Proposed Registration Decision PRD2022-11

Fenazaquin, Magister SC Miticide/Fungicide, and Magus SC Miticide

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Overview

Proposed registration decision for Fenazaquin, Magister SC Miticide/Fungicide, and Magus SC Miticide

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the Pest Control Products Act, is proposing registration for the sale and use of Fenazaquin Technical, Magister SC Miticide/Fungicide, and Magus SC Miticide, containing the technical grade active ingredient fenazaquin, to control certain mites, psylla, whitefly, and powdery mildew on a variety of crops and ornamental plants.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of fenazaquin, Magister SC Miticide/Fungicide, and Magus SC Miticide.

What does Health Canada consider when making a registration decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] 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 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.

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 (for example, children) as well as organisms in the environment.

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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."

These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the Health Canada regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides section of the Canada.ca website.

Before making a final registration decision on fenazaquin, Magister SC Miticide/Fungicide, and Magus SC Miticide, Health Canada's PMRA will consider any comments received from the public in response to this consultation document.[3] Health Canada will then publish a Registration Decision[4] on fenazaquin, Magister SC Miticide/Fungicide, and Magus SC Miticide, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What is Fenazaquin?

Fenazaquin is a conventional chemical miticide, insecticide and fungicide that acts by disrupting energy production within the cells of certain mites, insects and fungi. It is the active ingredient in the commercial class products Magister SC Miticide/Fungicide and Magus SC Miticide, which provide control of the target mite, insect and fungal pests on a variety of food crops as well as indoor and outdoor ornamental plants.

Health considerations

Can approved uses of Fenazaquin affect human health?

Magister SC Miticide/Fungicide and Magus SC Miticide, containing Fenazaquin, are unlikely to affect human health when used according to proposed label directions.

Potential exposure to fenazaquin may occur through the diet (food and drinking water), when handling and applying the end-use products, or when coming into contact with treated surfaces. When assessing health risks, two key factors are considered: 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 selected to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

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

In laboratory animals, technical-grade active ingredient, fenazaquin, was of high acute toxicity by the oral route and was considered to potentially cause an allergic skin reaction; consequently, the signal word "DANGER" and hazard statements "POISON" and "POTENTIAL SKIN SENSITIZER" are required on the label. It was of low acute toxicity by the dermal route, of slight acute toxicity by inhalation exposure, minimally irritating to the eyes, and non-irritating to the skin.

The end-use products Magister SC Miticide/Fungicide and Magus SC Miticide were of high acute toxicity by the oral route, mildly irritating to the eyes, and moderately irritating to the skin in laboratory animals; consequently, the signal word "DANGER" and hazard statements "POISON" and "EYE AND SKIN IRRITANT" are required on the labels. Both products were of low acute toxicity by the dermal route and of slight acute toxicity by inhalation exposure, and neither caused an allergic skin reaction.

Registrant-supplied short- and long-term (lifetime) animal toxicity tests, as well as information from the published scientific literature, were assessed for the potential of fenazaquin to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoint for risk assessment was reduced survival of the young. An increase in adrenocortical tumors in female hamsters could not clearly be attributed to treatment with fenazaquin. There was no evidence of increased sensitivity of the young compared to adult animals. The risk assessment protects against the effects noted above and other potential effects by ensuring that the level of exposure to humans is well below the lowest dose level at which these effects occurred in animal tests.

Residues in food and drinking water

Dietary risks from food and drinking water are not of health concern.

Aggregate acute dietary (food plus drinking water) intake estimates indicated that the general population and all population subgroups are exposed to less than 58% of the acute reference dose, and therefore are not of health concern.

Aggregate chronic (non-cancer and cancer) dietary (food plus drinking water) intake estimates indicated that the general population and all population subgroups are exposed to less than 10% of the acceptable daily intake, and therefore are not of health concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, 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.* Given that dietary risks from the consumption of foods are shown to be acceptable when fenazaquin is used according to the supported label directions, MRLs are being proposed as a result of this assessment

MRLs for fenazaquin determined from the acceptable residue trials conducted throughout the United States, including regions representative of Canada, on fruiting vegetables (pepper, tomato), cucurbit vegetables (cantaloupe, cucumber, zucchini), pome fruits (apple, pear), stone fruits (peach, cherry, plum), caneberries (raspberry), bushberries (blueberry), vine climbing small fruits (grape), low growing berries (strawberry) and citrus fruits (lemon, lime, grapefruit) can be found in the Science Evaluation of this consultation document.

Occupational risks from handling Magister SC Miticide/Fungicide and Magus SC Miticide

Occupational risks are not of health concern when Fenazaquin is used according to the proposed label directions, which include protective measures.

Workers mixing, loading or applying Magister SC Miticide/Fungicide or Magus SC Miticide, and workers entering recently treated fields, nurseries, non-cropland areas and ornamental plant greenhouses can be exposed to fenazaquin residues through direct skin contact or through inhalation. Therefore, the label specifies that anyone mixing, loading and applying Magister SC Miticide/Fungicide or Magus SC Miticide must wear coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves, protective eyewear (goggles or faceshield), socks and chemical-resistant footwear. Additionally, workers applying with open-cab airblast equipment must wear chemical-resistant headgear. Greenhouse workers and workers using mechanically-pressurized handguns must wear chemical-resistant coveralls instead of coveralls and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides. For berries and orchard crops, a restriction on the amount handled per day of up to 12 L is required when using mechanically-pressurized handguns.

The label also requires that workers do not enter treated fields up to a maximum of 22 days (depending on the crop or use and associated postapplication activity) after application. The restricted-entry intervals (REIs) for greenhouse vegetables, and for indoor/greenhouse and outdoor ornamental cut flowers were not considered agronomically feasible; therefore, these uses are not supported.

Taking into consideration the label statements, the number of applications and the duration of exposure for handlers and postapplication workers, the risks to these individuals from exposure to fenazaquin are not of health concern when the end-use products are used according to the proposed label directions.

Health risks in residential and other non-occupational environments

Health risks in residential and other non-occupational environments are not of health concern when Magister SC Miticide/Fungicide or Magus SC Miticide is used according to the proposed label directions and REIs are observed.

Residential exposure to fenazaquin during pick-your-own berries and orchard fruit activities, and from contact with treated ornamental plants and trees in residential, recreational, commercial, industrial and public areas are not of health concern when the end-use products are used according to the proposed label directions.

Health risks to bystanders

Bystander risks are not of health concern when Magister SC Miticide/Fungicide or Magus SC Miticide is used according to the proposed label directions for ornamental plants and trees and orchard trees in rights-of-way, easements and recreational areas and the public use of treated areas is allowed only when the sprays have dried. For interiorscapes or plantscapes in buildings, since Magister SC Miticide/Fungicide or Magus SC Miticide can only be applied when occupants and/or bystanders are not present, no health risks of concern are expected. In addition, a standard label statement to protect against drift during application is on the label. Therefore, health risks to bystanders from the other exposure scenarios are also not of concern.

Environmental considerations

What happens when Fenazaquin is introduced into the environment?

When fenazaquin and its end-use products are used according to label directions, the risks to the environment are acceptable.

Fenazaquin can enter the environment when its end-use products are applied as a foliar spray to control fungal diseases and insect and mite pests on various outdoor and greenhouse plants. Fenazaquin on plant surfaces is not expected to travel into plant tissues. Fenazaquin is not expected to be found in air. On land, fenazaquin may persist for months, but fenazaquin and its breakdown products have low potential to carry over to the next growing season and are not expected to move through the soil and reach groundwater. In water bodies, fenazaquin moves quickly into sediments and may persist for months. Fenazaquin is not expected to build up in aquatic organisms.

Use restrictions and hazard statements on end-use product labels are required to reduce risks to bees, other beneficial arthropods and aquatic organisms. When used according to label directions, fenazaquin and its breakdown products pose acceptable risk to terrestrial and aquatic organisms.

Value considerations

What is the value of Magister SC Miticide/Fungicide and Magus SC Miticide?

Magister SC Miticide/Fungicide and Magus SC Miticide provide a new active ingredient, and in most cases a new mode of action, for control of important mite and insect pests of food crops and ornamental plants, and for control of powdery mildew diseases of food crops.

Magister SC Miticide/Fungicide provides control of certain mites, including spider mites, and powdery mildew on a variety of terrestrial food crops, pear psylla on pear, spider mites on indoor and outdoor ornamental plants, and sweetpotato whitefly on indoor ornamentals. Magus SC Miticide provides control of certain spider mites on indoor and outdoor ornamental plants and sweetpotato whitefly on indoor ornamentals. These products provide a new active ingredient for all of their uses and a new mode of action for most of their uses, which will aid in the management of resistance to pest control products already registered for those uses.

Measures to minimize risk

Labels of 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 key risk-reduction measures being proposed on the label of Fenazaquin Technical, Miticide/Fungicide, and Magus SC Miticide to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Human health

To reduce the potential exposure of workers to fenazaquin through direct skin contact or inhalation of sprays, workers mixing, loading and applying Magister SC Miticide/Fungicide or Magus SC Miticide and performing cleaning and repair activities must wear coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves, protective eyewear (goggles or faceshield), socks and chemical-resistant footwear. Additionally, workers applying with open-cab airblast equipment must wear chemical-resistant headgear. Greenhouse workers and workers using mechanically-pressurized handguns must wear chemical-resistant coveralls instead of coveralls when applying to indoor plants and plantscapes and to outdoor ornamental plants and trees, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides when applying to berries and orchard crops. For berries and orchard crops, a restriction on the amount handled per day of up to 12 L is required when using mechanically-pressurized handguns.

Risks to workers are not of health concern when Magister SC Miticide/Fungicide or Magus SC Miticide is used according to the proposed label directions and REIs are observed. In addition, standard label statements to protect against drift during application are found on each product label.

Crop	Postapplication activity	Restricted-entry interval (REI) and/or Preharvest interval (PHI)
Bushberry (Subgroup 13-07B) and Caneberry (Subgroup 13-07A)	Harvesting	7 days
	Hand set irrigation	2 days
	All other activities	12 hours
Low Growing Berry Subgroup 13-07G	Harvesting	1 day
	Hand set irrigation	2 days
	All other activities	12 hours
Fruiting Vegetables	Harvesting; Hand set irrigation	3 days
	All other activities	12 hours
Cucurbit Vegetables	Harvesting	3 days
	Hand set irrigation	6 days
	All other activities	12 hours
Small Fruit Vine Climbing (Subgroup 13-07F)	Hand harvesting of grapes	15 days
	Mechanical harvesting of grapes and hand harvesting of all vine climbing berries	7 days
	Girdling of table grapes	22 days
	Tying and training	15 days for grapes 2 days for other vine climbing berries
	Thinning fruit by hand	7 days
	Hand set irrigation	3 days
	All other activities	12 hours
Pome Fruit and Stone Fruit	Harvesting	10 days
	Thinning fruit by hand	17 days
	Scouting, hand pruning and training	1 day
	All other activities	12 hours
Outdoor ornamental plants; Established outdoor ornamental landscape plantings; Ornamental plants in rights-of-way and other easements; Ornamental	Hand set irrigation	1 day
	All other activities	12 hours

Crop	Postapplication activity	Restricted-entry interval (REI) and/or Preharvest interval (PHI)
plants in recreational sites (such as campgrounds, golf courses, parks, athletic fields)		
Greenhouse ornamental plants; Shade house plants; Indoor plants, and Interiorscapes	All activities	12 hours

Health Canada is seeking comments from stakeholders on the agronomic feasibility of the 10-day restricted-entry interval (REI) for hand harvesting stone fruits, 17-day REI for hand thinning pome and stone fruits, and the 22- and 15-day REI for girdling and training grapes, respectively, in addition to any other proposed REIs.

Environment

- Hazard statements to protect bees and restrictions on outdoor application timing
- Hazard statements to protect beneficial arthropods, spiders, and mites and direction to minimize spray drift for outdoor applications
- Hazard statement to protect aquatic organisms and a requirement to observe specified spray buffer zones
- A standard statement prohibiting greenhouse effluent from entering natural water bodies

Next steps

Before making a final registration decision on fenazaquin, Magister SC Miticide/Fungicide, and Magus SC Miticide, Health Canada's PMRA will consider any comments received from the public in response to this consultation document. Health Canada will accept written comments on this proposal up to 45 days from the date of publication of this document. Please note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to Publications (contact information on the cover page of this document). Health Canada will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and Health Canada's response to these comments.

Other information

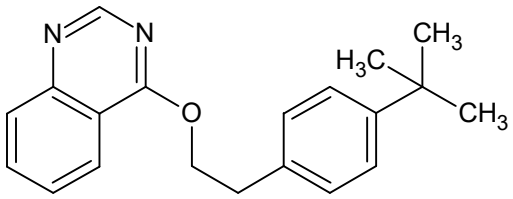
When the Health Canada makes its registration decision, it will publish a Registration Decision on fenazaquin, Magister SC Miticide/Fungicide, and Magus SC Miticide (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room. For more information, please contact the PMRA's Pest Management Information Service.

Science evaluation

Fenazaquin

1.0 The active ingredient, its properties and uses

1.1 Identity of the Active Ingredient

Active substance	Fenazaquin
Function	Insecticide / Miticide / Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	2-(4-*tert*-butylphenyl)ethyl quinazolin-4-yl ether
2. Chemical Abstracts Service (CAS)	4-[2-[4-(1,1-dimethylethyl)phenyl]ethoxy]quinazoline
CAS number	120928-09-8
Molecular formula	$C_{20}H_{22}N_2O$
Molecular weight	306.40
Structural formula	
Purity of the active ingredient	99.4 %

1.2 Physical and chemical properties of the active ingredient and end-use product

Technical product—Fenazaquin technical

Property	Result
Colour and physical state	light yellow powder
Odour	practically odourless
Melting range	77.5–80.0°C
Boiling point or range	> 300°C

Property	Result
Density	1.16 g/cm^3
Vapour pressure at 20°C	0.031–0.16 mPa (extrapolated)
Ultraviolet (UV)-visible spectrum	λ_{max} = 215 nm (ε ~4.16 × 10^4 L(mol cm)$^{-1}$) no significant absorption above 325 nm
Solubility in water at 20°C	0.21 mg/L
Solubility in organic solvents at 20°C	Solvent — Solubility (g/L) acetonitrile — 40–50 toluene — 40–50 methanol — 67–80 ethyl acetate — > 90 chloroform — > 1000
n-Octanol-water partition coefficient (K_{ow})	log K_{ow} = 5.51
Dissociation constant (pK_a)	2.44 (pKa for protonated base)
Stability (temperature, metal)	Stable at 54°C for 14 days

End-use product—Magister SC Miticide/Fungicide

Property	Result
Colour	pale brown
Odour	non-distinctive chemical odour
Physical state	liquid
Formulation type	suspension concentrate
Label concentration	205 g/L
Container material and description	plastic jug, tote or bulk 1–1000 L
Density	1.082 g/cm^3
pH of 1% dispersion in water	8.48
Oxidizing or reducing action	the product does not have oxidizing or reducing potential
Storage stability	stable for two years in commercial containers under warehouse conditions
Corrosion characteristics	not corrosive to commercial containers
Explodability	the product is not explosive

End-use product—Magus SC Miticide

Property	Result
Colour	pale brown
Odour	non-distinctive chemical odour
Physical state	liquid
Formulation type	suspension concentrate
Label concentration	205 g/L
Container material and description	plastic jug, tote or bulk 1–1000 L
Density	1.082 g/cm^3
pH of 1% dispersion in water	8.48
Oxidizing or reducing action	the product does not have oxidizing or reducing potential
Storage stability	stable for two years in commercial containers under warehouse conditions
Corrosion characteristics	not corrosive to commercial containers
Explodability	the product is not explosive

1.3 Directions for use

Magister SC Miticide/Fungicide and Magus SC Miticide are commercial class products formulated for foliar application using conventional ground equipment on all crops and use sites. Application rates range from 1.75 L/ha to 2.63 L/ha on food crops and from 300 mL to 1000 mL per 400 L of spray volume on ornamental plants. There is a maximum of one application per year for outdoor uses and a maximum of two applications per year with a minimum 14-day reapplication interval on indoor ornamentals. More details of the overall use pattern are outlined in Appendix I, Table 34.

1.4 Mode of action

Fenazaquin is a mitochondrial electron transport inhibitor, classified as a mode of action Group 21A acaricide/insecticide by the Insecticide Resistance Action Committee (IRAC) and as a Group 39 fungicide by the Fungicide Resistance Action Committee (FRAC). By inhibiting mitochondrial energy production, fenazaquin disrupts cellular metabolism, leading to mortality of mites and insects and disrupting the normal development of fungi by inhibiting spore germination and mycelial growth.

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 impurities in the technical product have been validated and assessed to be acceptable.

2.2 Method for formulation analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for residue analysis

Gas chromatographic or high-performance liquid chromatographic methods were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

Plant matrices

A high performance liquid chromatography method with tandem mass spectrometric detection (HPLC-MS/MS; Ricerca Method 024119-1) was developed and proposed for data generation and enforcement purposes in plant matrices. In addition, gas chromatography methods with mass spectrometric detection (GC-MS; DowElanco ERC 94.15, ERC 91.17, ERC 92.20, ERC 93.4, ERC 93.2, ERC 91.9, ERC 92.34, and ERC 92.4) and a HPLC method with ultraviolet light detection (HPLC-UV) (DowElanco ERC 92.5) were developed for data generation purposes in plant matrices. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (generally 70–120%) were obtained in plant matrices. The proposed enforcement method, Ricerca Method 024119-1, was successfully validated in plant matrices by an independent laboratory, and adequate extraction efficiencies were demonstrated using radiolabelled corn stover samples. Methods for residue analysis in plant matrices are summarized in Appendix I, Table 16.

3.0 Impact on human and animal health

3.1 Hazard assessment

3.1.1 Toxicology summary

Fenazaquin, also identified as EL-436, is an acaricide, fungicide, and insecticide belonging to the quinazoline chemical class. The insecticidal mode of action (MOA) of fenazaquin is through inhibition of the mitochondrial respiratory chain at the complex I site (nicotinamide adenine dinucleotide hydride (NADH)-ubiquinone reductase), leading to reduced synthesis of adenosine triphosphate (ATP) and the formation of reactive oxygen species (ROS).

A detailed review of the toxicology database for fenazaquin was conducted. The database is lacking an acceptable developmental toxicity study in the rabbit. The database is otherwise complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The applicant also submitted a special study in the mouse, investigating the mechanism for metabolic activation and induction of hepatocellular peroxisomal proliferation

following oral exposure to fenazaquin, as well as select toxicity studies on the fenazaquin transformation products 2-(4-*tert*-butylphenyl) ethanol (2,4-TBPE) and 4-hydroxyquizoline (4-OHQ). The required studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The human health risk assessment also considered any relevant information found in the published literature. Overall, the scientific quality of the toxicology database is acceptable, and the database is considered adequate to characterize the majority of the toxic effects that may result from exposure to fenazaquin.

Metabolism and toxicokinetic studies were conducted via the oral route in both intact and bile duct-cannulated rats, as well as in mice and hamsters. In these studies, fenazaquin was radiolabelled specifically on the phenyl ring, or uniformly on the t-butyl-phenyl ring and the quinazoline ring portions of the molecule. Fenazaquin was rapidly absorbed and distributed to tissues following a single low- or high-dose gavage administration. The highest levels of radioactivity were observed in the bile within eight hours of dosing with the phenyl ring label.

Radioactivity was readily excreted within 48 hours of administration of a single dose, with the majority of radioactivity excreted via the feces (in intact rats) and lower amounts in the urine. Results from bile duct-cannulated rats suggested that biliary excretion accounted for the majority of the eliminated radioactivity in the feces. The levels of radioactivity in urine, bile, and feces were similar across all dosing regimens. In these studies, bioavailability was not significantly different between sexes.

The toxicokinetics of radiolabelled fenazaquin were also examined following 14 days of gavage administration to intact rats. Peak tissue concentrations occurred seven days after the final dose with greatest concentrations in the fat of both sexes, and the ovaries of females. Concentrations of radioactivity observed in tissues following repeated dosing were similar to those observed after single dose administration. There was no notable sex difference in the distribution of radioactivity in the repeat-dose study, and the majority of the administered radioactivity was excreted via the feces.

Fenazaquin was readily metabolized in the rat with no significant sex differences identified. Following single gavage dosing with a low- or high-dose of radiolabelled test material, the major metabolite found in the urine was an acidic non-conjugate (AN-1). Metabolite F-2 was the primary fecal metabolite, and metabolites F-1, F-1A, and F-3 were also identified. These metabolites were formed by cleavage of the ether bridge, and oxidation of methyl groups on the alkyl sidechain to either an alcohol or a carboxylic acid. The minor metabolite 4-OHQ was also identified in the feces, which formed as a result of cleavage of the ether bridge in the fenazaquin molecule. The identification of select fenazaquin metabolites is presented in Appendix I, Table 2.

In a supplemental study designed to examine species differences in plasma kinetics, radiolabelled fenazaquin was administered as a single gavage dose to rats, mice and hamsters. A different range of doses was tested for each species, reflecting their differences in toxicity from exposure to fenazaquin, with fenazaquin showing highest acute oral toxicity in rats followed by hamsters and then mice. At a similar dose level across the three species (25 or 30 mg/kg bw), absorption of radiolabel in mice and hamsters was very rapid compared to rats. However, plasma

concentrations dropped very quickly in mice compared to rats and hamsters. Additionally, the plasma toxicokinetic profiles generated for each species showed that the absorption and elimination of radiolabelled fenazaquin were similar for rats and hamsters, but different in mice. Plasma concentrations in mice were not dose-proportional, demonstrating supralinearity relative to the administered dose level; additionally, a large secondary peak concentration was observed in female mice. In rats and hamsters, the mean peak plasma concentrations were proportional to the dose levels, and the elimination profiles showed dose-related decreases. These data were used, in part, to support the selection of the hamster as the second rodent species in carcinogenicity testing.

