AE 0317309 02 SE06 A1 and AE 0317309 03 EC23 A8 Magnitude of the Residue in/on Barley, Bayer CropScience, RAAIM004, DACO: 7.4.1,7.4.2,7.4.6

PMRA 1190059 2006, AE 0317309 02 SE06 A1 and AE 0317309 03 EC23 A8 Magnitude of the Residue in/on Oats, Bayer CropScience, RAAIM006, DACO: 7.4.1,7.4.2,7.4.6

PMRA 1190060 2006, AE 0317309 02 SE06 A1 and and AE 0317309 03 EC23 A8 - Magnitude of the Residue in/on Wheat, Bayer CropScience, RAAIM002, DACO: 7.4.1,7.4.2,7.4.6

PMRA 1190061 2006, AE B197555 - Magnitude of the Residue in Laying Hens, Bayer Corporation, RAAIP004, DACO: 7.5.1

PMRA 1190062 2006, AE0317309 - Magnitude of the Residue in Lactating Cows, Bayer CropScience, RAAIX017, DACO: 7.5.1

PMRA 1190082 2006, Storage Stability of AE 0317309, AE 1073910, and AE B197555 in Soybean and Wheat Matrices (Data to 11 Months of Storage), Bayer CropScience, RAAIX009, DACO: 7.3

PMRA 1190083 2006, The Accumulation of [Phenyl-UL-^{14}C] and [Pyrazole-3-14C] AE 0317309 in Confined Rotational Crops, Bayer CropScience, 201152, DACO: 7.4.3

PMRA 1190094 2004, Metabolism of [Phenyl-U-^{14}C]AE 0317309 in Wheat (Triticum aestivum) Following Treatment at a Nominal Application Rate of 100 g a.s./ha, Bayer CropScience GmbH, MEF-193/03, DACO: 6.3

PMRA 1190095 2004, Metabolism of [Phenyl-U-14C]AE 0317309 in Wheat Following Treatment at an Application Rate of 100 g/ha with and without Safener, Bayer CropScience AG, M-128001-01-2, DACO: 6.3

PMRA 1190096 2004, Metabolism of [Pyrazole-3-^{14}C]AE 0317309 in Wheat (Triticum aestivum) Following Treatment at a Nominal Application Rate of 100 g a.s./ha, Bayer CropScience GmbH, MEF-194/03, DACO: 6.3,7.4.3

PMRA 1190101 2006, Metabolism of [Phenyl-U-^{14}C]-AE 0317309 in the Laying Hen, Bayer CropScience, MEAIM012, DACO: 6.2

PMRA 1190102 2006, Metabolism of [pyrazole-3-^{14}C]-AE 0317309 in the laying hen, Bayer CropScience, MEAIM011, DACO: 6.2

PMRA 1190103 2006, AE 0317309 - Metabolism of [Pyrazole-3-^{14}C]-AE 0317309 in the Lactating Goat, Bayer CropScience, MEAIM010, DACO: 6.2

PMRA 1190108 2006, Metabolism of [phenyl-U-^{14}C]-AE 0317309 in the Lactating Goat, Bayer CropScience, MEAIM009, DACO: 6.2

3.0 Impact on the Environment

1189849 2006, AE 0317309 - Analytical Method for the Determination of AE 0317309 and its Meabolite AE B197555 in Soil and Sediment by LC/MS/MS, AI-002-S05-02, DACO: 8.2.2.1

1189854 2006, In House Laboratory Validation of an Analytical Method for the Determination of Residues of AE 00317309 and its Metabolite AE B197555 in Soil and Sediment Using LC/MS/MS, 04MEAIX017, DACO: 8.2.2.1

1189855 2005, Independent Laboratory Validation of Method AI002-S05-01 for the Determination of AE 0317309 and its Metabolite AE B197555 in Soil and Sediment by LC/MS/MS., MR-112/05, DACO: 8.2.2.1

1189856 2006, Stability of AE 0317309 and AE B197555 in Soil During Frozen Storage, USA, 2005 (Reported Through a Maximum of 320 Days Storage), RAAIX008, DACO: 8.2.2.1

1189857 2006, AE 0317309 - Analytical Method for the Determination of AE 0317309 and its Metabolite AE B197555 in Water by LC/MS/MS, AI-003-W05-02, DACO: 8.2.2.3