In acute toxicity testing, the active ingredient fenazaquin was highly toxic in rats and slightly toxic in mice via the oral route, of low acute toxicity via the dermal route in rabbits, and of slight acute toxicity in rats via inhalation exposure. Fenazaquin was minimally irritating to the eyes and non-irritating to the skin of rabbits. Sensitization studies conducted in guinea pigs using the Maximization test protocol or the Buehler test protocol yielded negative results, but were considered inadequate due to small group sizes. As such, fenazaquin is classified as a potential dermal sensitizer in the absence of an acceptable dermal sensitization study.

The end-use products Magister SC Miticide/Fungicide and Magus SC Miticide, containing fenazaquin, were of high acute toxicity via the oral route in rats, of low acute toxicity via the dermal route in rabbits, and of slight acute toxicity in rats via inhalation exposure. Both end-use products were mildly irritating to the eyes and moderately irritating to the skin of rabbits, and were negative for skin sensitization in guinea pigs using the Buehler test protocol.

Repeat-dose oral toxicity studies of short- and/or long-term duration with fenazaquin were available in mice (dietary), rats (gavage and dietary), hamsters (gavage and dietary), and dogs (dietary). In these studies, the most sensitive species appeared to be the rat and the dog, followed by the hamster, and then the mouse. In the rat and the dog, decreases in food consumption, body weight gains, and body weight were observed as the target effects. In hamsters after repeated oral administration, the target organs were the liver and the testes. Specifically, increased relative liver weight, decreased testes and prostate weight, and testicular atrophy were observed, in addition to decreases in body weight and food consumption. In rats and hamsters, other effects included decreased globulin and cholesterol, and changes in alanine aminotransferase (ALT) levels. Hamsters also had decreased alkaline phosphatase (ALP), total protein, glucose, creatinine, and triglycerides, while rats had decreased protein, bilirubin and albumin, along with a change in aspartate aminotransferase (AST) levels, decreased absolute spleen weight, increased liver weight, and increased lactate dehydrogenase (LDH). These studies demonstrated evidence of increased toxicity with increased duration of dosing for rats and hamsters.

In several repeat-dose oral studies in rodents, hepatic microsomal enzyme activity was assessed in non-guideline studies (14-day duration), as well as in guideline studies (90-day duration). Increased p-nitroanisole O-demethylase (PNA), benzphetamine N-demethylase (BNZ), and 7-ethoxyresorufin O-deethylase (7-ER) levels were observed in rats and hamsters. With repeated dosing in the mouse, rat, and hamster, increased hepatic peroxisomal β-oxidation was observed, as well as increased liver weight and other varied liver effects. In a 4-day oral gavage study,

mice were dosed with analogues of fenazaquin, created by altering portions of the molecule, in order to investigate which functional groups are likely responsible for the induction of hepatocellular peroxisome proliferation in rodents. Increased peroxisomal fatty acyl CoA oxidase (FAO) activity in this study indicated that oxidation of the t-butyl substituent on the alkylbenzene moiety of fenazaquin is the critical step for induction of hepatocellular peroxisome proliferation in mice. Analogues containing a substituent on the alkylbenzene portion of the molecule that were susceptible to oxidization to carboxylic acid were also active peroxisome proliferators.

In a 28-day immunotoxicity study in rats conducted via oral gavage, there was no evidence of immune system dysregulation. Additionally, there were no systemic effects up to the limit dose in a 21-day dermal toxicity study in rabbits. A request to waive the conditional requirement for a repeat-exposure inhalation toxicity study was accepted, based on the low volatility of fenazaquin, the difficulty in generating particle sizes in the respirable range with fenazaquin, and acceptable margins of exposure obtained for the inhalation exposure scenarios when oral endpoints were used in the risk assessment.

In a 2-generation reproductive toxicity study conducted in rats via oral gavage, the systemic toxicity observed in parental animals was generally consistent with findings reported in other repeat-dose toxicity studies in rats, and included decreased body weight, body weight gains, and food consumption, as well as excess salivation. A second 2-generation reproductive toxicity study was conducted under similar conditions as the first but using a single higher dose level to supplement the original study. In the second reproductive toxicity study, additional clinical signs and behavioural effects were observed in parental animals. In both studies, effects noted in the offspring were observed at the same dose levels as those resulting in parental toxicity. Effects in the offspring included reduced pup body weight and/or body weight gains, and increased pup mortality in the F1 generation between postnatal days (PND) 2 and 4 in both studies and PND 8 and 14 at the higher dose level in the second study. The findings identified in these 2-generation reproductive toxicity studies suggested that there was no increased sensitivity of the young animal when compared to the adult animal, although a serious endpoint (reduced offspring survival) was observed in the presence of parental toxicity. Reproductive effects consisted of a decreased fertility index in F1 parental animals, as well as inflammation of the prostate in P generation males at the highest dose level tested in the second study.

A developmental toxicity study was conducted in rats via oral gavage. Maternal rats administered fenazaquin exhibited decreases in body weight gain, food consumption, and food efficiency, similar to other repeat-dose studies in rats. There were no treatment-related effects on gestational parameters, and no treatment-related developmental effects.

Range-finding and main developmental toxicity studies conducted via oral gavage were available in the rabbit. Although no treatment-related maternal or developmental effects were apparent in the main study, a high number of maternal deaths caused by technical errors and several abortions that occurred after the cessation of dosing resulted in an insufficient number of litters available from the high-dose group for an adequate assessment of potential developmental toxicity. Furthermore, the lack of treatment-related effects in this study called into question the

adequacy of the dose levels selected. As such, this study on its own was not considered acceptable for regulatory purposes, and was therefore classified as supplemental. When considering the dose levels tested in this study in relation to the points of departure established in other studies in the database as well as those selected for human health risk assessment, there is a low level of concern for potential developmental toxicity that may have been observed at the high-dose level in the rabbit had a sufficient number of litters been available for evaluation. Therefore, additional uncertainty factors for the lack of an acceptable developmental toxicity study are not required in the human health risk assessment, and a new developmental toxicity study in the rabbit is not required at this time.

Fenazaquin was negative in a bacterial reverse mutation assay, as well as in several in vitro assays in mammalian cells assessing forward mutations, unscheduled DNA synthesis, and chromosomal aberrations. Fenazaquin was also negative in an in vivo unscheduled DNA synthesis assay, and two in vivo micronucleus assays. The weight of evidence indicated that fenazaquin was negative for potential genotoxicity.

There was no evidence of tumourigenicity in the 2-year dietary combined chronic toxicity/oncogenicity study in rats, and there was equivocal evidence of tumorigenicity in the 18-month gavage oncogenicity study in the hamster. In the hamster, increased incidences of adrenocortical adenomas in females at the mid- and high-dose levels were deemed to have an equivocal relationship to treatment based on several considerations. There was significantly greater survival at study termination at the mid- and high-dose levels where the adenomas were observed, indicating that the increased tumour incidences could have been due to the older age of the majority of the animals at termination when compared to the control. Historical control data suggested that the background incidence of adrenocortical adenomas in females sacrificed at 19–24 months increases by 2.7-fold compared to those necropsied at 13–18 months, demonstrating that the incidence of adrenocortical adenomas increases significantly later in life. Furthermore, the incidence of adrenocortical adenomas at the mid-dose level fell within the range of historical control incidences, and the incidence in high-dose females was slightly higher than the upper end of the historical range. Therefore, based on the available information, the evidence for tumorigenicity in this study was considered to be equivocal.

The hamster was selected as the second species for oncogenicity testing over the mouse due to toxicokinetic differences and the fact that the hamster was demonstrated to be more sensitive to the toxic effects of fenazaquin. Notably, in the supplemental toxicokinetics study, decreased body weight was observed in the hamster at 22 mg/kg bw/day, whereas no effects in body weight were observed in the mouse at up to 450 mg/kg bw/day. At dose levels that produced treatment-related reductions in body weight gain in the subchronic studies, rats and hamsters showed plasma elimination rates that did not differ considerably with dose level. In contrast, the half-life of elimination for fenazaquin in mice increased substantially at dose levels required to produce systemic toxicity, and it would therefore be necessary to dose mice to levels at which metabolic pathways would become saturated before any toxicity is apparent.

In an acute neurotoxicity study in rats conducted via oral gavage, decreased motor activity, sluggish arousal, abnormal respiration, unusual posture, spastic gait, and ataxia were observed predominantly on the day of dosing. In a 90-day neurotoxicity study conducted in rats via oral gavage, similar findings such as decreased motor activity, unusual posture, and ataxia were observed in females, as were excess salivation, urine-stained abdominal fur, and loss of righting reflex. General ataxia and mortality were also observed in the first few days of the 28-day gavage immunotoxicity study in rats conducted via oral gavage. Additionally, excess salivation, decreased motor activity, abnormal respiration, urine-stained fur, ataxia, and impaired righting reflex were noted in the 2-generation gavage reproductive toxicity study conducted in rats. Although these behavioural findings could be suggestive of possible neurotoxicity, all occurred at the same or higher dose levels as those that also caused generalized systemic toxicity and in some cases significant body weight loss and mortality, suggesting that the effects were attributable to generalized toxicity, rather than evidence of selective neurotoxicity. Therefore, there is an overall low level of concern for neurotoxicity within the fenazaquin database.

Two in vitro toxicity studies from the literature investigating the mechanism of toxicity of pesticides acting at the complex I site of the mitochondrial respiratory chain, including fenazaquin, were considered in the hazard characterization of fenazaquin. In one study, inhibition of the complex I site by fenazaquin and other pesticide active ingredients via oxidative damage was demonstrated. A ranked order of toxicity to neuroblastoma cells was included, with fenazaquin ranking at a lower potency in comparison to the other complex I inhibitors used in the study. In the second study, there was reduced neuronal survival in astrocytes deficient in the cytoprotective protein DJ-1 when treated with fenazaquin and other complex I inhibitors when compared to wild-type astrocytes, demonstrating a neuroprotective effect of DJ-1 against mitochondrial complex I inhibitor-induced neurotoxicity. Overall concern for these in vitro findings was low given the results of the in vivo acute and subchronic neurotoxicity studies discussed above, both of which employed various staining techniques specific to neurological tissue and did not provide any evidence of neuronal damage following oral exposure to fenazaquin.

A number of toxicity studies were provided for two fenazaquin transformation products: 2,4-TBPE and 4-OHQ. 2,4-TBPE was found to be of low acute toxicity via the oral and dermal routes in rats, and mildly irritating to the skin and corrosive to the eyes of rabbits. There were equivocal results for dermal sensitization in a guinea pig Maximization test with 2,4-TBPE. 2,4-TBPE was also found to be negative in a bacterial reverse mutation assay and in an in vivo micronucleus assay in mice. 4-OHQ was found to be of high acute toxicity via the oral route of exposure in rats, and tested negative in a bacterial reverse mutation assay.

Repeat-dose gavage toxicity studies in rats of 28 days duration were provided for 2,4-TBPE and 4-OHQ, which allowed a comparison of toxic effects with the 90-day repeat-dose dietary and gavage studies with fenazaquin. In the repeat-dose gavage studies conducted with 2,4-TBPE and 4-OHQ, toxic effects were produced at higher dose levels when compared to the 90-day oral gavage and dietary studies in rats conducted with fenazaquin. For both transformation products, decreased body weight, food consumption, and/or body weight gains were observed, and target tissues included the liver, kidney, and testes. Additionally, the adrenal gland was a target tissue

for 2,4-TBPE, and the uterus for 4-OHQ. Although toxic effects observed with these transformation products were observed at higher dose levels than with fenazaquin, there is insufficient information to conclude that they are generally of lower toxicity than fenazaquin.

The identification of select fenazaquin metabolites and transformation products is presented in Appendix I, Table 2. The toxicology reference values for use in the human health risk assessment are summarized in Appendix I, Table 3. Results of the toxicology studies conducted on laboratory animals with fenazaquin-containing end-use products, fenazaquin, and its metabolites, are summarized in Appendix I, Tables 4, 5, and 6, respectively.

3.1.2 *Pest Control Products Act* hazard characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the available rabbit developmental toxicity study was deemed supplemental due to issues with maternal survival and inadequacy of dosing. However, there is sufficient information to conclude that additional factors are not warranted in this situation and that a new study is not required to ensure the protection of human health for potential developmental toxicity. The other studies in the database include two gavage 2-generation reproductive toxicity studies in rats, and a gavage developmental toxicity study in rats.

With respect to potential prenatal and postnatal toxicity, there was no indication of increased sensitivity of fetuses or offspring compared to parental animals in the reproductive or developmental toxicity studies. In the 2-generation reproductive toxicity studies, both parents and offspring demonstrated effects on body weight at the same dose level. There was an increased incidence of pup mortality in both reproductive toxicity studies in rats; however, these effects occurred in the presence of parental toxicity. There were no developmental effects observed in the rat developmental toxicity study, or in the available information from the supplemental rabbit developmental toxicity study.

Overall, the database is adequate for determining the sensitivity of the young. There is a low level of concern for sensitivity of the young as effects in the young are well-characterized and occurred in the presence of maternal toxicity. The pup mortalities were considered serious endpoints although the concern was tempered by the presence of parental toxicity. On the basis of this information, the *Pest Control Products Act* factor (PCPA factor) was reduced to threefold for scenarios in which the endpoint of pup mortality was used to establish the point of departure for use in human health risk assessment.

3.2 Toxicology reference values

3.2.1 Route and duration of exposure

Potential exposure to fenazaquin may occur via the diet (food and drinking water). Workers are also expected to be exposed via the dermal route over short-, intermediate- and long-term durations and the inhalation route over the short-term. Application of fenazaquin-containing products in residential areas and on pick-your-own farms may result in non-occupational aggregate exposure via the oral (food and drinking water) and dermal routes over a short-term duration.

For outdoor crop, non-crop and ornamental uses and interiorscapes, occupational exposure for mixers, loaders and applicators to Magister SC Miticide/Fungicide or Magus SC Miticide is characterized as short- to intermediate-term in duration depending on the use scenario and is predominantly by the dermal and inhalation routes. For postapplication workers, occupational exposure is also characterized as short- to intermediate-term in duration and is predominantly by the dermal route.

For greenhouse ornamental uses, occupational exposure for mixers, loaders and applicators to Magister SC Miticide/Fungicide or Magus SC Miticide is characterized as long-term in duration and is predominantly by the dermal and inhalation routes. For postapplication workers, occupational exposure is also characterized as long-term in duration and is predominantly by the dermal route.

For the general public, contact with treated berries, orchard fruit trees and ornamental plants and trees should primarily occur via the dermal route of exposure. The duration is expected to be short-term.

3.2.2 Occupational and residential toxicology reference values

Short-, intermediate-, and long-term dermal and short-term inhalation

For short-, intermediate, and long-term dermal and short-term inhalation occupational exposures, the offspring NOAEL of 5 mg/kg bw/day from the 2-generation reproductive toxicity study in rats was selected for risk assessment. At the LOAEL of 25 mg/kg bw/day, an increased incidence of pup mortality was observed.

For residential scenarios, the target margin of exposure (MOE) selected for this endpoint is 300. Ten-fold factors were applied each for interspecies extrapolation and intraspecies variability. As outlined in the *Pest Control Products Act* Hazard Characterization Section, the PCPA factor was reduced to threefold. The selection of this study and target MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed women.

For occupational scenarios, the target MOE for this endpoint is 300. Ten-fold factors were applied each for interspecies extrapolation and intraspecies variability. As the worker population could include pregnant or lactating workers, it is necessary to afford adequate protection of the fetus or nursing infant who may be exposed via their mother. In light of the concerns outlined in the *Pest Control Products Act* Hazard Characterization Section, an additional threefold factor was applied to this endpoint to protect all subpopulations, including the nursing or unborn children of exposed female workers.

3.2.3 Acute reference dose (ARfD)

To estimate acute dietary risk, the offspring NOAEL of 5 mg/kg bw/day from the 2-generation reproductive toxicity study in rats via oral gavage was selected. At the LOAEL of 25 mg/kg bw/day, an increased incidence of pup mortality was observed between PND 2 and 4. At the same dose level, reductions in body weight and body weight gain were observed in parental animals. The possibility that the early postnatal deaths in offspring could be due to a single exposure could not be ruled out; therefore, this endpoint is considered relevant to an acute scenario. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization Section, the PCPA factor was reduced to threefold. The composite assessment factor (CAF) is thus 300.

The ARfD is calculated according to the following formula:

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{5 \text{ mg/kg bw/day}}{300} = 0.02 \text{ mg/kg bw of fenazaquin}$$

The ARfD provides a margin of 650 to the mid-dose level in the rabbit developmental toxicity study for which an acceptable number of litters was available for assessment, and at which there were no developmental effects noted.

3.2.4 Acceptable daily intake (ADI)

To estimate risk following repeated dietary exposure, the offspring NOAEL of 5 mg/kg bw/day from the 2-generation reproductive toxicity study in rats was selected. At the LOAEL of 25 mg/kg bw/day, an increased incidence of pup mortality was observed. At the same dose level, reductions in body weight and body weight gain were observed in parental animals. The points of departure established in the long-term studies in hamsters and rats were lower or comparable to the offspring NOAEL of 5 mg/kg bw/day. Despite this, the critical endpoint of pup mortality was selected for use in human health risk assessment because it ensured adequate protection for all populations, including nursing infants and the unborn children of exposed workers, when considering the application of the PCPA factor. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization Section, the PCPA factor was reduced to threefold. The CAF is thus 300.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{\text{5 mg/kg bw/day}}{300} = 0.02 \text{ mg/kg bw/day of fenazaquin}$$

The ADI provides a margin of 750 to the dose level at which an equivocal increase in adrenocortical adenomas was seen in female hamsters, and 650 to the mid-dose level in the rabbit developmental toxicity study for which an acceptable number of litters was available for assessment, and at which there were no developmental effects observed.

3.2.5 Cancer assessment

As previously discussed, an increase in the incidence of adrenocortical adenomas in female hamsters in the 18-month gavage oncogenicity study with fenazaquin was considered equivocal based on the weight of evidence. Overall, the toxicology reference values selected for the non-cancer risk assessment are protective of any residual concerns regarding the carcinogenic potential of fenazaquin.

3.2.6 Aggregate toxicology reference values

Aggregate exposure is the total exposure to a single pesticide that may occur from dietary (food and drinking water), residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation). Short-term aggregate exposure to fenazaquin may be comprised of food, drinking water, and residential exposure via the dermal route. The toxicology endpoint selected for aggregation for all populations was increased pup mortality. For the oral and dermal routes, the offspring NOAEL of 5 mg/kg bw/day from the 2-generation reproductive toxicity study in rats was selected with a target MOE of 300. The PCPA factor for all routes was threefold as set out in the *Pest Control Products Act* Hazard Characterization Section.

3.3 Dermal absorption

A human and rat in vitro dermal absorption study was reviewed. Based on the data presented in the study, dermal absorption values of 10% from the high-dose rat group for mixers and loaders handling the concentrated end-use products, and 28% from the low-dose human group for all other exposure scenarios were selected for the risk assessments of fenazaquin (Appendix I, Table 7). The dermal absorption value of 28% from the low-dose human group was deemed appropriate to use in the risk assessment and would not underestimate exposure as all the tape strips were included. For workers handling the concentrated product, it was deemed more appropriate to use the dermal absorption value of 10% from the rat high-dose group (which was similar to the 6% from the human high-dose group) as a Geiger counter was used in the study to determine remaining skin residues following extensive washes, which is not representative of a worker taking a shower at the end of the day. With this procedure, the potential amount of test material absorbed may be underestimated, therefore, the dermal absorption value from the rat was chosen.

3.4 Occupational and residential exposure assessment

3.4.1 Acute hazards of end-use products and mitigation measures

3.4.1.1 Magister SC Miticide/Fungicide and Magus SC Miticide

The acute hazard assessment indicated that Magister SC Miticide/Fungicide and Magus SC Miticide are of high acute toxicity by the oral route, mildly irritating to the eyes, and moderately irritating to the skin; consequently, the signal word "DANGER" and hazard statements "POISON" and "EYE AND SKIN IRRITANT" are required on both labels. Both products are of low acute toxicity by the dermal route, of slight acute toxicity by inhalation exposure, and did not cause an allergic skin reaction.

Based on these acute hazards, coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, chemical-resistant footwear, and goggles/face shield are required for workers during mixing, loading, application, clean-up and repair; and for open-cab airblast application, chemical-resistant headgear is also required.

3.4.2 Occupational exposure and risk assessment

3.4.2.1 Mixer, loader and applicator exposure and risk assessment

Individuals have potential for exposure to fenazaquin during mixing, loading, application, clean-up and repair. Dermal and inhalation exposure estimates were generated from the Agricultural Handlers Exposure Task Force (AHETF) database, and the Pesticide Handlers Database (PHED, v1.1) for mixers, loaders and applicators handling Magus SC Miticide or Magister SC Miticide/Fungicide and applying to crops and ornamental plants using airblast, groundboom and handheld equipment. The PPE in the risk assessment is based on handlers wearing a long-sleeved shirt, long pants and chemical-resistant gloves for groundboom, rights-of-way sprayer, backpack and manually-pressurized handwand application equipment. For airblast application, the PPE in the risk assessment is based on handlers wearing coveralls over a long-sleeved shirt, long pants and chemical-resistant gloves for mixers, loaders and applicators, and chemical-resistant headgear for applicators. For mechanically-pressurized handgun application to greenhouse crops and outdoor grown ornamentals, the risk assessment is based on handlers wearing coveralls over a long-sleeved shirt, long pants and chemical-resistant gloves. For mechanically-pressurized handgun application to indoor grown/greenhouse ornamental plants and tree seedlings, the risk assessment is based on handlers wearing chemical-resistant coveralls over a long-sleeved shirt, long pants and chemical-resistant gloves, and for application to orchard trees and berries, a respirator was added to the latter PPE for mixers, loaders and applicators.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day and the dermal absorption values of 10% for mixers and loaders, and 28% for applicators for groundboom, airblast and rights-of-way sprayers. The dermal absorption value of 28% was used for mixers, loaders and applicators for all handheld application equipment.

Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 80 kg adult body weight.

Exposure estimates were compared to the selected toxicological reference value to obtain the margin of exposure (MOE); the target MOE is 300. Dermal and inhalation MOEs were combined, since the dermal and inhalation endpoints are based on the same toxicological effects. Calculated MOEs are greater than the target MOE of 300 for all agricultural crops, non-crop areas and ornamental plants for all chemical handler scenarios, with the exception of mechanically-pressurized handgun application to caneberries (Crop Group 13-07A), bushberries (Crop Group 13-07B), small fruit vine climbing berries, except fuzzy kiwifruit (Crop Group 13-07F) and orchard crops (pome fruit and stone fruit). The exposure to workers from the berries and orchard fruit scenarios is mitigated by limiting to 12 L the amount of product that can be handled per day when using a mechanically-pressurized handgun. Therefore, when the required mitigation measures are followed, there are no health risks of concern (Appendix I, Tables 8 and 9).

3.4.2.2 Postapplication exposure and risk assessment

There is potential for exposure to workers entering areas treated with Magus SC Miticide or Magister SC Miticide/Fungicide to complete tasks such as scouting, setting irrigation lines, tying/training, hand harvesting, fruit thinning, disbudding and hand pruning. Given the nature of the activities performed, exposure should be primarily via the dermal route based on dermal contact with treated foliage. Inhalation exposure is not expected as fenazaquin is considered non-volatile with a vapour pressure of $< 3.1 \times 10^{-8}$ kPa (at 20°C), which is less than the North American Free Trade Agreement criterion for a non-volatile product for outdoor scenarios [1×10^{-4} kPa (7.5×10^{-4} mm Hg) at 20-30°C] and for indoor uses [1×10^{-5} kPa (7.5×10^{-5} mm Hg)]. As such, a quantitative inhalation risk assessment is not required. Inhalation risk is not of health concern for postapplication workers as fenazaquin is considered to be non-volatile and the required restricted-entry intervals (REIs) for specific postapplication activities will allow residues to dry, suspended particles to settle and vapours to dissipate.

Fenazaquin dislodgeable foliar residue (DFR) data in apples, grapes, squash and sweet corn for assessing human exposures during postapplication activities were reviewed (Appendix I, Table 10).

The apple DFR values were generated in Pennsylvania and Idaho. The DFR values derived from the Idaho site were selected since this site is more representative of Canadian-growing regions and represents the most conservative exposure estimates despite the fact that the daily dissipation rate could not be determined due to the high variability of the field recoveries from this site. The highest peak DFR value of 21% of the application rate and the standard daily dissipation value of 10% were used in the risk assessments for orchard trees.

The grape DFR values were generated in California and New York. The DFR values derived from the New York site were selected since this site is more representative of typical Canadian grape and berry growing regions in terms of climate. The statistics are more robust at this site compared to the values from the California site, and the R^2 value is adequate. The peak DFR of 8.9% of the application rate and the daily dissipation rate of 12.1% were used in the risk assessment.

The squash DFR values were generated in Pennsylvania and California. The DFR values derived from the Pennsylvania site were selected since this site is more representative of Canadian-growing regions and it represents the most conservative exposure estimates: the highest peak DFR value of 20% of the application rate and the slowest daily dissipation rate of 20%. In addition, the R^2 value for this site is adequate.

The sweet corn DFR values were generated in Pennsylvania and Oregon. The DFR values derived from the Oregon site were selected based on the application method and equipment, which are the typical application practice for sweet corn, fruiting vegetables, low growing berries and field grown ornamental trees and plants. In addition, the R^2 value for this site is adequate. The peak DFR value of 9.3% of the application rate and the daily dissipation rate of 9.9% were used in the risk assessment.

Dermal exposure to workers entering treated areas is estimated by coupling dislodgeable foliar residue (DFR) values with activity-specific transfer coefficients (TCs). Activity TCs are based on data from the Agricultural Re-entry Task Force (ARTF). The fenazaquin-specific DFR data were used for the applicable crops and ornamental plants in the postapplication exposure assessments. In those cases where specific DFR data were not applicable, a standard DFR value of 25% of the application rate coupled with 10% daily dissipation of residues for outdoor uses and 2% for indoor uses were applied in the exposure assessment.

Exposure estimates were compared to the toxicological reference value to obtain the margin of exposure (MOE); the target MOE is 300. Specific REIs are required for certain postapplication activities to meet the target MOE of 300. For some scenarios, the target MOE of 300 could not be reached with agronomically feasible REIs. Therefore, the uses on greenhouse vegetables, and on indoor/greenhouse and outdoor ornamental cut flowers could not be supported (Appendix I, Table 11).

3.4.3 Residential exposure and risk assessment

3.4.3.1 Handler exposure and risk assessment

Magus SC Miticide and Magister SC Miticide/Fungicide are not domestic class products, therefore, a residential handler exposure assessment is not required.

3.4.3.2 Postapplication exposure and risk assessment

Magus SC Miticide and Magister SC Miticide/Fungicide are proposed for use on pick-your-own berries and orchard fruits, as well as on indoor and outdoor ornamental plants and trees in public, industrial, recreational and commercial areas, including residential areas. As such, postapplication pick-your-own and residential risk assessments are required.

3.4.3.2.1 Pick-your-own (PYO) activities

Berries and orchard fruits can be treated with fenazaquin, and therefore, there is potential for exposure during pick-your-own activities. However, given that the postapplication occupational risk assessment is protective of the risk associated with dermal exposure to the patrons in a pick-your-own facility, a quantitative risk assessment is not required.

3.4.3.2.2 Ornamental plants and trees in residential areas treated with Magus SC Miticide or Magister SC Miticide/Fungicide

When a commercial applicator is hired to treat ornamental plants and trees in a residential area or a farmer treats ornamental plants and trees adjacent to residential areas, there is potential for residential postapplication dermal exposure to homeowners and their families.

The residential postapplication dermal risk assessment was conducted for adults (16 years old and over) and children (6 to less than 11 years old) when contacting treated ornamental plants and trees to perform activities such as thinning and pruning or from incidental contact as a result of climbing treated trees or playing in the foliage of treated plants.

Dermal exposure was estimated for ornamental trees and outdoor ornamental plants using the apple and sweet corn DFR values, respectively, and for indoor plants/plantscapes using the standard DFR values, and the indicated transfer coefficients, durations of exposure and body weights from the 2012 United States Environmental Protection Agency Residential Standard Operating Procedures. Using the dermal absorption value of 28% determined from the in vitro dermal absorption study and toxicological reference values, calculated MOEs were greater than the target MOE of 300 (Appendix 1, Table 12) for all residential postapplication exposure scenarios on Day 0. Therefore, health risks are not of concern and individuals can enter the treated areas once the sprays have dried.

3.4.4 Bystander exposure and risk assessment

As there is potential for exposure to recreational users and the general public contacting vegetation treated by commercial application of fenazaquin to ornamental plants and trees in rights-of-way, easements and recreational areas, a postapplication dermal risk assessment for bystanders was conducted for adults (>16 years old) and children (6 to <11 years old).

Dermal exposure was estimated using the standard DFR values, transfer coefficients for "scouting" of 1100 cm^2/hr for adults (>16 years old) and 605 cm^2/hr for children (6<11 years old), an exposure duration of 2 hours, and standard body weights of 80 kg for adults and 32 kg for children. Using the dermal absorption value of 28% determined from the in vitro dermal absorption study and the toxicological reference values, calculated MOEs for both subpopulations were greater than the target MOE of 300 (Appendix 1, Table 13). For bystanders, health risks are not of concern and the individuals can enter the treated areas once the sprays have dried.

For interiorscapes or plantscapes in buildings, Magister SC Miticide/Fungicide or Magus SC Miticide applications can occur only when the public or occupants are not present. With this restriction, bystanders are not expected to be in the vicinity during interiorscape spraying events (for example, inside public areas such as shopping malls and office buildings), but are expected to be in the vicinity postapplication once the sprays have dried. However, since adults and children do not usually contact interiorscapes and postapplication inhalation exposures are expected to be negligible when compared to workers that are exposed for 8 hours per day, no health risks of concern are expected.

For all other use sites, bystander exposure is considered negligible as application is limited when there is low risk of drift beyond the area to be treated, taking into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings. Therefore, exposure and risk to other bystanders are also not of health concern since the potential for drift is expected to be minimal.

3.5 Dietary exposure and risk assessment

3.5.1 Exposure from residues in food of plant origin

The residue definition for risk assessment and enforcement in plant commodities is fenazaquin. The data gathering/enforcement analytical method Ricerca Method 024119-1 (HPLC-MS/MS) is valid for the quantitation of fenazaquin residues in crops. The residues of fenazaquin are stable in representative matrices from four of the five commodity categories: high water content for up to 34.5 months, high oil content for up to 25.2 months, high starch content for up to 25.2 months and high acid content for up to 13.3 months when stored at ≤-10ºC. Fenazaquin residues concentrated in the following processed commodities (median processing factor): apple pomace (2×), citrus oil (79×), plum prunes (4.8×) and raisins (2.3×). Crop field trials conducted throughout the United States, including growing regions representative of Canada, using end-use products containing fenazaquin at the proposed rates in or on fruiting vegetables (pepper, tomato), cucurbit vegetables (cantaloupe, cucumber, zucchini), pome fruits (apple, pear), stone fruits (peach, cherry, plum), caneberries (raspberry), bushberries (blueberry), vine climbing small fruits (grape), low growing berries (strawberry) and citrus fruits (lemon, lime, grapefruit) are sufficient to support the proposed maximum residue limits. Confined rotational crop studies were conducted with lettuce, radish and wheat. The data are adequate to demonstrate that a 30-day plantback interval (PBI) is appropriate for non-labeled crops except for root, tuber and bulb vegetables where a 120-day PBI is required.

The use on greenhouse vegetables is not supported as the greenhouse trials submitted for cucumbers, peppers and tomatoes are not considered acceptable as they are not representative of the Canadian use pattern and the crops were not grown under conditions typical of greenhouses in Canada. Additionally, as plant metabolism was not demonstrated in three diverse crop categories, but only in cereals and fruits, the MRL request on imported tea is not supported.

3.5.2 Exposure from residues in drinking water

3.5.2.1 Concentrations in drinking water

Estimated environmental concentrations (EECs) of fenazaquin and its transformation products of concern for human health were calculated for potential drinking water sources (groundwater and surface water) using the Pesticide in Water Calculator (PWC) (version 1.52). A parent-daughter modelling approach considered fenazaquin and its transformation products of human health concern: 4-quinazolinol, 2-(4-*tert*-butylphenyl)ethanol (2,4-TBPE), 2-oxy-fenazaquin, and fenazaquin propionic acid.

In order to model groundwater EECs, PWC simulates leaching through a layered soil profile into groundwater. The EECs calculated using PWC are average concentrations in the top one meter of the water table. PWC also models surface water EECs by simulating pesticide runoff and drift from a treated field into an adjacent water body, and the fate of a pesticide within that water body. The model water body is a small reservoir, a vulnerable drinking water source.

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The Level 1 EEC estimates are expected to allow for future use expansion into other crops at application rate(s) equal to or lower than the modelled rate of one single application of 539.15 g a.i./ha. Appendix I, Table 19 in lists the major environmental fate characteristics of fenazaquin and its transformation products used in the model simulations. The model was run for 50 years for surface water simulations and 100 years for groundwater simulations. The highest EECs were selected from the various model scenarios as Level 1 EECs and are reported in Appendix I, Table 20.

Details of water modelling inputs and calculations are available upon request.

3.5.3 Dietary risk assessment

Acute and chronic (non-cancer and cancer) dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 4.02, 05-10-c), which incorporates consumption data from the National Health and Nutrition Examination Survey/What We Eat in America (NHANES/WWEIA) for the year 2005-2010.

3.5.3.1 Acute dietary exposure results and characterization

The following assumptions were applied in the refined (intermediate level) acute analysis for fenazaquin: 100% crop treated, HAFT (highest average field trial) residues from field trials, experimental processing factors, where available, and American tolerances for imported commodities.

The refined (intermediate level) acute dietary exposure for all supported fenazaquin commodities and including all imported commodities ranged from 12.6% to 56.3% of the ARfD for all population subgroups (95th percentile, deterministic). Aggregate exposure from food and drinking water (EEC value = 9.3 µg a.i./L, Level 1, surface water) is not of health concern. Specifically 23.6% (0.005 mg/kg bw/day) of the ARfD was obtained for the general population and 57.4% (0.011 mg/kg bw/day) of the ARfD for children 1-2 years old.

3.5.3.2 Chronic dietary exposure results and characterization

The following criteria were applied to the refined (intermediate level) chronic (non-cancer and cancer) exposure assessment: 100% crop treated, median residues from field trials, American tolerances for imported commodities and experimental processing factors, where available.

The refined (intermediate level) chronic dietary exposure from all supported fenazaquin food uses and including all imported commodities for the representative population subgroups ranged from 2.0% to 9.3% of the ADI. Aggregate exposure from food and drinking water (EEC value = 4.5 µg a.i./L, Level 1, surface water) is not of health concern. Specifically a range from 2.3% to 9.9% of the ADI was obtained for all population subgroups. The highest exposed population subgroup was children 1-2 years old (0.002 mg/kg bw/day).

3.6 Aggregate exposure and risk

There is potential for individuals to be exposed to fenazaquin via different routes of exposure concurrently. As such, the following scenarios were considered.

Aggregation of acute dietary (food and drinking water) and dermal exposure to fenazaquin from pick-your-own activities was not conducted, as the risk estimated for each individual route of exposure is well below the level of concern and therefore, protective of this scenario.

Aggregation of chronic dietary (food and drinking water) and dermal exposure to fenazaquin from contact with ornamental plants and trees in residential settings was conducted. When combining dermal and dietary exposure values and comparing the total exposure to the aggregate toxicological reference values, calculated MOEs were greater than the target MOE of 300 (Appendix I, Table 14) for the indicated life stages. As such, aggregate health risks are not of concern.

For recreational users and the general public entering rights-of-way, easements and outdoor recreational sites and contacting treated vegetation or foliage, the chronic dietary exposure values (food plus drinking water) for specific subpopulations for fenazaquin were aggregated with the dermal exposure values. Aggregate exposure estimates were compared to the aggregate toxicological reference value to obtain the MOE; the target MOE is 300. The results of the aggregate risk assessment are presented in Appendix I, Table 15. The calculated MOEs were greater than the target MOE of 300; as such, there are no health risks of concern and recreational users and the general public can enter areas where ornamental plants and trees have been treated once the sprays have dried.

3.7 Maximum residue limits

Dietary risks from the consumption of foods listed in Table 3.7.1 were shown to be acceptable when fenazaquin is used according to the supported label directions. Therefore, foods containing residues at these levels are safe to eat, and the PMRA recommends that the following MRLs be specified for residues of fenazaquin.

Table 3.7.1 Recommended maximum residue limits

MRL (ppm)	Food commodity
20	Citrus oil
2	Stone Fruits Crop Group 12-09; Low Growing Berries Crop Subgroup 13-07G
0.8	Bushberries Crop Subgroup 13-07B; Raisins
0.7	Caneberries Crop Subgroup 13-07A; Small Fruit, Vine Climbing, Except Fuzzy Kiwifruit Crop Subgroup 13-07F
0.6	Pome Fruits Crop Group 11-09
0.4	Citrus Fruits (Revised) Crop Group 10
0.3	Fruiting Vegetables Crop Group 8-09; Cucurbit Vegetables Crop Group 9

MRLs are proposed for each commodity included in the listed crop groupings in accordance with the Residue Chemistry Crop Groups webpage in the Pesticides section of Canada.ca.

For additional information on Maximum Residue Limits (MRLs) in terms of the international situation and trade implications, refer to Appendix II.

The nature of the residues in plant matrices, analytical methodologies, field trial data, and acute and chronic dietary risk estimates are summarized in Appendix I, Tables 16, 17 and 18.

3.8 Cumulative assessment

The *Pest Control Products Act* requires the Agency to consider the cumulative effects of pest control products that have a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pesticides was undertaken for fenazaquin. Fenazaquin is classified, based on its structure, as a quinazoline insecticide. No other quinazoline insecticides are registered for use in Canada, and other quinazoline insecticides to which Canadians may be exposed via imported food commodities (for example, pyrifluquinazon, fluquinconazole) demonstrate different pesticidal modes of action and toxicological profiles, and as such are not considered to have a common mechanism of toxicity with fenazaquin. The insecticidal MOA for fenazaquin, inhibition of the mitochondrial electron transport at the complex I site, is common to several other pesticide active ingredients, including fenpyroximate, pyridaben, pyrimidifen, tebufenpyrad, tolfenpyrad, and rotenone. Although the mechanism of toxicity for fenazaquin in mammals in unknown, the available in vitro studies from the literature suggested exposure of human neuroblastoma cells to several complex I inhibitors resulted in ATP depletion, cell death, and displacement of dihydrorotenone binding from complex I, suggesting a common mechanism of cellular toxicity in vitro. However, specific toxicity was not demonstrated in the available mammalian in vivo studies conducted with fenazaquin that could be linked to this mode of action. Overall, the observed effects with fenazaquin are indicative of more generalized toxicity and there is insufficient evidence to link the apical endpoints observed in the toxicology databases for fenazaquin and other complex I inhibitors with a specific mechanism of toxicity. Therefore, a common mechanism of toxicity has not been identified, and a cumulative risk assessment is not required at this time.

4.0 Impact on the environment

4.1 Fate and behaviour in the environment

Terrestrial environment

Fenazaquin applied by foliar spray is expected to remain mostly on leaves and not translocate throughout the plant. It is relatively non-volatile and is not likely to volatilize from moist soil surfaces. Fenazaquin is moderately persistent to persistent in soil depending on environmental conditions, and dissipates through biotransformation and phototransformation. Phototransformation results in the production of 4-quinazolinol and 2,4-TBPE as major transformation products (in other words, greater than 10% of initially applied fenazaquin), while biotransformation results largely in mineralization or residues that remain strongly bound to the soil and are thus not bioavailable.

In field soils, fenazaquin is non-persistent to moderately persistent and has low potential to carry over to the next growing season. A large portion of fenazaquin and its residues may become incorporated into the soil matrix. Considering the results of laboratory studies including K_{oc} values, assessments using Groundwater Ubiquity Scores and the criteria of Cohen et al. (1984), and field studies, fenazaquin and its transformation products are unlikely to leach to groundwater.

Aquatic environment

Fenazaquin is sparingly soluble in water and is unlikely to volatilize from water surfaces. Fenazaquin is slightly to moderately persistent in aquatic systems. There is low potential for hydrolysis and photolysis in aquatic systems due to preferential partitioning of fenazaquin to sediments. Fenazaquin is transformed by micro-organisms into two major transformation products, mostly in the sediment phase: 2-oxyfenazaquin and fenazaquin propionic acid. Fenazaquin is also eventually transformed to large quantities of CO_2, in addition to residues strongly bound to sediment that are not bioavailable. Bioaccumulation of fenazaquin in aquatic organisms is not likely.

A summary of terrestrial and aquatic environmental fate characteristics for fenazaquin is in Appendix I, Table 21.

4.2 Environmental risk characterization

The environmental risk assessment integrates environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing estimated environmental concentrations (EECs) in various environmental media (food, water, soil and air) with the concentrations at which adverse effects occur. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for organisms (invertebrates, vertebrates, and plants) from both terrestrial and aquatic habitats.

Toxicity endpoints and effects for fenazaquin are summarized in Appendix I, Tables 22 and 23 for terrestrial and aquatic organisms, respectively. Acute toxicity endpoints (for example, LC_{50}, LD_{50}, and EC_{50}) used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level). The magnitude of the uncertainty factor depends on the group of organisms being evaluated as follows: 10 for fish, birds, and mammals, 2 for aquatic invertebrates, freshwater plants, and earthworms, and 1 for bees, other beneficial arthropods, and terrestrial plants. The difference in the value of the uncertainty factor reflects, in part, the ability of organisms at a certain trophic level (in other words, feeding position in a food chain) to withstand, or recover from, a stressor at the level of the population. When assessing chronic risk, a no-observed (adverse) effect concentration (NOEC, NOAEC, or similar chronic endpoint) is used and an uncertainty factor is not applied. Toxicity endpoints used in the risk assessment and their associated uncertainty factors are in Appendix I, Table 24.

Initially, a screening level risk assessment is performed to identify specific uses and/or groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 0.4 for acute risk to pollinators,

2 for glass plate studies using the standard beneficial arthropod test species *Typhlodromus pyri* and *Aphidius rhopalosiphi*, and 1 in all other cases). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary.

If the screening level risk quotient is equal to or greater than the level of concern, a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to terrestrial organisms

Fenazaquin end-use products are applied as a foliar spray to crops. Terrestrial organisms, such as earthworms, bees and other beneficial arthropods, birds, mammals and terrestrial vascular plants may be exposed to fenazaquin through direct contact with spray or spray drift, contact with sprayed surfaces, or from ingestion of contaminated food. A risk assessment for fenazaquin and its end-use products Magister SC Miticide/Fungicide and Magus SC Miticide was performed based on available toxicity data for earthworms, bees and other beneficial arthropods, birds, mammals, and terrestrial plants.

Screening level calculation details and risk quotients are in Appendix I, Table 25 (all organisms except birds and mammals) and Appendix I, Table 26 (birds and mammals). At the screening level, the risk quotients were below the level of concern for earthworms (acute basis), Collembola (chronic basis), plants (seedling emergence and vegetative vigour), and birds. Risk quotients exceeded the level of concern for earthworms (chronic basis), bees and other beneficial arthropods, and mammals. Risk assessment refinements for these organisms are described below. There was a slight exceedance of the level of concern for seedling germination of terrestrial plants. As this was based on an indeterminate endpoint, and no significant effects were observed in any of the plant toxicity studies, terrestrial plants were not included in the refined risk assessment.

Earthworms

The screening level risk quotient exceedance for chronic exposure was based on a significant reduction (34%) in the mean number of juveniles observed at the highest tested treatment rate of 624 g a.i./ha, which is higher than the maximum Canadian outdoor application of 539.15 g a.i./ha. There were no significant effects on earthworm survival or growth. As a refinement, when considering the lowest observed adverse effect rate (LOAER) in the risk quotient instead of the no observed adverse effect rate (NOAER) as a more representative endpoint for potential effects on earthworm populations, the chronic risk quotient does not exceed the level of concern. Therefore, the use of fenazaquin is not expected to pose a chronic risk of concern to earthworms.

Bees

Due to the potential risk suggested at the screening level, the risk to bees was further characterized by considering results from a foliar residue test and semi-field studies.

A foliar residue test with adult honey bees was conducted on alfalfa treated with a 200 g/L SC fenazaquin end-use product formulation at 504 g a.i./ha (similar to the maximum outdoor Canadian application rate) in order to characterize the duration of time during which residues remain toxic to bees (Appendix I, Table 22). Honey bees showed no treatment-related mortality when exposed for 24 hours to aged residues of fenazaquin on alfalfa foliage. The residual time required to bring bee mortality down to 25% following exposure to weathered residues (in other words, the RT_{25} value) in this study was less than three hours, suggesting minimal risk from exposure to weathered residues.

Two semi-field studies were conducted with flowering *Phacelia tanacetifolia* sprayed with a 200 g/L SC fenazaquin end-use product formulation at a rate of 80 or 300 g a.i./ha (Appendix I, Table 22). The study results over the three- to four-day observation periods suggest initial, transient effects on foraging activity and adult mortality are possible. There were no effects on bee brood development. The applicability of these results to a Canadian context is uncertain due to the study application rates which were approximately half, or less, than the maximum Canadian outdoor application rate of 539.15 g a.i./ha. In addition, the study duration of three to four days does not allow reliable determination of effects on bee brood since a full brood cycle is approximately 24 days. The study duration is also insufficient for assessment of chronic effects on adult honey bees in the field as the majority of mortality in the adult chronic toxicity test in the laboratory was observed as of day 4.

Overall, the risk to honey bees and other pollinators is expected to be greatest from direct applications of fenazaquin to blooming crops, weeds, and ornamental plants, or through spray drift to these areas. The semi-field study results do not allow for reliable determination of effects on bee brood or adult bees in a Canadian context. In addition, there is uncertainty about risks to other non-*Apis* bees such as bumble bees or solitary bees. Considering the risk identified at the screening level, and the uncertainties associated with the semi-field studies and effects on non-*Apis* bees, risk mitigation is required for pollinators.

The pollinator risk mitigation for Magister SC Miticide/Fungicide and Magus SC Miticide is based in part on exposure potential. The majority of labelled crops can be attractive to honey bees, bumble bees and solitary bees. For the proposed orchard crops, there may be flowering groundcover which can also be attractive to pollinators. There is further potential for pollinator exposure through pollen and nectar for those crops which require insect pollination (for example, cucurbit vegetables, pome and stone fruits). Outdoor applications of Magister SC Miticide/Fungicide and Magus SC Miticide will not be permitted during bloom for crops with high exposure potential, while application during bloom will be restricted to evenings for all other crops. For greenhouse uses, there is potential for exposure to managed pollinators used in greenhouse production. There is also potential for exposure to pollinators when greenhouse ornamentals or vegetables are planted outside; however, this exposure route from pollen and

nectar is minimal given that the product is not systemic, that blooms would have to present when sprayed in the greenhouse, and that blooms are unlikely to last through or after transplant. For greenhouse uses, a precautionary statement indicating toxicity to managed pollinators used in greenhouse production will be required. With these label mitigation measures, the risk to pollinators is acceptable.

Beneficial arthropods

The risk to beneficial arthropods was further characterized using results from extended laboratory and field toxicity studies with various foliar-dwelling arthropod species (Appendix I, Table 22). Extended laboratory studies demonstrated minimal effects of fenazaquin end-use product formulations to different species of non-target arthropods after application at rates up to 252 g a.i./ha; however, this rate was less than half of the maximum Canadian outdoor application rate of 539.15 g a.i./ha. In field studies conducted at rates of 100 to 500 g a.i./ha, initial transient effects on population density were noted, indicating potential for recovery between seasons. Lower toxicity to eggs was also consistently demonstrated in the various studies, suggesting that long-term impact on beneficial arthropod populations is unlikely. Based on the available data, risk to beneficial arthropods from extended residual toxicity following application of fenazaquin is considered minimal. In order to mitigate for potential toxicity to beneficial arthropods at the time of spray applications, precautionary label statements will be required for both outdoor and greenhouse uses. With these label mitigation measures, the risk to beneficial arthropods is acceptable.

Mammals

The risks to mammals were further characterized considering endpoint selection, other feeding guilds, on-field (diet exposed to direct pesticide application) and off-field exposures (diet exposed to drift only), and maximum and mean food item residue levels. In the screening level assessment, the acute oral toxicity endpoint was indeterminate (in other words, >37.8 mg a.i./kg bw, the lowest tested dosage), and was a conservative estimate for a study in which a clear dose-response relationship could not be established. The data suggest the endpoint may actually be closer to the mid-point of the study range, in other words, 113.4 mg a.i./kg bw. This is in agreement with the other available acute oral toxicity study with a determinate endpoint of 134 mg a.i./kg bw. In the refined risk assessment, the determinate endpoint of 134 mg a.i./kg bw was used to assess acute risk.

Risk quotients and calculation details for the refined risk assessment are in Appendix I, Table 27. Considering multiple feeding groups and the revised acute endpoint, risk quotients only exceeded the level of concern for a few combinations of weight class and feeding group when considering maximum food residue levels on-field (RQs up to 3.65). Assuming that food items all contain maximum residue levels is conservative; levels will likely vary. On-field risk quotients calculated using mean residues of fenazaquin only exceeded the level of concern for a few feeding groups of small and medium-sized mammals on an acute basis (RQs up to 1.30). Off-field risk quotients did not exceed the level of concern for any combination of weight class and feeding group when considering mean residues off-field. It should be noted that the other

methods of application for Magister SC Miticide/Fungicide and Magus SC Miticide involve less spray drift than early season airblast application and consequently would result in even lower off-field risk quotients. Furthermore, outdoor application rates range from 153.75 to 539.15 g a.i./ha; therefore, use of the maximum application rate in the risk assessment is considered conservative with respect to exposures.

Relatively few risk quotients for mammals exceeded the level of concern following refinement. Risk quotients were no larger than 3.65 and involved mostly maximum residues. Levels on food items are likely variable and thus assuming that 100% of food items contain maximum residue levels is conservative. The assumption that the mammalian diet is composed entirely of one food item is also conservative; mammals typically roam over a large area to seek alternate food sources. Very few risk quotients exceeded the level of concern when considering mean residues on-field (maximum RQ of 1.30), and no risk quotient exceeded the level of concern when considering mean residues off-field. Based on these results, fenazaquin is not expected to pose a risk of concern to mammals.

4.2.2 Risks to aquatic organisms

At the screening level, aquatic organisms are assumed to be exposed to fenazaquin via direct spray to a small water body. Screening level calculation details and risk quotients are in Appendix I, Table 28. At the screening level, all risk quotients were exceeded except for some freshwater algae, and for the transformation products 2,4-TBPE and fenazaquin propionic acid. Though the screening level risk quotient (less than 1.8) exceeded the level of concern for freshwater plants, the risk was determined to be of low concern due to the low magnitude of exceedance and lack of treatment-related effects observed at the maximum treatment rate of 75.1 µg a.i./L, which was approximately the same as the PMRA's estimated exposure concentration at screening level, 67 µg a.i./L, corresponding to the maximum Canadian outdoor application rate. Therefore, the risk to aquatic plants was not included in the refined risk assessment.

Since cranberry cultivation presents a unique scenario from the perspective of aquatic risk assessment relative to other uses of fenazaquin, it was considered separately, only for those organisms with level of concern exceedances at the screening level. The cranberry risk assessment model methods, resulting exposure estimate, and risk quotients are in Appendix I, Table 29. The risk quotients were below the level of concern for all organisms except for *Daphnia* exposed to fenazaquin as an end-use product on a chronic basis (RQ = 1.55). Considering the conservative use of the peak simulated concentration in floodwater as the exposure concentration, dilution of floodwater in recipient water bodies, and preferential partitioning of fenazaquin to sediments, it is unlikely that aquatic organisms would be exposed to water column concentrations as high as the estimated concentration on a chronic basis. Thus, the risk to aquatic organisms from exposure to fenazaquin due to cranberry cultivation is acceptable.

The refined risk assessment considered spray drift and runoff separately. The spray drift risk assessment calculations and risk quotients are in Appendix I, Table 30. Model inputs used to generate exposure estimates for the runoff risk assessment are in Appendix I, Table 19. The runoff model methods and resulting exposure estimates are in Appendix I, Table 31, and the risk quotients are in Appendix I, Table 32.

Spray drift

The refined risk quotients for fenazaquin exposure due to spray drift still exceeded the level of concern on an acute and chronic basis for all freshwater and marine invertebrates (RQs up to 249.4), freshwater and marine fish (RQs up to 127.9), amphibians (RQ up to 682), and freshwater and marine algae (RQs up to 118.7). A hazard statement and spray buffer zones are required for the use of Magister SC Miticide/Fungicide and Magus SC Miticide in order to protect aquatic organisms from spray drift in adjacent aquatic habitats.

Runoff

The refined risk quotients for fenazaquin exposure due to runoff still exceeded the level of concern on an acute and/or chronic basis for all organisms (RQs up to 24.5) except freshwater algae and the marine shrimp *Crangon crangon*. Many of the risk quotients that exceeded the level of concern corresponded to chronic exposure. Given that fenazaquin will preferentially partition to sediment, it is unlikely that fenazaquin would be available in the water column on a chronic basis. The rapid partitioning of fenazaquin to sediments in aquatic systems in the field is demonstrated by the single submitted outdoor microcosm study during which no treatment-related effects on *Daphnia* or fish were observed under a spray and runoff exposure scenario. A slurry meant to simulate runoff was added to the microcosms, resulting in a nominal maximum of 6.0 µg a.i./L of microcosm water, which is within the range of the PMRA's estimated exposure concentrations, 4.8 to 7.1 µg a.i./L, for the runoff refinement. However, the maximum measured concentration in microcosm water two hours following slurry addition was only 2.87 µg a.i./L. The study suggests fenazaquin concentrations in the water column of aquatic systems may not even be sustained on the shorter time scales corresponding to the acute toxicity endpoints used in the risk assessment. Nevertheless, in order to mitigate potential risk to aquatic organisms, a hazard statement for aquatic organisms and standard label statements to mitigate runoff and other contamination of aquatic habitats are required on the labels of Magister SC Miticide/Fungicide and Magus SC Miticide.

With label mitigation measures, the risk to aquatic organisms from exposure to fenazaquin is acceptable.

5.0 Incident reports

Fenazaquin is a new active ingredient pending registration for use in Canada and as of 24 March 2022, no incident reports had been submitted to the PMRA.

6.0 Value

Fenazaquin is a new conventional pesticide active ingredient for management of certain mite and insect pests and powdery mildew pathogens in Canada. Alternative pesticides for control of the target pests and pathogens on the same crops are registered in Canada, representing various FRAC and IRAC mode of action groups. Magister SC Miticide/Fungicide and Magus SC Miticide will provide Canadian growers additional options for use against the target mite and insect pests and powdery mildew on the food crops and ornamentals listed on the product labels. These options represent a new active ingredient for all uses and a new mode of action for most uses on the product labels, which will aid in the management of resistance to the pesticides already registered for those uses.

Scientific rationales and efficacy data from 15 field trials demonstrated that Magister SC Miticide/Fungicide controls powdery mildew on cucurbit vegetables (Crop Group 9), pome fruits (Crop Group 11-09), stone fruits (Crop Group 12-09) and grapes (Amur river grape and grape). Efficacy data from 33 field and greenhouse trials demonstrated that Magister SC Miticide/Fungicide and/or Magus SC Miticide control blueberry bud mite, pear rust mite, twospotted spider mite, Pacific spider mite, European red mite, sweetpotato whitefly and pear psylla. Those trials included a wide variety of food crops as well as indoor and outdoor ornamentals. No phytotoxicity or crop injury was reported in any of the submitted studies; therefore, application of Magister SC Miticide/Fungicide or Magus SC Miticide to the crops on the product labels is not expected to result in crop injury.

The value information reviewed was sufficient to support claims for control of blueberry bud mite, certain rust mites and spider mites, pear psylla, sweetpotato whitefly and powdery mildew with one application (outdoors) or two applications (indoors) per year at rates of 1.75–2.63 L of product per hectare on food crops or 300–1000 mL of product per 400 L of spray volume on ornamentals. Details of the supported use pattern are outlined in Appendix I, Table 34.

7.0 Pest Control Product Policy considerations

7.1 Assessment of the active ingredient under the Toxic Substances Management Policy

The *Toxic Substances Management Policy* (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, in other words, those that meet all four criteria outlined in the policy: persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*. The *Pest Control Products Act* requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, fenazaquin and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that fenazaquin and its transformation products do not meet all of the TSMP Track 1 criteria.

Further information on the TSMP assessment is in Appendix I, Table 33.

7.2 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.*[6] The list is used as described in the PMRA Science Policy Note SPN2020-01[7] and is based on existing policies and regulations, including the *Toxic Substances Management Policy* and *Formulants Policy*,[8] and taking into consideration the *Ozone-depleting Substances and Halocarbon Alternatives Regulations* under the *Canadian Environmental Protection Act, 1999, (*substances designated under the *Montreal Protocol).*

The end-use products, Magister SC Miticide/Fungicide and Magus SC Miticide contain the preservative 1,2-benzisothiazolin-3-one which contains low levels of dioxins and furans. These are being managed as outlined in the PMRA Regulatory Directive DIR99-03 for the implementation of the TSMP. The end-use products also contain the allergen “sulfites”.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

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5 DIR99-03*, The Pest Management Regulatory Agency’s Strategy for Implementing the Toxic Substances Management Policy*.

6 SI/2005-114, last amended on June 24, 2020. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.*

7 PMRA’s Science Policy Note SPN2020-01, *Policy on the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* under paragraph 43(5)(b) of the *Pest Control Products Act*.

8 DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

8.0 Proposed regulatory decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the Pest Control Products Act, is proposing registration for the sale and use of Fenazaquin Technical, Magister SC Miticide/Fungicide, and Magus SC Miticide, containing the technical grade active ingredient fenazaquin, to control certain mites, psylla, whitefly, and powdery mildew on a variety of crops and ornamental plants.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

Additional information being requested

Since this technical product is manufactured only at pilot scale before registration, five-batch data representing commercial-scale production will be required as post-market information after registration.

List of abbreviations

°C	degree Celsius
°N	degrees North
^{14}C	carbon-14 radioactive isotope
2,4-TBPE	2-(4-*tert*-butylphenyl)ethanol
4-OHQ	4-hydroxyquizoline
↑	increased
↓	decreased
♂	male
♀	female
µg	micrograms
µmol	micromolar
7-ER	7-ethoxyresorufin O-deethylase
a.i.	active ingredient
abs	absolute
AD	administered dose
ADI	acceptable daily intake
AHETF	Agricultural Handlers Exposure Task Force
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AN-1	acidic non-conjugate
AOPWIN	Atmospheric Oxidation Program for Microsoft Windows
AR	applied radioactivity
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
AST	aspartate aminotransferase
ATP	adenosine triphosphate
ATPD	area treated per day
AUC	area under the concentration-time curve
BAF	bioaccumulation factor
BBCH	Biologishe Bundesanstalt, Bundessortenamt and Chemical industry
BCF	bioconcentration factor
BNZ	benzphetamine N-demethylase
BUN	blood urea nitrogen
bw	body weight
bwg	body weight gain
CAS	Chemical Abstracts Service
CAF	composite assessment factor
CEPA	*Canadian Environmental Protection Act*
CHO	Chinese hamster ovary
cm	centimetres
Cmax	maximum plasma concentration
CO_2	carbon dioxide
CR	chemical-resistant
d	day(s)

DA	dermal absorption
DAT	days after treatment
DEEM-FCID	Dietary Exposure Evaluation Model
DFOP	double first-order in parallel
DFR	dislodgeable foliar residue
DHR	^{3}H-dihydrorotenone
DIR	Regulatory Directive
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
dw	dry weight
EC	emulsifiable concentrate
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure
EEC	estimated environmental exposure concentration
EFSA	European Food Safety Authority
EPI Suite	Estimation Programs Interface Suite
ER_{25}	effective rate on 25% of the population
F1	first generation
F2	second generation
fc	food consumption
fe	food efficiency
FAO	peroxisomal fatty acyl CoA oxidase
FDA	*Food and Drugs Act*
FIR	food ingestion rate
FL	Florida
FRAC	Fungicide Resistance Action Committee
g	gram
GC-FID	Gas Chromatography Flame Ionization Detector
GC-MS	Gas Chromatography Mass Spectrometry
GC-NPD	Gas Chromatography Nitrogen Phosphorus Detector
GIT	gastrointestinal tract
h	hour(s)
ha	hectare(s)
HAFT	highest average field trial
Hg	mercury
HPLC-UV	high pressure liquid chromatography ultra-violet detector
HPLC-MS	high pressure liquid chromatography mass spectrometry
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
hr(s)	hour(s)
IUPAC	International Union of Pure and Applied Chemistry
ILV	independent laboratory validation
IN	Indiana
IORE	indeterminate order rate equation

IRAC	Insecticide Resistance Action Committee
kg	kilogram
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
kPa	kilopascal(s)
L	litre
LAFT	lowest average field trial
LC_{50}	concentration estimated to be lethal to 50% of the test population
LD_{50}	dose estimated to be lethal to 50% of the test population
LDH	lactate dehydrogenase
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
LOAER	lowest observed adverse effect rate
LOC	level of concern
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
LUFA	Landwirtschaftliche Untersuchungs- und Forschungsanstalt
m^3	cubic metre(s)
M/L/A	mixer/loader/applicator
mg	milligram(s)
mL	millilitre(s)
mm	millimetre(s)
mol	mole(s)
mPa	milliPascal
MAS	maximum average score
MIS	maximum irritation score
MOA	mode of action
MOE	margin of exposure
MRL	maximum residue limit
N/A	not applicable
NADH	nicotinamide adenine dinucleotide hydride
NER	non-extracted residues
NHANES/WWEIA	National Health and Nutrition Examination Survey/What We Eat in America
nM	nanomolar
nm	nanometer
NIOSH	National Institute for Occupational Safety and Health
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOAER	no observed adverse effect rate
NOEC	no observed effect concentration
NZW	New Zealand white
OC	organic carbon content
P	parental generation
Pa	Pascal(s)
PBI	plantback interval

PCPA	*Pest Control Product Act*
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PNA	p-nitroanisole O-demethylase
PND	postnatal day
PPE	personal protective equipment
ppm	parts per million
PWC	Pesticide in Water Calculator
PYO	pick-your-own
R^2	coefficient of determination
RAC	raw agricultural commodity
REI	restricted-entry interval
rel	relative
ROS	reactive oxygen species
RQ	risk quotient
RT_{25}	residual time needed to reduce the activity of the test substance and bring bee mortality down to 25%
SC	suspension concentrate
SDEV	standard deviation
SFO	single first-order
SL	single layer of clothing
SPN	Science Policy Note
$t_{1/2}$	half-life
TC	transfer coefficient
Tmax	time of maximum plasma concentration
TP	transformation product
t_R	representative half-life
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution
w	week(s)
wc	water consumption
wt	weight
ww	wet weight

Appendix I Tables and figures

Table 1 Residue analysis

Matrix	Method type	Analyte	LOQ	Reference
Soil (four various types)	HPLC-MS	Fenazaquin	0.010 µg/g	PMRA# 2962746, 3047643
Soil (four various types)	HPLC-MS	2-oxyfenazaquin	0.010 µg/g	PMRA# 2962746, 3047643
Soil (four various types)	HPLC-MS	4-hydroxyquinazoline	0.010 µg/g	PMRA# 2962746, 3047643
Soil (three various types)	HPLC-MS	2,4-TBPE	0.001 µg/g	PMRA# 3168980
Water (drinking, ground and surface)	GC-NPD	Fenazaquin	0.05 µg/L	PMRA# 2962538
Water (synthetic surface water)	GC-MS	2-oxyfenazaquin	10 µg/L	PMRA# 3168974,
Water (synthetic surface water)	HPLC-UVD	4-hydroxyquinazoline	3 mg/L	PMRA# 3168976, 3168977
Water (synthetic surface water)	HPLC-UVD	Fenazaquin propionic acid	10 µg/L	PMRA# 2962595, 3168978
Water (synthetic surface water)	GC-FID	2,4-TBPE	10 µg/L	PMRA# 2962596, 3102692

Table 2 Identification of select metabolites and transformation products of fenazaquin

Code name	Chemical name (IUPAC)	Source
2,4-TBPE	2-(4-*tert*-butylphenyl)ethanol	Growing crops, soil
4-OHQ	4-hydroxylquinazoline	Growing crops, animal commodities, soil, and rat
F-1	2-methyl-2-{4-[2-(quinazolin-4-yloxy)ethyl]phenyl}-propan-1-ol	Growing crops and rat
F-1A	4-[2-[4-(1,1-dimethylethyl)phenyl]-2-(hydroxy)ethoxy]quinazoline	Rat
F-2	2-methyl-2-(4-(2-((4-quinazolinyl)oxy)ethyl)phenyl)propionic acid	Growing crops, animal commodities, soil, aquatic systems, and rat

Code name	Chemical name (IUPAC)	Source
F-3	2-methyl-2-(4-{2-[(2-oxo-1,2-dihydroquinazolin-4-yl)oxy]ethyl}phenyl) propanoic acid	Growing crops, animal commodities, soil, and rat
AN-1	2-(4-carboxymethylphenyl)-2-methylpropanoic acid	Animal commodities, soil, aquatic systems, and rat

Table 3 Toxicology reference values for use in health risk assessment for fenazaquin

Exposure scenario	Study	Point of departure and endpoint	CAF[1] or target MOE
Acute dietary	2-generation oral reproductive toxicity study in rats	Offspring NOAEL = 5 mg/kg bw/day Pup deaths PND 2-4	300
ARfD = 0.02 mg/kg bw			
Repeated dietary	2-generation oral reproductive toxicity study in rats	Offspring NOAEL = 5 mg/kg bw/day Pup deaths PND 2-4	300
ADI = 0.02 mg/kg bw/day			
Short-, intermediate- and long-term dermal[2]	2-generation oral reproductive toxicity study in rats	Offspring NOAEL = 5 mg/kg bw/day Pup deaths PND 2-4	300
Short-term inhalation[3]			
Short-term aggregate Oral and dermal[2]	Oral and dermal: 2-generation oral reproductive toxicity study in rats	Common endpoint: pup deaths Oral and dermal: offspring NOAEL = 5 mg/kg bw/day	Oral and dermal: 300
Cancer	Equivocal increase in adrenocortical adenomas in female hamsters. Toxicology reference values selected for non-cancer risk assessment are protective of any residual concerns regarding carcinogenic potential.		