1189860 2006, In House Laboratory Validation of an Analytical Method for the Determination of Residues of AE 00317309 and its Metabolite AE B197555 in Water Using LC/MS/MS, MEAIX018, DACO: 8.2.2.3

1189861 2005, Independent Laboratory Validation of Method AI-003-W05-01 for the Determination of AE 0317309 and its Metabolite AE B197555 in Water, MR-139/05, DACO: 8.2.2.3

1190109 2005, (Phenyl-UL-14C) and (Pyrazole-3-14C)AE 0317309: Anaerobic Soil Metabolism, 04MEAIP001, DACO: 8.2.3.4.4

1190112 2004, [Pyrazole-3-14C] AE 0317309: Phototransformation on Soil, 200638, DACO: 8.2.3.3.1

1190115 2005, AE 0317309: Calculation of the Chemical Lifetime in the Troposphere, MEAIM006, DACO: 8.2.3.3.3

1190116 2006, Aquatic Ecological and Drinking Water Exposure Assessment for AE 0317309 and its Major Metabolite AE B197555 (Canada), M-267796-02-1, DACO: 8.5.1,8.6

1190117 2006, Aquatic Ecological and Drinking Water Exposure Assessment for AE 0317309 and its Major Metabolite AE B197555 (United States), MEAIY010, DACO: 8.5.1,8.6

1190131 2006, Terrestrial Field Dissipation of AE 0317309 in Washington soil, 2004, MEAIY009, DACO: 8.5.1,8.6

1190133 2006, Terrestrial Field Dissipation of AE 0317309 in Canada, 2003-2004, MEAIM004, DACO: 8.5.1,8.6

1190134 2006, Terrestrial Field Dissipation of AE 0317309 in Kansas Soil, 2004, MEAIY008, DACO: 8.5.1,8.6

1190135 2006, Terrestrial Field Dissipation of AE 0317309 in North Dakota Soil, 2004, MEAIY007, DACO: 8.5.1,8.6

1190136 2005, [phenyl-U-14C]- and [pyrazole-3-14C]-AE 0317309: Aerobic soil metabolism in a loamy sand soil of US origin under laboratory conditions at 25¿¿C, MEF-386/03, DACO: 8.2.3.4.2

1190137 2004, [phenyl-U-14C]- and [pyrazole-3-14C]-AE 0317309: Aerobic Soil Metabolism in a Silt Loam Soil of US Origin Under Laboratory Conditions at 25 degrees Celsius, MEF-387/03, DACO: 8.2.3.4.2

1190138 2005, [Phenyl-UL-14C] and [Pyrazole-3-14C]AE 0317309: Aerobic Soil Metabolism in a European Soil, MEF-05/459, DACO: 8.2.3.4.2

1190145 2003, Adsorption/Desorption of AE 0317309 on Five Souls and One Sediment, MEF-186/03, DACO: 8.2.4.2

1190148 2004, (14C)-RPA 203328: Adsorption / Desorption in Five Soils, C040534, DACO: 8.2.4.2

1190151 2004, [Pyrazole-3-14C] AE0317309: Hydrolytic Degradation, 200578, DACO: 8.2.3.2

1190154 2005, [14C-UL-phenyl] and [14C-3-pyrazole] AE 0317309: Phototransformation in Water, M-248236-02-1, DACO: 8.2.3.3.2

1190155 2006, [Pyrazol-3-14C]AE 0317309 and [Phenyl-UL-14C]AE 0317309: Aerobic Aquatic Metabolism, MEAIM008, DACO: 8.2.3.5.2,8.2.3.5.4

1190158 2005, [Phenyl-UL-14C]AE 0317309: Anaerobic Aquatic Metabolism, 200593, DACO: 8.2.3.5.5,8.2.3.5.6

1190159 2005, [Pyrazole-3-14C]AE 0317309: Anaerobic Aquatic Metabolism, 200495, DACO: 8.2.3.5.5,8.2.3.5.6

1188989 2006, Non-target terrestrial plants: seedling emergence and growth test (Tier 2) suspo-emulsion: 50 + 12.5 g/L (Code: AE 0317309 02 SE06 A102), EBAIX020, DACO: 9.8.4

1188992 2006, Non-target terrestrial plants: vegetative vigour test (Tier 2) AE 0317309 + mefenpyr di-ethyl (AE F107892); suspo-emulsion: 50 + 12.5 g/L (Code: AE 0317309 02 SE06 A102), VV04/005, DACO: 9.8.6