[1] CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments; MOE refers to a target MOE for occupational and residential assessments.
[2] Since an oral NOAEL was selected, a dermal absorption factor of either 10% for mixer/loaders or 28% for all other exposure scenarios was used in route-to-route extrapolation.
[3] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Table 4 Toxicity profile of end-use products containing fenazaquin

Effects are known or assumed to occur in both sexes unless otherwise noted.

Study Type/Animal/PMRA#	Study Results
Magister SC Miticide/Fungicide and Magus SC Miticide	
Acute oral (gavage) Rat (F344) PMRA# 2962734	LD_{50} > 300 mg/kg bw (♀) LD_{50} = 425 mg/kg bw (♂) Clinical signs of toxicity included hypoactivity, hunched posture, posterior soiling, soft stool, diarrhea, ataxia, lethargy, coma. High acute toxicity
Acute dermal Rabbit (NZW) PMRA# 2962735	LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity. Low acute toxicity
Acute inhalation Rat (F344) PMRA# 2962736	LC_{50} = 1.1 mg/L (♂/♀) Clinical signs of toxicity included hypoactivity, dyspnea, poor grooming, lethargy, ataxia, prostration, rales, thinness, weakness of extremities. Slight acute toxicity
Primary eye irritation Rabbit (NZW) PMRA# 2962737	MAS = 17.2/110 MIS = 26.2/110 at 24 hrs Mildly irritating
Primary skin irritation Rabbit (NZW) PMRA# 2962735	MAS = 3.13/8 MIS = 4.3/8 at 24 hrs Moderately irritating
Dermal sensitization (Buehler) Guinea pig (Hartley, albino) PMRA# 2962733	Negative

Study Type/Animal/PMRA#	Study Results
Dermal sensitization (Buehler) Guinea pig (Hartley albino) PMRA# 2962484	Negative

Table 5 Toxicity profile of technical fenazaquin

Effects observed in both sexes are presented first followed by sex-specific effects in males, then females, each separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to body weights unless otherwise noted. Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.

Study Type/Animal/PMRA#	Study results
Toxicokinetic studies	
Toxicokinetics – single and repeated oral doses (gavage) Rat (F344) PMRA# 2962518	[^{14}C]-labelled fenazaquin (uniformly labelled on the t-buty-phenyl ring and the quinazoline ring) was administered via gavage as a single dose at 1 and 30 mg/kg bw, and after 14 days of repeated oral dosing with unlabelled fenazaquin at 1 mg/kg bw/day. Excretion: Excretion was predominantly via feces, accounting for 72–89% of the AD (all dosing regimens). Excretion via urine accounted for 19–21% of the AD (all dosing regimens). Most of the radiolabel was eliminated within 48 hours of dosing. Negligible radioactivity (<0.1% of the AD) was excreted as CO_2 through expired air. Distribution: At 7 days post-dosing, individual tissues contained <0.04% of the AD, with highest levels in the fat of both sexes and the ovaries of ♀. Metabolism: There was no detectable unchanged fenazaquin in the urine indicating that absorbed fenazaquin was readily metabolized. The major metabolite in the urine was an acidic non-conjugate (AN-1) formed as a result of cleavage of the ether bridge in the fenazaquin molecule and represented 24-29% of the total urine radioactivity (4.1–5.8% of the AD). The remaining metabolites were divided among 10 or more unidentified metabolites, none of which represented >5% of the total urine radioactivity.

Study Type/Animal/PMRA#	Study results
	Radioactivity detected in feces that was attributed to unchanged fenazaquin was as follows: 1.2–4.2% of fecal radioactivity or 1.0–3.5% of the AD for the single and repeat low-dose groups; 12–21% of fecal radioactivity or 8.3–15% of the AD for the single high-dose group. Metabolite F-2 was the primary fecal metabolite identified, accounting for 16–23% of the fecal radioactivity (14–20% of the AD). Metabolites F-1, F-1A, and F-3 represented 4.6–9.4%, 0.6–2.6%, and 6.5–13% of the fecal radioactivity, respectively. Other minor components represented ≤ 2% of the total fecal radioactivity. One of these minor components was identified as 4-OHQ, which was formed as a result of cleavage of the ether bridge in the fenazaquin molecule. Metabolism involved cleavage of the ether bridge, and oxidation of methyl groups on the alkyl sidechain to either an alcohol or a carboxylic acid.
Absorption and excretion – single oral dose (gavage) Rat (F344; ♂); bile duct-cannulated PMRA# 2962517	[Phenyl-U-^{14}C]-fenazaquin was administered via gavage as a single dose at 1 mg/kg bw. Absorption: Absorption was rapid (highest residues in bile within 8 hrs of dosing), and represented 65% of the AD (based on radioactivity measured in urine, bile, cage wash, whole blood, GIT, carcass). Excretion: Excretion via bile, urine and feces accounted for 61%, 3.8%, and 32% of the AD, respectively, at 48 hrs after dosing.
Plasma kinetics – single oral dose (gavage) Non-guideline Rat (F344) Mouse (CD-1) Hamster (Syrian Golden) PMRA# 3077821	Supplemental [^{14}C]-labelled fenazaquin (position of radiolabel not reported) was administered via gavage as a single dose to rats at 1, 10, or 30 mg/kg bw; to mice at 30, 300, or 750 mg/kg bw; and to hamsters at 5, 25, or 125 mg/kg bw. Rat: AUC was proportional to dose. Cmax for ♀ dosed with 30 mg/kg bw was nearly twofold higher than that for ♂. Tmax was 8 hrs in all groups, except for ♂ dosed with 30 mg/kg bw for which the Tmax was 24 hrs. The half-life of elimination from plasma was generally similar between the sexes and dose levels. Radioactivity was still detectable in plasma at 7 days post-dosing. Mouse: AUC was proportional to dose except for ♀ at 750 mg/kg bw (AUC ↑ by 56-fold compared to a 25-fold ↑ in dose). Tmax ranged from 0.5 to 4 hrs at 30 and 300 mg/kg bw. The 750 mg/kg

Study Type/Animal/PMRA#	Study results
	bw dose group demonstrated two peak plasma concentrations at 2-4 and 48 hrs. The half-life of elimination from plasma was similar between the sexes at 30 mg/kg bw. At 300 mg/kg bw, elimination from plasma for ♂ was threefold slower than for ♀ at the same dose level, and ninefold slower than for ♂ at 30 mg/kg bw. The determination of plasma elimination half-lives at 750 mg/kg bw was confounded by the large secondary Cmax at 48 hrs. Hamster: AUC was generally proportional to dose. Tmax was 1–2 hrs for the 5 and 25 mg/kg bw dose groups and 4 hrs for ♂ and 8 hrs for ♀ at 125 mg/kg bw. The half-life of elimination from plasma was generally similar between the sexes and dose levels. Limitations: limited reporting.
Acute Toxicity Studies	
Acute oral (gavage) Mouse (CD-1) PMRA# 3077793	LD_{50} = 2449 mg/kg bw (♂) LD_{50} = 1480 mg/kg bw (♀) Clinical signs included hypoactivity, hunched posture, low carriage, ataxia, generalized leg weakness, ptosis, piloerection, tremors, coma. Slight acute toxicity
Acute oral (gavage) Rat (F344) PMRA# 2962479	LD_{50} = 134 mg/kg bw (♂) LD_{50} = 138 mg/kg bw (♀) Clinical signs of toxicity included hypoactivity, hunched posture, straub tail, low carriage, soft stool, diarrhea, perineal/posterior soiling, piloerection, clear ocular discharge, generalized leg weakness, ataxia, immobilization, coma. High acute toxicity
Acute oral (gavage) Rat (F344) PMRA# 3077792	LD_{50} > 50 mg/kg bw, < 500 mg/kg bw (♂/♀) Clinical signs of toxicity included hypoactivity, diarrhea, posterior soiling, hunched posture, poor grooming, lethargy, piloerection, ataxia, gasping, coma, clear ocular discharge, chromorhinorrhea, absence of feces and urine. High acute toxicity

Study Type/Animal/PMRA#	Study results
Acute dermal Rabbit (NZW) PMRA# 2962485	LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity. Low acute toxicity
Acute inhalation Rat (F344) PMRA# 2962480	LC_{50} = 1.9 mg/L (♂/♀) Clinical signs of toxicity included hypoactivity, dyspnea, ataxia, poor grooming, nasal discharge, lethargy, rales, tympanites. Slight acute toxicity
Primary eye irritation Rabbit (NZW) PMRA# 2962481	MAS and MIS could not be calculated due to limitations in reporting; MAS estimated to be <15 Slight corneal dullness, slight iritis, and slight conjunctival redness and swelling observed within 1 hr. All animals free were from irritation by 48 hrs. Minimally irritating
Primary skin irritation Rabbit (NZW) PMRA# 2962485	No dermal irritation was observed at any of the test sites during the study Non-irritating
Dermal sensitization (Buehler) Guinea pig (Hartley Albino) PMRA# 2962482	Supplemental Study yielded negative results but group size considered inadequate
Dermal sensitization (Maximization) Guinea pig (Dunkin-Hartley) PMRA# 2962483	Supplemental Study yielded negative results but group size considered inadequate
Short-Term Toxicity Studies	
14-day oral (dietary) – pilot /non-guideline	Supplemental NOAEL and LOAEL not established

Study Type/Animal/PMRA#	Study results
Mouse (CD-1) PMRA# 2962494, 3077801, 3077802	Effects at ≥ 225 mg/kg bw/day: ↑ hepatic peroxisomal β-oxidation (♂/♀) Effects at ≥ 450 mg/kg bw/day: ↑ liver wt, centrilobular hepatocellular cytoplasmic eosinophilic change, hepatocellular cytomegaly, ↑ number and size of hepatic peroxisomes (♂/♀) Effects at 900 mg/kg bw/day: ↓ bwg, single-cell necrosis in liver (♂/♀); ↑ hepatocellular proliferation (♀) Limitations: limited reporting.
14-day oral (dietary) – pilot /non-guideline Rat (F344) PMRA# 2962494, 3077803, 3077804, 3077805, 3077806	Supplemental NOAEL and LOAEL not established Effects at ≥ 46/48 mg/kg bw/day: ↓ bw, ↓ bwg, ↓ fc, ↑ hepatic peroxisomal β-oxidation, ↑ rel. liver wt, hepatocellular cytomegaly (♂/♀) Effects at ≥ 79/93 mg/kg bw/day: ↓ fe (♂/♀); ↓ triglycerides (♂); ↑ abs. liver wt (♀) Effects at 168/180 mg/kg bw/day: ↑ hepatic peroxisomal proliferation (♂/♀) Limitations: limited reporting.
14-day oral (dietary) – pilot study/non-guideline Hamster (Syrian Golden) PMRA# 2962494	Supplemental NOAEL and LOAEL not established Effects at ≥ 23/22 mg/kg bw/day: ↓ hepatic microsomal enzyme activity (♂/♀); ↓ bw (♂) Effects at ≥ 70/66 mg/kg bw/day: ↓ fc (♂/♀); ↓ bwg (♂) Effects at ≥ 186 mg/kg bw/day: ↓ bw, ↓ bwg (♀) Effects at 420/607 mg/kg bw/day: mortality (2 animals near end of study) (♀) Limitations: limited reporting.
14-day oral (gavage) –	Supplemental

Study Type/Animal/PMRA#	Study results
pilot /non-guideline Hamster (Syrian Golden) PMRA# 2962494, 3077807, 3077808, 3077809, 3077810	NOAEL and LOAEL not established Effects at ≥ 5 mg/kg bw/day: ↓ bilirubin (♀) Effects at ≥ 25 mg/kg bw/day: ↑ PNA, ↑ BNZ (♀) Effects at ≥ 75/50 mg/kg bw/day: ↓ bwg, ↓ ALP (♂/♀); ↑ triglycerides, ↑ PNA, ↑ BNZ (♂); ↑ 7-ER (♀) Effects at 150/100 mg/kg bw/day: ↓ fe, ↑ rel. liver wt (♂/♀); ↑ hepatic peroxisomal β-oxidation, ↑ 7-ER (♂); ↓ bw, ↓ fc, centrilobular hepatocellular hypertrophy (♀) Limitations: limited reporting.
90-day oral (dietary) Rat (F344) PMRA# 2962486	NOAEL = 9.6/12 mg/kg bw/day (♂/♀) LOAEL = 29/33 mg/kg bw/day (♂/♀) Effects at LOAEL: ↓ bw, ↓ bwg, ↓ fc, ↓ protein, ↓ globulin (♂/♀); ↓ fe, ↓ cholesterol, ↑ rel. liver wt, ↑ ALT, ↑ AST, ↑ LDH, ↑ 7-ER (♂); ↑ PNA, ↑ abs. liver wt (♀)
90-day oral (gavage) Rats (F344) PMRA# 2962488	NOAEL = 10 mg/kg bw/day (♂/♀) LOAEL = 30 mg/kg bw/day (♂/♀) Effects at LOAEL: ↓ bw, ↓ bwg, ↓ fc, ↓ fe, ↓ abs. spleen wt (♂/♀); ↑ rel. liver wt (♂); ↑ PNA, ↓ cholesterol, ↓ globulin (♀) Recovery group: Effects at LOAEL: ↓ bw, ↑ bwg, ↑ fe, ↓ ALT, ↓ AST, ↓ abs. spleen wt (♂/♀); ↑ PNA, ↓ cholesterol (♀)
90-day oral (gavage) Hamster (Syrian Golden) PMRA# 2962487	NOAEL = 5/25 mg/kg bw/day (♂/♀) LOAEL = 25/50 mg/kg bw/day (♂/♀) Effects at LOAEL: ↓ bw, ↓ bwg, ↓ ALP, ↑ PNA (♂/♀); ↓ total protein, ↓ globulin, ↓ ALT, ↓ creatinine, ↓ triglycerides, ↑ rel. liver wt (♀)

Study Type/Animal/PMRA#	Study results
10-day and 14-day oral (dietary) – palatability and dose range-finding/non-guideline Dog (Beagle) PMRA# 2962490	Supplemental No issues with palatability of a test diet prepared to deliver a dose of 15 mg/kg bw/day. Dietary dose levels of ≥20 mg/kg bw/day were not palatable. No treatment-related effects reported up to 15 mg/kg bw/day in 14-day study. Limitations: limited reporting.
90-day oral (dietary) Dog (Beagle) PMRA# 2962489	NOAEL = 5 mg/kg bw/day (♂/♀) LOAEL = 15 mg/kg bw/day (♂/♀) Effects at LOAEL: bw loss weeks 1–2, ↓ bw, ↓ bwg, ↓ fc, ↓ fe, ↑ incidence of ↓ liver vacuolation (considered secondary to ↓ bw/fc) (♂/♀)
1-year oral (dietary) Dog (Beagle) PMRA# 2962491	NOAEL = 5 mg/kg bw/day (♂/♀) LOAEL = 12 mg/kg bw/day (♂/♀) Effects at LOAEL: bw loss weeks 1–4, ↓ bw, ↓ bwg ↓ fc, ↓ fe (♂/♀)
21-day dermal Rabbit (NZW) PMRA# 2962492	NOAEL = 1000 mg/kg bw/day (♂/♀) No treatment-related systemic toxicity. Dermal effects at ≥ 100 mg/kg bw/day: ↑ erythema and edema (♂/♀) Recovery group: Dermal effects at 1000 mg/kg bw/day: complete resolution of skin irritation (♂), persistence of skin irritation with some lessening in severity (♀)
Short-term inhalation toxicity Waiver Request PMRA# 3077824	The applicant's request to waive the short-term inhalation toxicity study was found to be acceptable based on (1) the low volatility of fenazaquin (vapour pressure = 1.9×10^{-8} kPa), (2) the fact that it is difficult to generate particle sizes in the respirable range with fenazaquin, and (3) acceptable margins of exposure obtained for the inhalation exposure scenarios when oral endpoints were used in the risk assessment.

Study Type/Animal/PMRA#	Study results
Chronic Toxicity / Oncogenicity Studies	
18-month chronic toxicity/oncogenicity (gavage) Hamster (Syrian Golden) PMRA# 2962499, 2962500, 2962501, 2962502, 2962503, 2962494	NOAEL = 2 mg/kg bw/day (♂/♀) LOAEL = 15 mg/kg bw/day (♂/♀) Effects at LOAEL: ↓ bw, ↓ thrombocyte count, ↓ incidence and severity of amyloidosis (♂/♀); ↓ bwg (♂); equivocal ↑ adrenocortical adenomas (♀) Incidence of enteritis higher at ≥ 15 mg/kg bw/day, which the study author postulated was evidence that fenazaquin may alter gut flora thus increasing susceptibility to infection. An additional study was performed to assess the oral bioavailability of an antibiotic that was added to all dosing solutions to treat enteritis starting on day 232. The additional bioavailability study consisted of dosing for 1 or 7 days, and demonstrated that the plasma levels of the antibiotic were low, indicating little systemic availability. Equivocal evidence of tumorigenicity
2-year chronic toxicity/oncogenicity (dietary) Rat (F344) PMRA# 2962495, 2962496, 2962497, 2962498, 3077811, 3077812, 3077813	NOAEL= 4.5/5.7 mg/kg bw/day (♂/♀) LOAEL = 9.2/12 mg/kg bw/day (♂/♀) Effects at LOAEL and higher: ↓ bw, ↓ bwg, ↓ fc, ↓ fe, ↓ cholesterol (♂/♀) No evidence of tumorigenicity
Developmental/Reproductive toxicity studies	
2-generation reproductive toxicity (gavage) Rats (Sprague Dawley) PMRA# 2962504, 2962505	Parental NOAEL = 5 mg/kg bw/day Parental LOAEL = 25 mg/kg bw/day Effects at LOAEL: ↑ salivation [P, F1], ↓ bw [F1], ↓ bwg [F1], ↓ fc [F1] (♂/♀); ↑ bw [P] (LD21) (♀) Offspring NOAEL = 5 mg/kg bw/day Offspring LOAEL = 25 mg/kg bw/day Effects at LOAEL: ↓ pup bwg PND 4-14 [F1, F2], ↑ pup deaths [F1, PND 2-4] (♂/♀) Reproductive NOAEL = 25 mg/kg bw/day Reproductive LOAEL not established

Study Type/Animal/PMRA#	Study results
	No treatment-related effects on the reproductive parameters assessed No evidence of sensitivity of the young Serious endpoint (pup deaths) in the presence of parental toxicity
2-generation reproductive toxicity (gavage) Rat (Sprague Dawley) PMRA# 2962506	Supplemental Study was conducted under similar conditions as PMRA# 2962504 and 2962505 and included a single higher dose level and concurrent control group. Parental effects at 40 mg/kg bw/day: ↑ salivation [P, F1], emaciation [P], ↓ motor activity [P, F1], bradypnea [F1], irregular breathing [F1], ↓ premating bw [P, F1], ↓ premating bwg [P, F1], ↓ fc [P, F1], ↓ fe [P] (♂/♀); chromodacryorrhea [P], ungroomed appearance [P, F1], urine-stained fur [P], dyspnea [P], rales [P], swollen snout [F1], red exudate on penis [F1] (♂); one mortality [P], alopecia [P], bradypnea [P], ataxia [P, F1], impaired righting reflex [P], ptosis [P], pallor [P], labored breathing [P, F1], chromorrhinorhea [F1] (♀) Offspring effects at 40 mg/kg bw/day: ↓ pup bw [F1 PND 4-21; F2 PND 1-21], ↓ pup bwg [F1, F2; PND 1-21], ↑ pup deaths [F1, PND 2-4 and 8-14] Reproductive effects at 40 mg/kg bw/day: ↓ fertility index [F2 litters] (♂/♀); inflammation of the prostate [P adults] (♂) Limitations: only one dose level tested.
Developmental toxicity (gavage) Rat (Sprague Dawley) PMRA# 2962510	Maternal NOAEL = 10 mg/kg bw/day Maternal LOAEL = 40 mg/kg bw/day Effects at LOAEL: ↓ bwg, ↓ fc, ↓fe Developmental NOAEL = 40 mg/kg bw/day Developmental LOAEL not established No treatment-related developmental effects No evidence of sensitivity of the young No treatment-related malformations