1189109 2006, Non-target terrestrial plants: seedling emergence and seedling growth test (Tier 2), AE 0317309 + mefenpyr di-ethyl + bromoxynil, (Code: AE 0317309 03 EC23 A8), EBAIX028, DACO: 9.8.4

1189110 2006, Non-target terrestrial plants: vegetative vigour test (Tier 2), AE 0317309 + mefenpyr di-ethyl + bromoxynil, (Code: AE 0317309 03 EC23 A8), VV05/002, DACO: 9.8.4

1190166 2006, Technical AE 0317309: An acute oral LD50 with northern bobwhite, 201125, DACO: 9.6.2.1,9.6.2.2,9.6.2.3

1190171 1998, RPA 203328: A Dietary LC50 Study with the Northern Bobwhite, B004404, MRID: 44693501, DACO: 9.6.2.4,9.6.2.5

1190172 2005, Technical AE0317309: A subacute dietary LC 50 with mallards, EBAIM003, DACO: 9.6.2.4,9.6.2.5

1190173 2005, Technical AE0317309: A subacute dietary LC 50 with northern bobwhite, EBAIM002, DACO: 9.6.2.4,9.6.2.5

1190178 2006, Effect of technical AE 0317309 on mallard reproduction, EBAIX017, DACO: 9.6.3.1,9.6.3.2,9.6.3.3

1190179 2006, Effect of technical AE 0317309 on northern bobwhite reproduction, EBAIX016, DACO: 9.6.3.1,9.6.3.2,9.6.3.3

1190180 2004, Acute Toxicity of AE 0317309 Technical to the Sheepshead Minnow (Cyprinodon variegatus) Under Static Conditions, 200820, DACO: 9.4.2,9.4.3,9.4.4

1190181 2004, AE 0317309 - Acute Toxicity to Eastern Oysters (Crassostrea virginica) Under Flow-Through Conditions, EBAIX013, DACO: 9.4.2,9.4.3,9.4.4

1190182 2004, AE 0317309 - Acute Toxicity to Mysids (Americamysis bahia) Under Static Conditions, EBAIX011, DACO: 9.4.2,9.4.3,9.4.4

1190187 1998, RPA 203328 - Acute Toxicity to Mysids (Mysidopsis bahia) Under Static Acute Conditions, C026471, MRID: 44718801, DACO: 9.4.2,9.4.3,9.4.4

1190188 2004, Toxicity of AE 0317309 technical to the saltwater diatom Skeletonema costatum, 200697, DACO: 9.4.2,9.4.3,9.4.4

1190189 1997, Amendment to the final study report - RPA203328 - Determination of effects on vegetative vigor of ten plant species, R005076, MRID: 44399906, DACO: 9.8.4

1190190 1997, RPA203328 - Determination of effects on seedling emergence of ten plant species, R005075, MRID: 44399907, DACO: 9.8.4

1190191 1997, A Laboratory Assessment of the Effect of RPA 203328 on Soil Microflora Respiration and Nitrogen Transformations According to EPPO Bulletin 24, 1-16 (1994), R000492, DACO: 9.3.4,9.6.6,9.9

1190192 2004, AE 0317309 tech. (AE 0317309 00 1C96 0001): Determination of Effects on Carbon Transformation in Soil, LKC-C-23/04, DACO: 9.3.4,9.6.6,9.9

1190193 2004, AE 0317309 tech. (AE 0317309 00 1C96 0001): Determination of Effects on Nitrogen Transformation in Soil, LKC-N-26/03, DACO: 9.3.4,9.6.6,9.9

1190194 2004, Isoxaflutole-RPA203328 (AE B197555): Reproduction Toxicity to Earthworm Eisenia fetida in Artificial Soil, C041342, DACO: 9.3.4,9.6.6,9.9

1190195 1995, RPA203328 - Acute Toxicity to Rainbow Trout (Oncorhynchus mykiss) Under Flow-Through Conditions, R005254, MRID: 43904825, DACO: 9.3.4,9.6.6,9.9

1190198 2006, The 96 hour acute toxicity to the rainbow trout, Oncorhynchus mykiss, in a static system - AE 0317309 technical, 97.4%w/w (Amended report), 02DT35541-a, DACO: 9.5.2.1,9.5.2.3

1190201 2006, The 96 hour acute toxicity to the bluegill sunfish, Lepomis macrochirus, in a static system - AE 0317309 technical, 98.2% w/w (Amended report), 02DT35540-a, DACO: 9.5.2.2,9.5.2.3