Study Type/Animal/PMRA#	Study results
Developmental toxicity (gavage) – dose range-finding Rabbit (NZW) Report not submitted (summary of results in PMRA# 2962519)	Supplemental NOAEL and LOAEL not established Maternal effects at ≥ 30 mg/kg bw/day: ↓ fc Maternal effects at ≥ 60 mg/kg bw/day: soft stools Limitations: limited details pertaining to developmental assessments
Developmental Toxicity (gavage) Rabbit (NZW) PMRA# 2962519	Supplemental NOAEL and LOAEL not established No treatment-related maternal or developmental findings observed in 15 litters assessed at 13 mg/kg bw/day or in 8 available litters assessed at 60 mg/kg bw/day. Limitations: small group size at highest dose due to abortions (after dosing ceased) and maternal deaths caused by technical errors; dose levels considered inadequate due to lack of adverse, treatment-related effects.
Genotoxicity Studies	
Bacterial reverse mutation assay *S.* Typhimurium (TA 1535, TA 1537, TA 98, TA 100) and *E. coli* (WP2uvrA) PMRA# 2962511	Negative ± metabolic activation Tested up to the highest concentration that did not cause precipitation
In vitro forward mutation assay in mammalian cells Mouse L5178Y $TK^{+/-}$ lymphoma cells PMRA# 2962512	Negative ± metabolic activation Increase in forward mutations with metabolic activation at cytotoxic concentrations only

Study Type/Animal/PMRA#	Study results
In vitro unscheduled DNA synthesis Primary rat (Fischer 344) hepatocyte cultures PMRA# 2962516	Negative Tested up to cytotoxic concentrations
In vitro chromosomal aberration assay CHO cells PMRA# 3077817	Negative ± metabolic activation Tested up to cytotoxic concentrations
In vitro chromosomal aberration assay CHO cells PMRA# 3077819	Equivocal Non-concentration-related ↑ in chromosomal aberrations in the presence of metabolic activation at the 30-hour harvest time-point only Tested up to cytotoxic concentrations
In vivo unscheduled DNA synthesis (gavage) ♂ Rat (Sprague-Dawley) PMRA# 2962515	Negative Clinical signs of toxicity included altered respiratory rate, exophthalmos, lethargy, limbs splayed. Deaths occurred at 180 (1 rat) and 600 (2 rats) mg/kg bw.
In vivo micronucleus assay (gavage) Mice (ICR) PMRA# 2962514, 3077820	Negative No clinical signs of toxicity reported
In vivo micronucleus (gavage) Mouse (ICR) PMRA# 3077818	Negative Clinical signs of toxicity included lethargy

Study Type/Animal/PMRA#	Study results
Neurotoxicity Studies	
Acute neurotoxicity (gavage) Rat (Sprague Dawley) PMRA# 2962507, 2962508, 2962509	NOAEL = 20 mg/kg bw (♂/♀) LOAEL = 65/60 mg/kg bw (♂/♀) Effects at LOAEL and higher: ↓ fc, bw loss, ↓ bwg (♂/♀); ↓ bw (♂); mild dehydration (♀) Effects at 130/120 mg/kg bw: ↓ body temperature, abnormal gait - ataxia (♂/♀); mild dehydration, ↓ motor activity (time and incidence of movement) (♂); ↓ bw, sluggish arousal, abnormal respiration, unusual posture, abnormal gait - spastic (♀) Most behavioural findings were observed on the day of dosing, and were considered secondary to generalized toxicity. No evidence of selective neurotoxicity
90-day neurotoxicity (gavage) Rat (Sprague Dawley) PMRA# 3286205	NOAEL = 10/20 mg/kg bw/day (♂/♀) LOAEL = 20/40 mg/kg bw/day (♂/♀) Effects at LOAEL: ↓ bw, ↓ bwg (♂/♀); ↓ motor activity (during daily clinical observations), urine-stained abdominal fur, prostrate position, ataxia, loss of righting reflex (♀) No evidence of selective neurotoxicity
Other Studies	
Immunotoxicity – 28-day oral (gavage) Rat (Sprague Dawley) (♀) PMRA# 2962493	NOAEL = 15 mg/kg bw/day (♀) LOAEL = 30 mg/kg bw/day (♀) Effects at LOAEL: general ataxia, mortality (♀) No evidence of immune system dysregulation
In vitro evaluation of the mechanism of toxicity of pesticides acting at mitochondrial complex I SK-N-MC human neuroblastoma cells Mitochondria isolated from rat brain PMRA# 2356217	Effects on cell death, ATP depletion, and DHR binding assessed for fenazaquin along with several other pesticide active ingredients. Cell death and ATP depletion: Dose-response observed for all compounds. Effect of fenazaquin only seen at the highest concentration tested, 1 µmol/L. Rank order of toxicity to neuroblastoma cells: pyridaben > rotenone > fenpyroximate > fenazaquin > tebufenpyrad. DHR binding: All compounds were able to displace DHR binding in the nanomolar range. Fenazaquin demonstrated the lowest potency among the pesticides tested.

Study Type/Animal/PMRA#	Study results
	Study authors concluded that the pesticides tested directly inhibit mitochondrial complex I via oxidative damage.
In vitro assessment of effects of DJ-1 deficiency in astrocytes on mitochondrial complex I inhibitor-induced neurotoxicity Astrocyte cultures from PND 1 CD-1 mouse cerebral cortex tissues PMRA# 2356215	Protective effect of DJ-1 against Complex-I inhibition assessed for fenazaquin along two other pesticide active ingredients. Astrocytes that were engineered to suppress or overexpress DJ-1 protein levels were significantly less protective of neuronal survival against all three complex I inhibitors when compared to the wild-type astrocytes. For fenazaquin, the LD_{50} for wild-type astrocyte co-cultured neurons was approximately 200 nM, compared to approximately 12 nM with DJ-1 knock-down astrocytes. For pyridaben, the LD_{50} for wild-type astrocyte co-cultured neurons was approximately 20 nM, whereas with DJ-1 knock-down astrocytes it shifted to approximately 1 nM. For fenpyroximate, the LD_{50} for wild-type astrocyte co-cultured neurons was approximately 8 nM, whereas with DJ-1 knock-down astrocytes it was approximately 2 nM A significant deficiency in astrocyte-mediated neuroprotection was seen at the following levels: Pyridaben: 0.8 to 25 nM Fenazaquin: 15.6 to 250 nM Fenpyroximate: 1.6 to 12.5 nM The study authors concluded that DJ-1 deficiency in astrocytes, a genetic deficiency linked to familial Parkinson's Disease, selectively enhances mitochondrial complex I inhibitor-induced neurotoxicity.
4-day oral (gavage) study to investigate the mechanism of hepatic hypertrophy and induction of hepatocellular peroxisomal proliferation by fenazaquin and various analogues – non-guideline Mouse (CD-1)	Supplemental Mice were dosed with analogues of fenazaquin, created by altering portions of the molecule, in order to investigate which functional groups are likely responsible for the induction of hepatocellular peroxisome proliferation in rodents. NOAEL and LOAEL not established Dose-response trial:

Study Type/Animal/PMRA#	Study results
PMRA# 2962521	Effects at ≥ 250 mg/kg bw/day: ↑ liver wt, ↑ FAO activity (plateaued at ≥ 500 mg/kg bw/day) Effects at ≥ 500 mg/kg bw/day: mortality Relative potency trials: Effects at ≥ 300 mg/kg bw/day: mortality Increased toxicity (mortality) seen with substitution of the ether tether with a nitrogen tether, substitution of the t-butyl functional group on the alkylbenzene moiety with a trifluoromethoxy, and halogenation of the quinazoline moiety coupled with a substitution of the t-butyl group on the alkylbenzene group with a blocking group. Only the nitrogen tether analog increased FAO activity greater than unchanged fenazaquin. The nitrogen tether is considered to be relatively resistant to hydrolysis and oxidation to a carboxylic acid; therefore, these findings indicate that it is plausible that another mechanism other than carboxylic acid analogs are potent inducers of hepatocellular peroxisomal proliferation in mice. Most compounds induced eosinophilia in hepatocytes and had panlobular or lobular hypertrophy in the centrilobular or midzonal regions of the liver. No consistent relationship was observed between histopathological changes and the potency of the test materials to induce peroxisomal proliferation. 2,4-TBPE did not cause any mortalities in mice, and resulted in similar increases in liver weights and FAO activity in mice relative to the vehicle control group compared to fenazaquin. The study authors concluded that it is plausible that multiple metabolite intermediates of fenazaquin are responsible for the hepatocellular peroxisomal proliferation activation in mice.

Table 6 Toxicity profile of metabolites of fenazaquin

Effects observed in both sexes are presented first followed by sex-specific effects in males, then females, each separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted. Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.

Study Type/Animal/PMRA #	Study Results
2-(4-*Tert*-Butylphenyl) Ethanol (2,4-TBPE)	
Acute oral (gavage) Rat (Sprague Dawley) PMRA# 3077790	LD_{50} > 2000 mg/kg bw Clinical signs of toxicity included lethargy, hunched posture, piloerection, ↓ motor activity, staggering gait, prone position, unconsciousness, slow deep respiration, hairloss, ungroomed appearance. Low acute toxicity
Acute dermal Rat (Sprague Dawley) PMRA# 3077798	LD_{50} > 2000 mg/kg bw Clinical signs of toxicity included irritability, ↓ motor activity, ungroomed appearance, serous discharge from eyes, pigmented staining of the snout, hunched posture. Skin observations: erythema, oedema, eschar formation, exfoliation, loss of elasticity, loss of flexibility, sensitive to the touch, brown discoloration. Low acute toxicity
Primary skin irritation Rabbit (NZW) PMRA# 3077794	MAS = 2.8 MIS = 3.0 (at 48 hrs and 6 days) Mildly irritating
Primary eye irritation Rabbit (NZW) PMRA# 3077797	MAS/MIS not calculated (only 1 animal tested due to severity of irritation response) Corrosive
Dermal sensitization (Maximization) Guinea pig (Dunkin-Hartley) PMRA# 3077799	Indications of a positive response in 40% of ♂ challenged with 50% 2,4-TBPE No positive control data included Equivocal

Study Type/Animal/PMRA #	Study Results
28-day oral (gavage) Rat (Sprague-Dawley) PMRA# 3077796	NOAEL= 20 mg/kg bw/day LOAEL = 150 mg/kg bw/day Effects at LOAEL: underactivity, salivation, ↑ wc, ↓ WBC, ↓ lymphocytes, ↑ urine volume, ↑ rel. kidney wt (♂/♀); ↑ AST, ↑ BUN, ↑ urinary ketones, ↑ liver wt, papillary necrosis of kidneys, dilated renal tubules, vacuolation and degeneration of renal tubules, fatty microvesicular vacuolation of the liver, bilateral degeneration of tubular germinal epithelium of testes (♂); hunched posture, ↓ neutrophils, ↓ platelets, ↑ ALP (♀)
Bacterial reverse mutation assay *S.* Typhimurium (TA 1535, TA 1537, TA 98, TA 100) PMRA# 3077814	Negative ± metabolic activation Tested up to cytotoxic concentrations
In vivo micronucleus assay (gavage) Mouse (ICR) PMRA# 3077815	Negative Clinical signs of toxicity included hunched posture, underactivity, piloerection, slow respiration, prone posture Early sacrifice of 3 ♀ at 1000 mg/kg bw
4-Hydroxyquiazoline (4-OHQ)	
Acute Oral (Up-and-down) Rat (Wistar) (♀) PMRA# 3077791	LD_{50} = 300 mg/kg bw (♀) Clinical signs of toxicity included altered activity, ruffled fur, slight tachypnea, collapse, dragging of forelimbs and hindlimbs, ptosis, clear lacrimation, prostration, hunched posture, ↓ body temperature High acute toxicity
28-day oral (gavage) Rat (Sprague-Dawley) PMRA# 3077800	NOAEL = 100/30 mg/kg bw/day (♂/♀) LOAEL = not established/100 mg/kg bw/day (♂/♀) Effects at LOAEL: ↓ bwg,↑ phospholipids, ↑ locomotor activity, ↑ creatine kinase, ↓ creatinine, ↑ uterine wt, ↑ rel. liver wt, ↑ rel. kidney wt (♀) All effects resolved after the recovery period (locomotor activity not measured in recovery group)

Study Type/Animal/PMRA #	Study Results
Bacterial reverse mutation assay *S.* Typhimurium (TA 1535, TA 1537, TA 98, TA 100) and *E. coli* (WP2 uvrA) PMRA# 3077816	Negative ± metabolic activation Tested up to the limit concentration

Table 7 Dermal absorption of fenazaquin residues in human and rat skin in vitro (Skin wash at 8 hours)

Matrix	Average % of applied dose[1]			
	High Dose (2000 µg/cm^2)		Low Dose (0.5 µg/cm^2)	
	Human	Rat	Human	Rat
Skin wash at 8 hours	88.36	84.27	63.57	46.58
Skin wash at termination	0.05	0.52	0.25	6.56
Donor chamber wash	2.73	0.54	1.68	0.29
Total tape strips	5.72	9.9	27.67	45.08
Receptor fluid+ chamber	0.058	0.068	0.23	0.76
Total recovery	96.92	95.30	93.40	99.27
Dermal absorption	**5.78 ± 3.3**	**9.97 ± 5.7**	**27.9 ± 16.0**	**45.8 ± 25.8**

[1] Mean of 3 skin donors/organism, 6-7 diffusion cells per dose group

Table 8 AHETF/PHED Unit exposure estimates for mixer/loaders and applicators (µg/kg a.i. handled)

Exposure Scenario and PPE[1]		Dermal	Dermal adjusted[2]	Inhalation[3]	Total Unit Exposure[4]
Mixer/loader AHETF estimates – Open Mix/Load					
A1	SL + CR gloves	58.5	5.85	0.63	6.48
A2	Cotton coveralls, CR gloves	31.3	3.13	0.63	3.76
A3	CR coveralls, CR gloves	25.5	2.55	0.63	3.18

Exposure Scenario and PPE[1]		Dermal	Dermal adjusted[2]	Inhalation[3]	Total Unit Exposure[4]
Applicator AHETF/PHED estimates					
B	Open Cab Groundboom Application (SL + CR gloves)	25.4	7.11	1.68	8.79
C1	Open Cab Airblast Application (Cotton coveralls + CR gloves)	3399.2	951.78	9.08	960.86
C2	Open Cab Airblast Application (Cotton coveralls + CR gloves + CR hat)	157.98	44.23	9.08	53.31
C3	Open Cab Airblast Application (CR coveralls + CR gloves)	3323.5	930.58	9.08	939.66
C4	Open Cab Airblast Application (CR coveralls + CR gloves + CR hat)	106.77	29.86	9.08	38.94
D	Rights-of-way sprayer (SL + CR gloves)	872.54	244.31	5	249.31
Mixer/loader + applicator AHETF/PHED estimates					
A1 + B	Open mixing/loading + open-cab groundboom (SL + CR gloves for M/L/A)	83.90	12.96	2.31	15.27
A2 + C2	Open mixing/loading + open-cab airblast (Cotton coveralls + CR gloves for M/L/A, CR hat for A)	189.28	47.36	9.71	57.07
A3 + C4	Open mixing/loading + open-cab airblast (CR coveralls + CR gloves for M/L/A, CR hat for A)	440.43	32.45	9.71	42.16
E	Backpack (SL + CR gloves for M/L/A)	5445.85	1524.84	62.1	1586.94
F	Manually-pressurized handwand (SL + CR gloves for M/L/A)	943.37	264.14	45.2	309.34
G1	Mechanically-pressurized handgun (Cotton coveralls + CR gloves for M/L/A)	2453.52	686.99	151	837.99
G2	Mechanically-pressurized handgun (CR coveralls + CR gloves for M/L/A)	1827.13	511.97	151	662.60
G3	Mechanically-pressurized handgun (CR coveralls + CR	1827.13	511.97	15.1	526.70

Exposure Scenario and PPE[1]		Dermal	Dermal adjusted[2]	Inhalation[3]	Total Unit Exposure[4]
	gloves + respirator for M/L/A)				
A+D	Open M/L Liquid + Rights-of-way sprayer (SL + gloves)	931.04	250.16	5.63	255.79

[1] SL: single layer of clothing; CR: chemical-resistant; M/L/A: mixer/loader/applicator
[2] A dermal absorption factor of 10% from the human and rat in vitro dermal absorption study was applied to the AHETF values for mixers/loaders. A dermal absorption value of 28% from the human and rat in vitro dermal absorption study was applied to the AHETF values for applicators and to the PHED value for rights-of-way spray applicators, and to the PHED values for mixers/loaders/applicators for all handheld equipment.
[3] Light inhalation rate for all exposure scenarios except backpack sprayers and moderate inhalation for backpack sprayer (M/L/A).
[4] Total unit exposure = Dermal exposure + inhalation exposure. Dermal and inhalation exposures were combined, since the dermal and inhalation endpoints are based on the same toxicological effects.

Table 9 Mixer/loader/applicator exposure and risk assessment

Exposure scenario	Target	Unit exposure (µg/kg ai handled)[1]	ATPD (ha/day)[2]	Rate (kg ai/ha)	Daily exposure (mg/kg bw/day)[3]	MOE[4]
Groundboom sprayer Open mixing/ loading + open-cab (SL + CR gloves for M/L/A)	Fruiting vegetables Caneberries Bushbberries Low growing berries (except lowbush blueberries)	15.27	26	0.48	2.38×10^{-3}	2098
	Lowbush blueberries		60		5.50×10^{-3}	909
	Cucurbit vegetables		26	0.54	2.68×10^{-3}	1869
	Outdoor ornamental plants including non-bearing fruit/nut trees (field grown, nursery)		26	0.513	2.55×10^{-3}	1964
Airblast sprayer (Open mixing/loading + open-cab; coveralls and CR gloves for	Fruiting vegetables Caneberries Bushberries Low growing berries (except lowbush blueberries)	57.07	20	0.48	6.85×10^{-3}	730
	Lowbush blueberries		40		1.37×10^{-2}	365

Exposure scenario	Target	Unit exposure (µg/kg ai handled)[1]	ATPD (ha/day)[2]	Rate (kg ai/ha)	Daily exposure (mg/kg bw/day)[3]	MOE[4]
M/L/A, and CR hat for A)	Ornamental plants including non-bearing fruit/nut trees (field grown, nursery)		20	0.513	7.32×10^{-3}	683
	Pome fruits Stone fruits Small Fruit Vine Climbing Subgroup, Except Fuzzy Kiwifruit		20	0.54	7.71×10^{-2}	649
Backpack Sprayer (SL + CR gloves for M/L/A)	Caneberries Bushberries Low growing berries	1586.94	0.3	0.48	2.86×10^{-3}	1750
	Greenhouse crops; Outdoor ornamentals including non-bearing fruit/nut trees (field grown, nursery)		0.15	0.384	1.14×10^{-3}	4376
	Indoor ornamentals (greenhouse, shadehouse, indoor plants and plantscapes) Non-bearing fruit trees (shadehouse, outdoor)		0.15	0.513	1.53×10^{-3}	3276
	Pome fruits Stone fruits Small Fruit Vine Climbing Subgroup, Except Fuzzy Kiwifruit		0.3	0.54	3.21×10^{-3}	1559
Manually-pressurized handwand (SL + CR	Greenhouse crops; Outdoor ornamental plants including non-bearing fruit/nut trees	309.34	0.15	0.384	2.23×10^{-4}	22339

Exposure scenario	Target	Unit exposure (µg/kg ai handled)[1]	ATPD (ha/day)[2]	Rate (kg ai/ha)	Daily exposure (mg/kg bw/day)[3]	MOE[4]
gloves for M/L/A)	(field grown, nursery)					
	Caneberries Bushberries Low growing berries		0.3	0.48	5.57×10^{-4}	8980
	Indoor ornamentals (greenhouse, shadehouse, indoor plants and plantscapes)		0.15	0.513	2.98×10^{-4}	16804
	Pome fruits Stone fruits Small Fruit Vine Climbing Subgroup, Except Fuzzy Kiwifruit		0.3	0.54	6.25×10^{-4}	7996.66
Mechanically-pressurized handgun (Coveralls and CR gloves for M/L/A)	Greenhouse crops; Outdoor ornamental plants including non-bearing fruit/nut trees (field grown, nursery)	837.99	3.8	0.384	1.53×10^{-2}	327
Mechanically-pressurized handgun (CR coveralls and CR gloves for M/L/A)	Indoor ornamentals (greenhouse, shadehouse, indoor plants and plantscapes)	662.60	3.8	0.513	1.61×10^{-2}	310
Mechanically-pressurized handgun (CR coveralls, CR gloves and respirator for M/L/A)	Pome fruits Stone fruits CSG13-07F	526.70	7.6	0.54	2.70×10^{-2}	300 when restricted to 12 L product handled per day
	Caneberries Bushberries Low growing berries			0.48	2.40×10^{-2}	301 when restricted to

Exposure scenario	Target	Unit exposure (µg/kg ai handled)[1]	ATPD (ha/day)[2]	Rate (kg ai/ha)	Daily exposure (mg/kg bw/day)[3]	MOE[4]
						12 L product handled per day
Right-of-way Sprayer (Open mix/load; SL and CR gloves for M/L/A)	Rights-of-way, easements	255.79	3.8	0.384	4.67×10^{-3}	1072

[1] Unit exposure based on AHETF/PHED.
[2] Default Area Treated per Day (ATPD) table (updated on 2017-09-20). For handheld equipment, volume in L/day was converted to ATPD using the minimum recommended spray volumes of 500 L/ha for all berries and orchard crops, 1000 L/ha for indoor/greenhouse ornamentals and greenhouse crops, and 250 L/day for cucurbits and fruiting vegetables. The spray volumes were used to divide the volume applied per day as per the ATPD table (150 L/day for backpack sprayers and manually-pressurized handwands, and 3800 L/day for mechanically-pressurized handguns) as applicable.
[3] Daily exposure = ([Unit exposure × 28% DA] × ATPD × Rate) / (80 kg bw × 1000 µg/mg)
[4] Based on NOAEL = 5 mg/kg bw/day, target MOE = 300.