1190204 2004, Early life stage toxicity of AE 0317309 technical to fathead minnow (Pimephales promelas) under flow-through conditions, EBAIX015, DACO: 9.5.3.1

1190207 1994, RPA203328 - Acute Toxicity to Ddaphnids (Daphnia magna) Under Flow-Through Conditions, R005204, MRID: 43573241, DACO: 9.3.2

1190208 2005, The 48 Hour Acute Toxicity to the Water Flea, Daphnia magna, in a Static System - AE 0317309 Technical, 97.4%w/w (Amended Report), 02DT35542-a, DACO: 9.3.2

1190211 2004, Chronic Toxicity of AE 0317309 Technical to the Daphnia magna Under Static Renewal conditions, EBAIX014, DACO: 9.3.3

1190212 1995, 5-day toxicity to the freshwater green alga, Selenastrum capricornutum RPA203328 Final Report, R005374, MRID: 43904826, DACO: 9.8.2,9.8.3

1190219 2004, Toxicity of AE 0317309 technical to the freshwater diatom Navicula pelliculosa, 200761, DACO: 9.8.2,9.8.3

1190220 2004, Toxicity of AE 0317309 technical to the green alga Pseudokirchneriella subcapitata (a.k.a. Selenastrum capricornutum), 200714, DACO: 9.8.2,9.8.3

1190221 2004, Toxictiy of AE 0317309 technical to the blue-green algae Anabaena flos-aquae, 200752, DACO: 9.8.2,9.8.3

1190224 1997, RPA203328 technical - Toxicity to the duckweed, Lemna gibba, R004953, MRID: 44399910, DACO: 9.8.5

1190225 2006, Toxicity of AE 0317309 05 EC15 A103 to duckweed (Lemna gibba G3) under static conditions, EBAIP008, DACO: 9.8.5

1190226 2004, Toxicity of AE 0317309 technical to duckweed (Lemna gibba G3) under static conditions, 200641, DACO: 9.8.5

1190229 2002, Oral Toxicity (LD50) to Honey Bees (Apis mellifera L.) Substance Technical code: AE 0317309 00 1C98 0001, C027636, DACO: 9.2.4.2

1190232 2002, Contact Toxicity (LD50) to Honey Bees (Apis mellifera L.) Substance Technical Code: AE 0317309 00 1C98 0001, CW02/048, DACO: 9.2.4.1

1190233 2004, Toxicity to the Parasitoid Wasp Aphidius rhopalosiphi (DeStephani-Perez) (Hymenoptera: Braconidae) in the Laboratory - AE 0317309 + AE F107892 - Suspo-emulsion - 50 + 12.5 g/L, CW04/030, DACO: 9.2.6

1190234 2004, Toxicity to the Predatory Mite Typhlodromus pyri SCHEUTEN (Acari, Phytoseiidae) in the laboratory - AE 0317309 + AE F107892 - Suspo-emulsion - 50 + 12.5 g/L, CW04/049, DACO: 9.2.5

1190235 2004, AE 0317309, Substance, Technical (Code: AE 0317309 00 1C96 0001): Acute Toxicity to Earthworms (Eisenia fetida) tested in Artificial Soil, LKC/Rg-A-27/04, DACO: 9.2.3.1

1190238 1997, RPA 203328 - Acute Toxicity (14-Day) to Earthworms (Eisenia foetida) - Artificial Soil Method, C026475, DACO: 9.2.3.1

4.0 Value

PMRA 1188998 AE 0317309 02 SE06 Herbicide (Pyrasulfotole) for Broadleaf Weed Control in Cereals and Timothy- Canadian Value Package. 1274 pp. DACOs 10.2.3.3, 10.3.2, 10.3.3, 10.4, 10.5.1, 10.5.2.1, 10.5.4

PMRA 1189072 AE 0317309 03 EC23 Herbicide (Pyrasulfotole + Bromoxynil) for Broadleaf Weed Control in Cereals and Timothy- Canadian Value Package. 2531 pp. DACOs 10.2.3.3, 10.3.2, 10.3.3, 10.4, 10.5.1, 10.5.2.1, 10.5.4

ADDITIONAL INFORMATION

Impact on the Environment

The US EPA RED document (Bromoxynil, EPA CASE # 2070) is available on the "Office of Pesticide Program website at www.regulations.gov.