Table 10 Summary of fenazaquin dislodgeable foliar residue (DFR) values

Apples		
Location	Pennsylvania	Idaho
Actual peak residue	0.403 µg/cm^2 on Day 0	1.095 µg/cm^2 on Day 0
% DFR on Day 0 based on the rates of each application	8%	21%
Equation of the linear regression	y = -0.1742x – 1.413	Not calculated as results were not considered reliable due to unacceptable field recoveries.
Coefficient of determination (R^2)	0.93	
Correlation coefficient (R)	-0.96	
% dissipation per day[1]	16%	
Slope	-0.1742	
Half-life[2]	4.0 days	
Grapes		
Location	New York	California
Actual peak residue	0.451 µg/cm^2 on Day 0	1.080 µg/cm^2 on Day 0.3 (1.015 µg/cm^2 on Day 0)
% DFR on Day 0 based on the rates of each application	8.9%	20.5%
Equation of the linear regression	y = -0.1295x – 0.908	y = -0.3028x + 0.5225
Coefficient of determination (R^2)	0.9607	0.9561
Correlation coefficient (R)	-0.98	-0.88
% dissipation per day[1]	12.1%	19.1%
Slope	-0.1295	-0.3028
Half-life[2]	5.4 days	2.3 days

Apples		
Location	Pennsylvania	Idaho
Squash		
Location	Pennsylvania	California
Actual peak residue	1.093 µg/cm^2 on Day 0	0.769 µg/cm^2 on Day 0
% DFR on Day 0 based on the rates of each application	20%	15%
Equation of the linear regression	y = -0.2197x – 0.9154	y = -0.5007x – 0.4365
Coefficient of determination (R^2)	0.9001	0.9926
Correlation coefficient (R)	-0.95	-1.00
% dissipation per day[1]	20%	39%
Slope	-0.2197	-0.5007
Half-life[2]	3.2 days	1.4 days
Sweet Corn		
Location	Pennsylvania	Oregon
Actual peak residue	1.144 µg/cm^2 on Day 0	0.468 µg/cm^2 on Day 0.3 (0.310 µg/cm^2 on Day 0)
% DFR on Day 0 based on the rates of each application	22.6%	9.3%
Equation of the linear regression	y = -0.3971x + 0.323	y = -0.1482x – 1.2611
Coefficient of determination (R^2)	0.9147	0.8684
Correlation coefficient (R)	-0.85	-0.92
% dissipation per day[1]	32.8	9.9%
Slope	-0.3971	-0.1482
Half-life[2]	1.7	4.7 days

[1] % dissipation per day = $(1 - e^{slope}) \times 100$
[2] Half-life = - LN 2 ÷ slope

Table 11 Postapplication dermal exposure and risk estimates for fenazaquin

Postapplication activity	**Peak DFR (µg/cm^2)[1]**	**Transfer coefficient (cm^2/hr)[2]**	**Dermal exposure (mg/kg bw/day)[3]**	**MOE[4]**	**REI[5]/PHI**
Caneberries (CSG13-07A) and Bushberries (CSG13-07B)					
Harvesting	0.1730	1400	6.8×10^{-3}	737	7 days
Hand set irrigation	0.4267	1750	2.1×10^{-2}	309	2 days
All other activities		1100	1.3×10^{-2}	380	12 hours
Low Growing Berry Subgroup (CSG13-07G)					
Harvesting	0.4022	1100	1.2×10^{-2}	404	1 day
Hand set irrigation	0.4464	1750	2.2×10^{-2}	313	3 days
All other activities		230	2.9×10^{-3}	1739	12 hours
Fruiting Vegetables (CG8-09)					
Harvesting	0.3265	1100	1.01×10^{-2}	497	3 days
Hand set irrigation	0.4464	1750	2.2×10^{-2}	313	3 days
All other activities		230	2.9×10^{-3}	1739	12 hours

Postapplication activity	Peak DFR (µg/cm²)[1]	Transfer coefficient (cm²/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI[5]/PHI
Cucurbit Vegetables (CG9)					
Harvesting	0.5530	550	8.5×10^{-3}	587	3 days
Hand set irrigation	1.080	1750	5.3×10^{-3}	360	6 days
All other activities		230	7.0×10^{-3}	719	12 hours
Small Fruit Vine Climbing Subgroup (CSG13-07F)					
Hand harvesting of grapes	0.1949	8500	4.5×10^{-2}	303	15 days
Mechanical harvesting of grapes and hand harvesting of all vine climbing berries		1400	7.6×10^{-3}	655	7 days
Girdling/turning of table grapes	0.4806	19 300	2.6×10^{-1}	329	22 days
Tying and training; leaf pulling by hand		8500 (grapes)	1.1×10^{-1}	303	15 days
Hand set irrigation		1750	2.4×10^{-1}	313	3 days
All other activities		640	8.6×10^{-3}	581	12 hours
Pome Fruit (CG11-09) and Stone Fruit (CG12-09); Non bearing ornamental trees (field and nursery grown)					
Harvesting	0.5424	1400	2.1×10^{-2}	323	10 days
Thinning fruit by hand	1.134	3000	9.5×10^{-2}	315	17 days
Scouting, hand pruning and training		580	1.8×10^{-2}	302	1 day
All other activities		230	7.3×10^{-3}	686	12 hours
Outdoor ornamental plants; Established outdoor ornamental landscape plantings; Ornamental plants in rights-of-way and other easements; Ornamental plants in recreational sites (such as campgrounds, golf courses, parks, athletic fields)					
Cut flowers: hand harvesting, disbudding, hand pruning	0.3571	4000	4.0×10^{-2}	319	**9 days Not agronomically feasible**
Hand set irrigation		1750	1.8×10^{-2}	317	1 day
All other activities		1100	1.1×10^{-2}	455	12 hours
Greenhouse ornamental plants; Shadehouse plants; Indoor plants and Interiorscapes					
Cut flowers: hand harvesting,	1.3389	4000	1.5×10^{-1}	324	**10 days Not**

Postapplication activity	Peak DFR (µg/cm²)[1]	Transfer coefficient (cm²/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI[5]/PHI
disbudding, hand pruning					**agronomically feasible**
All other activities		230	8.6×10^{-3}	580	12 hours
Greenhouse tomatoes, peppers and cucumbers					
Harvesting; all other activities	1.5845	1400	6.2×10^{-2}	304	**41 days Not agronomically feasible**

[1] Calculated using the following:

- Caneberries, bushberries and small vine climbing berries except fuzzy kiwifruit: the DFR values of 8.9% dislodgeable on the day of application and 12% dissipation per day from the grape DFR study.
- Low growing berries and fruiting vegetables: the DFR values of 9.3% dislodgeable on the day of application and 9.9% dissipation per day from the sweet corn DFR study.
- Cucurbit vegetables: the DFR values of 20% dislodgeable on the day of application and 20% dissipation per day from the squash DFR study.
- Pome and stone fruits and ornamental trees: the DFR values of 21% dislodgeable on the day of application from the apple DFR study and the standard value of 10% dissipation per day.
- Outdoor ornamental plants; established outdoor ornamental landscape plantings; ornamental plants in rights-of-way and other easements; ornamental plants in recreational sites (such as campgrounds, golf courses, parks, athletic fields): values of 9.3% dislodgeable on the day of application and 9.9% dissipation per day from the sweet corn study.
- Greenhouse vegetables and indoor and greenhouse ornamentals: standard indoor values of 25% dislodgeable on the day of application and 2% dissipation per day.

[2] Transfer coefficients obtained from PMRA Agricultural TCs Table (07.29.2020).
[3] Exposure = (Peak DFR [µg/cm²] × TC [cm²/hr] × 8 hours × 28% dermal absorption) / (80 kg bw × 1000 µg/mg)
[4] Based on a NOAEL of 5 mg/kg bw/day, target MOE = 300.
[5] Minimum REI is 12 hours to allow residues to dry and vapours to dissipate.

Table 12 Public exposure and risk estimates for fenazaquin on day 0 after the last application from treated ornamental trees and plants in residential, commercial and industrial areas

Scenario	Life stage	DFR[1] (µg/cm²)	Weight unit conversion factor (mg/µg)	Transfer coefficient[2] (cm²/hr)	Exposure time (hr)	Dermal exp.[3] (mg/kg bw/day)	Dermal MOE[4]
Gardens and Retail plants	Adult (>16 years)	0.468	0.001	1700	1	2.8×10^{-3}	1796
	Children (6 <11 yrs)			930	0.5	1.9×10^{-3}	2626
Trees	Adult (>16 years)	1.095		1700	1	6.5×10^{-3}	767

	Children (6 <11 yrs)			930	0.5	4.5×10^{-3}	1122
Indoor plants	Adult (>16 years)	1.283		220	1	9.9×10^{-4}	5063
	Children (6 <11 yrs)			120	0.5	6.7×10^{-4}	7426

[1] Calculated using the Gardens and Trees SOP Dermal Postapplication Calculator and an application rate of 384 g a.i./ha for outdoor gardens, trees and retail plants and of 513 g a.i./ha for indoor plants (including greenhouse and shadehouse cultivated plants, indoor plants and plantscapes in residences, commercial buildings and shopping malls) and the following values:

- For gardens and retail plants: values from the sweet corn DFR study of 9.3% retained on the day of application and 9.9% dissipation per day.
- For ornamental trees grown outdoors in fields or nurseries: values of 21% retained on the day of application from the apple DFR study and the standard default of 10% dissipation per day.
- For indoor plants (without DFR): standard 25% retained on the day of application and 2% dissipation per day.

[2] Transfer coefficients as per the Review of USEPA Residential SOPs (2012), Section 4: Gardens and Trees.
[3] Exposure = (Peak DFR [µg/cm^2] × TC [cm^2/h] × 8 hours × 28% dermal absorption) / (kg bw [80 kg, adults; 32 kg youth] × 1000 µg/mg).
[4] Based on a dermal NOAEL of 5 mg/kg bw/day, target MOE = 300.

Table 13 Public exposure and risk estimates for fenazaquin on day 0 after the last application from treated rights-of-way, easements and recreational areas

Scenario	Life stage	DFR[1] (µg/cm^2)	Weight unit conversion factor (mg/µg)	Transfer coefficient[2] (cm^2/hr)	Exposure time (hr)	Dermal exp.[3] (mg/kg bw/day)	Dermal MOE[4]
Public in rights-of-way, easements and recreational areas	Adult (>16 years)	0.950	0.001	1100	2	7.3×10^{-3}	684
	Children (6 <11 yrs)			605	2	1.01×10^{-2}	497

[1] Calculated using an application rate of 384 g a.i./ha and the default 25% dislodgeable on the day of application and 10% dissipation per day.
[2] Transfer coefficients for "scouting" for each subpopulation.
[3] Exposure = (Peak DFR [µg/cm^2] × TC [cm^2/h] × 8 hours × 28% dermal absorption) / (kg bw [80 kg, adults; 32 kg youth] × 1000 µg/mg).
[4] Based on a dermal NOAEL of 5 mg/kg bw/day, target MOE = 300.

Table 14 Aggregate public exposure and risk estimates for fenazaquin on day 0 after the last application from treated ornamental trees and plants in residential, commercial and industrial areas

Scenario	Life stage	Exposure source[1]	Exposure (mg/kg bw/day)	Calculated MOE[2]	Aggregate MOE[3]
Gardens and Retail Plants	Adult (>16 years)	Dietary	8.0×10^{-4}	6250	1395
		Dermal	2.8×10^{-3}	1796	
	Children (6 <11 yrs)	Dietary	8.0×10^{-4}	6250	1849
		Dermal	1.9×10^{-3}	2626	
Trees	Adult (>16 years)	Dietary	8.0×10^{-4}	6250	683
		Dermal	6.5×10^{-3}	767	
	Children (6 <11 yrs)	Dietary	8.0×10^{-4}	6250	951
		Dermal	4.5×10^{-3}	1122	
Indoor plants	Adult (>16 years)	Dietary	8.0×10^{-4}	6250	2797
		Dermal	9.9×10^{-4}	5063	
	Children (6 <11 yrs)	Dietary	8.0×10^{-4}	6250	3394
		Dermal	6.7×10^{-4}	7426	

1 Dermal exposure values from Table 6.
2 MOE = NOAEL ÷ Exposure; based on a dermal and chronic dietary NOAEL of 5 mg/kg bw/day for both adults and children.
3 Aggregate (total) margin of exposure = $MOE_{Aggregate} = 1/(1/MOE_{Oral} + 1/MOE_{Dermal})$; the target MOE is 300.

Table 15 Aggregate public exposure and risk estimates for fenazaquin on day 0 after the last application from treated ornamental trees and plants in rights-of-way, easements and recreational sites

Scenario	Life stage	Exposure source[1]	Exposure (mg/kg bw/day)	Calculated MOE[2]	Aggregate MOE[3]
Public in rights-of-way, easements and recreational areas	Adult (>16 years)	Dietary	8.0×10^{-4}	6250	617
		Dermal	7.3×10^{-3}	684	
	Children (6 <11 yrs)	Dietary	8.0×10^{-4}	6250	460
		Dermal	1.01×10^{-2}	497	

1 Dermal exposure values from Table 7.
2 MOE = NOAEL ÷ Exposure; based on a dermal and chronic dietary NOAEL of 5 mg/kg bw/day for both adults and children.
3 Aggregate (total) margin of exposure = $MOE_{Aggregate} = 1/(1/MOE_{Oral} + 1/MOE_{Dermal})$; the target MOE is 300.

Table 16 Residue analysis

Analytical methods	Matrix	Analyte	Method ID [Type]	LOQ	Reference
Plant Commodities					
Enforcement Method	Corn grain, tomato, almond, lemon, mint	Fenazaquin	Ricerca 024119-1 [HPLC-MS/MS]	0.01 ppm	PMRA# 2962744
Data-Gathering Method	Orange, mandarin [whole fruit]	Fenazaquin	DowElanco ERC 94.15 [GC-MS]	0.01 ppm	PMRA# 2962794
	Orange, mandarin, lemon [flesh and peel]	Fenazaquin	DowElanco ERC 91.17 [GC-MS]	0.01 ppm	PMRA# 2962794
	Orange, lemon [juice]	Fenazaquin	DowElanco ERC 92.20 [GC-MS]	0.01 ppm	PMRA# 2962794
	Marmalade	Fenazaquin	DowElanco ERC 93.4 [GC-MS]	0.01 ppm	PMRA# 2962794
	Orange oil, water-soluble orange oil, molasses	Fenazaquin	Dow Elanco ERC 93.2 [GC-MS]	0.01 ppm [water-soluble orange oil and molasses]; 0.10 ppm [orange oil]	PMRA# 2962794
	Apple [whole fruit]	Fenazaquin	DowElanco ERC 91.9 [GC-MS]	0.01 ppm	PMRA# 2962794
	Pear [whole fruit]	Fenazaquin	DowElanco ERC 92.34 [GC-MS]	0.01 ppm	PMRA# 2962794
	Apple [puree and pomace]	Fenazaquin	DowElanco 92.4 [GC-MS]	0.01 ppm	PMRA# 2962794

Analytical methods	Matrix	Analyte	Method ID [Type]	LOQ	Reference
	Apple [juice]	Fenazaquin	DowElanco 92.5 [HPLC-UV]	0.01 ppm	PMRA# 2962794
ILV of Enforcement Method	Almond, tomato and corn	Fenazaquin	Ricerca 024119-1 [HPLC-MS/MS]	0.01 ppm	PMRA# 2962745
Radiovalidation	Corn stover	Fenazaquin	Ricerca 024119-1 [HPLC-MS/MS]	N/A	PMRA# 2962743

Table 17 Integrated food residue chemistry summary

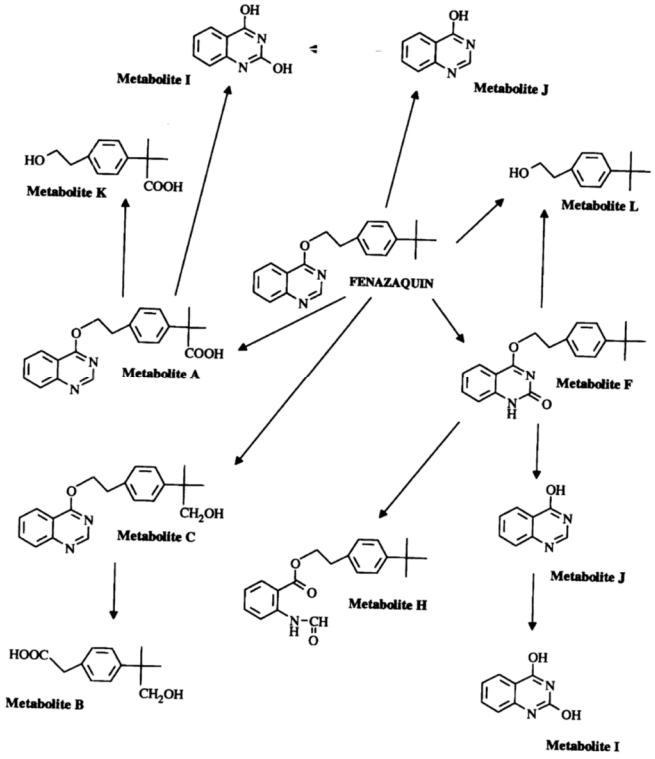
Nature of the residue in grapes	PMRA# 2962533 (or 2962783)
Radiolabel Position	[^{14}C-quinazoline phenyl]-fenazaquin (specific activity: 64.3 µCi/mg; 7.7748 Bq/mol); [^{14}C-*tert*-butyl-phenyl]-fenazaquin (specific activity: 26.6 µCi/mg; 3.2164 Bq/mol)
Test Site	Conducted outdoors at the Nimes field station in France. A plastic sheet was placed under the grape vines (Cabernet Sauvignon variety) to be treated. Each bunch of grapes or any area of the vines to be sprayed was enclosed in a plastic bag to eliminate drift of radioactive treatment emulsion. A small slit was made in each bag to allow for the insertion of the sprayer nozzle. Vines for each radiolabelled test substance and for each of the application timings were in different rows. The vines were bottom irrigated in addition to normal precipitation.

Treatment	A single application of the test substance was made to run-off to grape bunches or branches using a spray gun. Two different application timings were tested: • early application stage, approximately 2–3 weeks after the end of flowering (growth stage BBCH 68). The approximate size of the berries was between 3–6 mm in diameter. • late application stage, approximately 9–10 weeks after the end of flowering (growth stage BBCH 72). The approximate size of the berries was between 10–15 mm in diameter. Translocation Experiment: To assess whether fenazaquin and/or any of its degradation products may be translocated within the grape vine, a number of branches were sprayed and grape bunches were sampled from the same vines as the treated branches. Results indicated that the treated branches had approximately 10 mg/kg equivalents of fenazaquin. The grape bunches, however, had no detectable levels of radioactivity, thereby confirming that translocation from sprayed leaves to the fruit did not occur.		
Total Rate	15 g a.i./hL for each application timing; 150 g a.i./hL for the late season application timing to aid in residue identification.		
Formulation	Emulsifiable concentrate (EC)		
Harvest	Early application: Grape bunches were sampled at random at 0 days after treatment (DAT) (in other words, within 24 hours of spraying), at 49-DAT, and at normal harvest (76-DAT). Late application: Grape bunches were harvested at 0- and 28-DAT.		
Extraction solvent	Grape bunches were washed sequentially with 10% methanol:water, 100% dichloromethane and 100% methanol. Grape bunches were extracted with acetonitrile:water (9:1; v/v), and partitioned with ethyl acetate, and with hexane and 5% aqueous solution of sodium bicarbonate (0-DAT early application).		
Matrices	PHI (days)	[^{14}C-quinazoline] %TRR	[^{14}C-phenyl] %TRR
Early season application (2–3 weeks after flowering)			
Surface washes (Total)	0	80.9	77.5
	49	43.5	60.3
	76	29.3	33.7
Grape bunches	0	19.1	22.5
	49	56.5	39.7
	76	70.7	66.3
Late season application (9–10 weeks after flowering)			
Surface washes	28	61.3	71.4

Grape bunches	28	38.7		28.6		
Summary of major identified metabolites in grape matrices						
Radiolabel Position	Early season application [PHI = 49 days]		Early season application [PHI = 76 days]		Late season application [PHI = 28 days]	
	[^{14}C-quinazoline]	[^{14}C-phenyl]	[^{14}C-quinazoline]	[^{14}C-phenyl]	[^{14}C-quinazoline]	[^{14}C-phenyl]
Grape bunches (including surface wash)	Fenazaquin	Fenazaquin; Fenazaquin alcohol [Metabolite C]	Fenazaquin; Dihydroxyquinazoline [Metabolite I]	Fenazaquin	Fenazaquin	Fenazaquin

Proposed metabolic scheme in grapes

Photolysis is likely a key process by which residues of fenazaquin may be broken down. The cleavage products formed either remain on the surface or penetrate into the grapes where further transformations may occur. A large proportion of these cleavage products may become associated with the natural constituents of the grapes in the bound residue fraction.



Nature of the residue in oranges	**PMRA# 2962528, 2962531**
Radiolabel Position	[^{14}C-quinazoline phenyl]-fenazaquin (specific activity: 19.8 µCi/mg as received; isotopically diluted to 2.1 µCi/mg); [^{14}C-*tert*-butyl-phenyl]-fenazaquin (specific activity: 26.6 µCi/mg; isotopically diluted to 2.1 µCi/mg) Each formulated radioactive test substance was diluted with water to a final concentration of 400 ppm.
Test Site	Five bearing Valencia orange trees located in Fresno, California were used. Separate trees were treated with each radiolabeled fenazaquin test substance (2 trees per radiolabel). The remaining untreated tree was used for the control. Rainfall was supplemented with irrigation as needed. The trees were enclosed in a wooden, plastic-lined structure and the ground under the trees was covered with plastic sheeting to minimize ground contamination.
Treatment	Single foliar spray application of the test substance. Two different application timings were tested: • Early season application when immature fruit were 3.2 cm in diameter (191 days prior to harvest); and • Late season application 2 months before harvest to mature unripe fruit 6.5 cm in diameter (63 days prior to harvest). In order to determine the role of photolysis, nine oranges treated with a late season application were wrapped in muslin cloth immediately after the spray solution had dried.
Total Rate	450 g a.i./ha
Formulation	Emulsifiable concentrate (EC)
Harvest	Early season application: Fruit were collected immediately after the treatment solution dried (0-DAT), in addition to 28-, 112- and 191-DAT. Late season application: Fruit were collected 0-, 19- and 63-DAT. Samples of wrapped fruit (3 oranges) were removed for residue analysis 9-, 19- and 63-DAT for comparison with radioactive residues present in unwrapped fruit. Whole fruits were collected for surface washes, subsequent homogenization and total sample analysis, and for separation into peel and pulp (early and late season applications).

Extraction solvents	Oranges were washed sequentially with 10% methanol in water, dichloromethane and 100% methanol. The 10% methanol washes that contained sufficient radioactivity were partitioned with ethyl acetate after removal of the methanol. Oranges were extracted with acetonitrile, and partitioned with ethyl acetate.		
Matrices	PHI (days)	[^{14}C-quinazoline]-fenazaquin TRR (ppm)	[^{14}C-phenyl]-fenazaquin TRR (ppm)
Early season application			
Unwashed fruit	0	2.603	2.049
Surface washes		2.444	1.854
Washed fruit		0.158	0.197
Unwashed fruit	28	0.835	0.700
Surface washes		0.182	0.163
Washed fruit		0.653	0.537
Unwashed fruit	112	0.331	0.381
Surface washes		0.026	0.055
Washed fruit		0.305	0.326
Unwashed fruit	191	0.323	0.361
Surface washes		0.039	0.078
Washed fruit		0.284	0.283
Late season application			
Unwashed fruit	0	0.547	0.504
Surface washes		0.528	0.491
Washed fruit		0.019	0.014
Unwashed fruit	19	0.757	0.531
Surface washes		0.659	0.476
Washed fruit		0.098	0.055
Unwashed fruit	63	0.903	0.451
Surface washes		0.592	0.344
Washed fruit		0.311	0.107
Late season application (wrapped fruit)			
Unwashed fruit	9	0.839	0.480
Surface washes		0.816	0.456
Washed fruit		0.023	0.024
Unwashed fruit	19	0.894	0.617
Surface washes		0.830	0.584
Washed fruit		0.064	0.033
Unwashed fruit	63	0.566	0.178
Surface washes		0.503	0.163
Washed fruit		0.063	0.015
Early season application			
Whole fruit	191	0.270	0.356

Peel		0.231	0.338
Pulp		0.039	0.018
Late season application			
Whole fruit	63	0.484	0.676
Peel		0.471	0.670
Pulp		0.013	0.006

Summary of major identified metabolites in orange matrices

Radiolabel Position	Early season application [PHI = 191 days]		Late season application [PHI = 63 days]	
	[^{14}C-quinazoline]-fenazaquin	[^{14}C-phenyl]-fenazaquin	[^{14}C-quinazoline]-fenazaquin	[^{14}C-phenyl]-fenazaquin
Whole oranges (including surface wash)	Fenazaquin	Fenazaquin	Fenazaquin	Fenazaquin
Peel	Fenazaquin	Fenazaquin	N/A	N/A
Pulp	None	None	N/A	N/A
Unwrapped fruit	N/A	N/A	Fenazaquin	Fenazaquin
Wrapped fruit	N/A	N/A	Fenazaquin	Fenazaquin

Proposed metabolic scheme in oranges

The data indicate that fenazaquin is the major residue in/on citrus fruits, and that residues are largely confined to the fruit peel. Hydroxylation of fenazaquin was the major pathway, yielding Metabolite 1 (2-hydroxy-fenazaquin). The minimal amount of degradation of fenazaquin that occurred in/on wrapped fruits suggests that photolysis of surface residues plays an important role in the degradation of fenazaquin residues on the fruit surface.

Nature of the residue in apples (1992 Study)	**PMRA# 2962535, 2962530**
Radiolabel Position	[^{14}C-quinazoline phenyl] (specific activity: 19.8 µCi/mg); [^{14}C-*tert*-butyl phenyl] (specific activity: 26.6 µCi/mg) Prior to spraying, each radiolabeled test substance was isotopically diluted to a final specific activity of 3.0 µCi/mg.
Test Site	The study was conducted outdoors using four semi-dwarf Golden Delicious apple trees. Prior to spraying, a 3 m x 3 m area under each tree was covered with plastic and a plastic walled wooden enclosure (3 m x 3 m x 3 m) was erected around each tree. This was done to prevent spray drift and to minimize soil contamination. Equal portions of the spray solution were applied from each of the four sides of the tree through small cuts made in the plastic walls. Immediately following the application, the plastic enclosure was cut open to allow ventilation for drying. When dry (1–2 hours after spraying), all plastic from around each tree was removed.

Treatment	Single foliar spray application. Two application timings were tested: • Early season application: Two trees (one tree per radiolabel) were sprayed when apples were 2–3 cm in size; • Late season application: Two trees (one tree per radiolabel) were sprayed approximately 4–5 weeks prior to harvest when apples were 6-7 cm in size and were nearly mature. In order to study the effect of photolysis, six apples were individually covered 2-3 hours after application with bags made from white muslin cloth.		
Total Rate	450 g a.i./ha		
Formulation	Emulsifiable concentrate (EC)		
Harvest	Apples from the two trees treated with the early season application were harvested 0-, 4-, 7-, 14-, 29-, 57- and 92-DAT. Apples from the two trees treated with the late season application were harvested 0-, 7-, 14-, 28- and 42-DAT. The wrapped apples were harvested at 7- and 14-DAT. Some of the mature apples collected from each tree were separated into peel and pulp (peeled fruit).		
Extraction solvents	Apples were sequentially washed with hexane, chloroform and methanol. Following the methanol wash, apples were peeled. Apple peel samples were extracted with dichloromethane, acetonitrile:water (75:25, v/v) and ethyl acetate. Apple pulp samples were extracted with acetonitrile:water (75:25, v/v), and partitioned with dichloromethane and ethyl acetate.		
Matrices	PHI (days)	[^{14}C-quinazoline]-fenazaquin %TRR	[^{14}C-phenyl]-fenazaquin %TRR
Early season application			
Surface wash (total)	0	94.0	95.7
	4	81.8	90.9
	7	69.9	64.6
	14	54.0	57.6
	29	49.2	54.6
	57	33.4	36.4
	92 [mature]	29.4	32.5
Peel	0	6.1	4.3
	4	15.7	8.0
	7	27.5	32.2

	14	40.4	37.0
	29	50.8	36.2
	57	53.4	49.3
	92 [mature]	55.9	52.5
Pulp	0	-	-
	4	2.5	1.0
	7	2.6	3.3
	14	5.7	5.5
	29	6.9	9.2
	57	13.3	14.2
	92 [mature]	14.7	15.0
Late season application			
Surface wash	0	98.8	99.1
	7	73.8	81.4
	14	60.0	69.9
	28	47.8	53.0
	42 [mature]	40.0	49.3
Peel	0	1.1	0.8
	7	22.4	16.8
	14	32.9	25.4
	28	39.7	37.3
	42 [mature]	50.3	40.1
Pulp	0	0.1	<0.1
	7	3.8	1.9
	14	7.0	4.8
	28	12.5	9.7
	42 [mature]	9.7	10.6
Late season application (wrapped fruit; phenyl label only)			
Surface wash	0	-	99.1
	7	-	98.0
	14	-	96.1
Peel	0	-	0.8
	7	-	1.6
	14	-	2.6
Pulp	0	-	<0.1
	7	-	0.4
	14	-	1.3

Early season application			
Peel	92	0.802	0.653
Pulp		0.029	0.026
Whole apples		0.161	0.136
Late season application			
Peel	42	2.473	1.919
Pulp		0.063	0.050
Whole apples		0.489	0.367

Summary of Major Identified Metabolites in Apple Matrices				
Radiolabel Position	Early season application [PHI = 92 days]		Late season application [PHI = 42 days]	
	[^{14}C-quinazoline]-fenazaquin	[^{14}C-phenyl]-fenazaquin	[^{14}C-quinazoline]-fenazaquin	[^{14}C-t-phenyl]-fenazaquin
Apple peel	Fenazaquin	Fenazaquin	Fenazaquin	Fenazaquin
Apple pulp	None	None	None	None

Nature of the residue in apples (1997 Study)	**PMRA# 2962529, 2962534, 2962536**
Radiolabel Position	[^{14}C-quinazoline phenyl]-fenazaquin (specific activity: 88.89 µCi/mg); [^{14}C-*tert*-butyl-phenyl]-fenazaquin (specific activity: 23.87 µCi/mg)
Test Site	Apple trees (*Malus pumila* cv Golden Delicious), approximately 5-year old bushes, were potted in containers using compost and cultivated in a glass house. After approximately 4 months, the pots were transferred to an outside fruit cage.
Treatment	Fenazaquin was applied as a directed spray to the apple fruit and to run-off. Each group of trees was enclosed in polyethylene during spraying to prevent spray drift between the groups. The early season application was made when the average fruit diameter was approximately 2.5 cm; the late season application was made five weeks later. There were nine different treatment groups designated Groups A to I: • Groups A (phenyl-label) and B (quinazoline-label): 5 trees each received the early application at the low rate; • Groups C (phenyl-label) and D (quinazoline-label): 4 trees each received the early application at the high rate; • Groups E (phenyl-label) and F (quinazoline-label): one tree each received the late application at the low rate; • Groups G (phenyl-label) and H (quinazoline-label): one tree each received the late application at the high rate; and

	• Group I (photolysis experiment; phenyl-label): one tree received the late application at the low rate. Following treatment, the fruit were enclosed with aluminum foil-covered plastic plant pots, the open end being covered with mesh to exclude light, but allow some air exchange.		
Total Rate	Low application rate: 3.3 g a.i./hL; High application rate: 13.3 g a.i./hL		
Formulation	Suspension concentrate (SC)		
Harvest	• Early season application: On the day of application (1-2 hours after application), 7-, 14- and 28-DAT, and at maturity (105-DAT). • Late season application: On the day of application (1.5-2.5 hours after application) and at maturity (70-DAT). • Photolysis experiment: 14-DAT. Apples were washed with solvent (see below), and the washed fruit was peeled.		
Extraction solvent	Each fruit sample was washed sequentially with hexane:chloroform (1:1 v/v; Wash 1) and methanol (Wash 2). Peel and pulp samples were extracted with acetonitrile:water (1:1; v/v).		
Matrices	PHI (days)	[^{14}C-quinazoline]-fenazaquin TRR (ppm)	[^{14}C-phenyl]-fenazaquin TRR (ppm)
Early season application (3.3 g a.i./hL)			
Wash 1	0	0.342	0.340
Wash 2		0.020	0.019
Peel		0.005	0.004
Pulp		0.001	0.001
Whole fruit		0.369	0.364
Wash 1	7	0.114	0.115
Wash 2		0.012	0.012
Peel		0.026	0.014
Pulp		0.005	0.004
Whole fruit		0.158	0.145
Wash 1	14	0.079	0.063
Wash 2		0.005	0.003
Peel		0.033	0.013
Pulp		0.005	0.003
Whole fruit		0.122	0.082
Wash 1	28	0.021	0.017
Wash 2		0.022	0.001
Peel		0.018	0.013
Pulp		0.004	0.003

Whole fruit		0.045	0.033
Wash 1	105 [mature]	0.002	0.002
Wash 2		<0.001	<0.001
Peel		0.006	0.002
Pulp		0.002	0.001
Whole fruit		0.010	0.005
Early season application 13.3 g a.i./hL			
Wash 1	0	0.948	1.099
Wash 2		0.059	0.044
Peel		0.015	0.015
Pulp		0.004	0.002
Whole fruit		1.026	1.160
Wash 1	7	0.462	0.443
Wash 2		0.050	0.045
Peel		0.082	0.049
Pulp		0.013	0.011
Whole fruit		0.607	0.547
Wash 1	14	0.309	0.356
Wash 2		0.019	0.017
Peel		0.087	0.047
Pulp		0.019	0.011
Whole fruit		0.434	0.433
Wash 1	28	0.120	0.095
Wash 2		0.006	0.009
Peel		0.071	0.031
Pulp		0.017	0.010
Whole fruit		0.214	0.146
Wash 1	105 [mature]	0.012	0.018
Wash 2		0.001	0.001
Peel		0.022	0.016
Pulp		0.006	0.012
Whole fruit		0.040	0.048
Late season application (3.3 g a.i./hL)			
Wash 1	0	0.158	0.200
Wash 2		0.003	0.004
Peel		0.004	0.004
Pulp		0.002	0.002
Whole fruit		0.166	0.210
Wash 1	70 [mature]	0.017	0.016
Wash 2		0.001	0.001
Peel		0.018	0.011
Pulp		0.004	0.003
Whole fruit		0.040	0.030

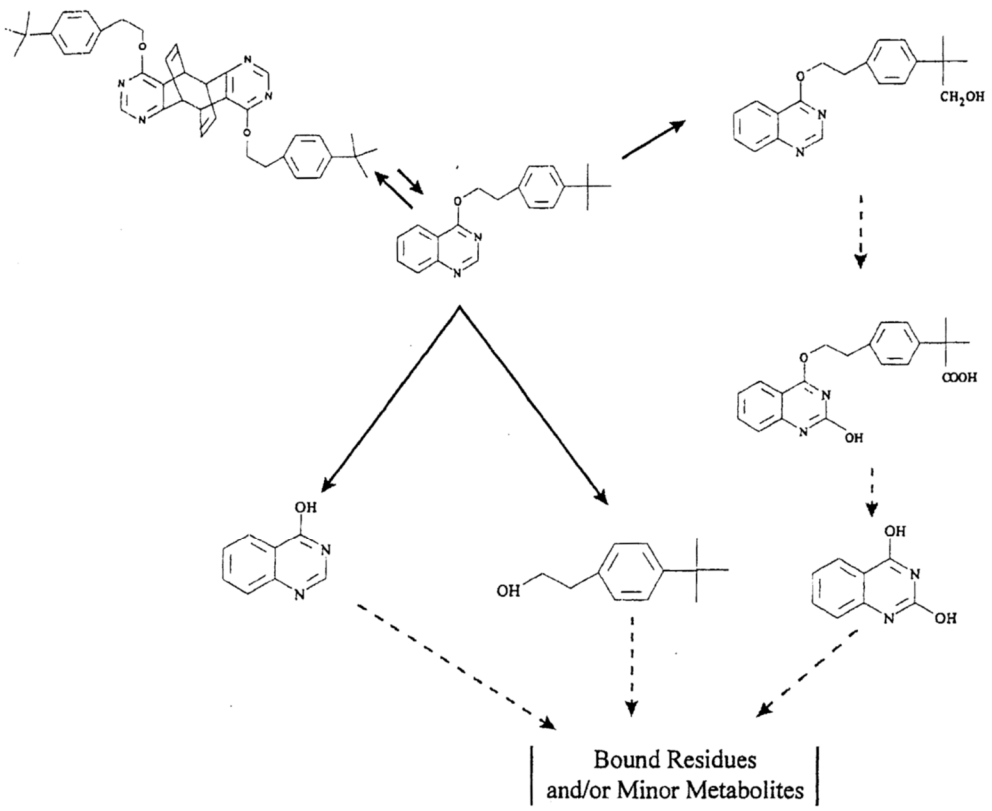
Late season application (13.3 g a.i./hL)			
Wash 1	0	0.774	0.874
Wash 2		0.017	0.019
Peel		0.017	0.019
Pulp		0.015	0.013
Whole fruit		0.823	0.925
Wash 1	70 [mature]	0.076	0.067
Wash 2		0.004	0.003
Peel		0.066	0.038
Pulp		0.021	0.011
Whole fruit		0.168	0.120
Photolysis experiment: Late season application (3.3 g a.i./hL)			
Wash 1	14 [mature]	N/A	0.120
Wash 2		N/A	0.003
Peel		N/A	0.007
Pulp		N/A	0.002
Whole fruit		N/A	0.131
Note: The TRR in whole fruit was calculated as the sum of the TRR in the washes, peel and pulp.			

Summary of Major Identified Metabolites in Apple Matrices		
Radiolabel Position	[^{14}C-quinazoline]-fenazaquin	[^{14}C-phenyl]-fenazaquin
Early season application (3.3 g a.i./hL; PHI = 105 Days)		
Hexane:Chloroform (wash 1)	None	Fenazaquin; Fenazaquin dimer
Methanol (wash 2)	None	None
Peel	None	None
Pulp	None	None
Early season application (13.3 g a.i./L; PHI = 105 days)		
Hexane:Chloroform (wash 1)	Fenazaquin; Fenazaquin dimer	Fenazaquin; Fenazaquin dimer
Methanol (wash 2)	None	None
Peel	None	None
Pulp	None	None
Late season application (3.3 g a.i./hL; PHI = 70 Days)		
Hexane:Chloroform (wash 1)	Fenazaquin	Fenazaquin; Fenazaquin dimer
Methanol (wash 2)	None	None
Peel	None	None
Pulp	None	None
Late season application (13.3 g a.i./hL; PHI = 70 Days)		
Hexane:Chloroform (wash 1)	Fenazaquin; Fenazaquin dimer	Fenazaquin; Fenazaquin dimer
Methanol (wash 2)	None	None

Peel	None	None
Pulp	None	None
Late season application – wrapped fruit (3.3 g a.i./hL; PHI = 14 Days)		
Hexane:Chloroform (wash 1)	N/A	Fenazaquin
Methanol (wash 2)	N/A	None
Peel	N/A	None
Pulp	N/A	None

Proposed metabolic scheme in apples

The primary pathway of metabolism of fenazaquin occurs in the first 7-14 days and is the result of photolysis. Cleavage of the ether linkage in fenazaquin results in production of photoproducts which are incorporated into the peel and pulp. Fenazaquin was the primary residue in the surface solvent washes. A dimer of fenazaquin was also observed. In the peel and in the pulp of washed apples, Metabolite I (dihydroxyquinazoline), Metabolite J (4-hydroxyquinazoline) and Metabolite C/L (2,4-TBPE) were also seen.

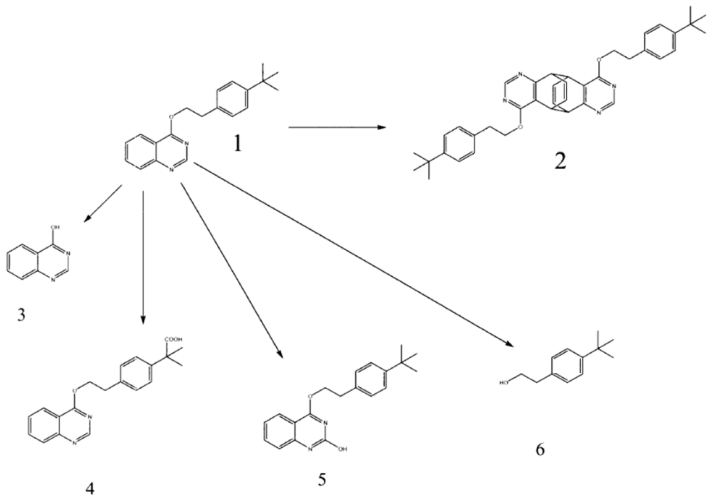


Nature of the residue in corn			**PMRA# 2962537**
Radiolabel Position	[^{14}C-quinazoline phenyl]-fenazaquin (specific activity: 3.20×10^8 dpm/mg, 5.33 MBq/mg; isotopically diluted to 1.50×10^8 dpm/mg, 2.50 MBq/mg); [^{14}C-*tert*-butyl-phenyl]-fenazaquin (specific activity: 3.66×10^8 dpm/mg, 6.10 MBq/mb; isotopically diluted to 1.49×10^{-8} dpm/mg, 2.48 MBq/mg).		
Test Site	Field corn (Hybrid 66P 32 variety) was grown from seed outdoors in above ground wooden boxes filled with sandy loam soil. Plot 1 was an untreated control plot, Plot 2 was treated once with [^{14}C-quinazoline]-fenazaquin and Plot 3 was treated once with [^{14}C-phenyl]-fenazaquin. All the plots were 1 m x 1 m and approximately 36 cm deep. The interior of each wooden box was lined with a heavy gauge plastic liner. Each plot contained two rows spaced approximately 69 cm apart. There were between 18 and 20 plants per row which were spaced 8 cm apart. The control plot was located more than 61 m from the treated plots. Plastic sheeting approximately 2.1 m high was erected all around the plot to block wind. All plastic barriers were removed after each application.		
Treatment	Single postemergence foliar treatment when the corn plants were at the milk stage of development.		
Total Rate	[^{14}C-quinazoline]-label: 549 g a.i./ha; [^{14}C-phenyl]-label: 556 g a.i./ha		
Formulation	Suspension concentrate (SC)		
Harvest	Mature whole ears and stover were collected 20 days after treatment. The husks were removed from the ears of corn. The cobs after removal of the grain were not added to the stover sample.		
Extraction solvents	Corn grain and stover samples were extracted with acetonitrile:water (1:1; v/v) and acetonitrile. The corn grain extracts were partitioned with hexane and acetonitrile.		
Matrices	PHI (days)	[^{14}C-quinazoline phenyl]-fenazaquin	[^{14}C-t-butyl phenyl]-fenazaquin
		TRR (ppm)	TRR (ppm)
Grain	20	0.013	0.003
Cobs		0.012	0.010
Corn ears*		0.013	0.005
Stover		6.544	6.434
*Calculated as weighted average of the TRR in grain + cobs. Note: The nature of the radioactive residues in phenyl-labelled grain, and phenyl- and quinazoline-labeled cobs was not further investigated due to the low levels of radioactivity.			

Summary of major identified metabolites in field corn matrices		
Radiolabel position	[^{14}C-quinazoline phenyl]-fenazaquin	[^{14}C-t-butyl phenyl]-fenazaquin
Field corn grain	Fenazaquin	N/A
Field corn stover	Fenazaquin; Fenazaquin dimer	Fenazaquin; Fenazaquin dimer

Proposed metabolic scheme in field corn

The major route of transformation is conversion to the fenazaquin dimer. The presence of the minor metabolites 4-hydroxyquinazoline and 2,4-TBPE suggests cleavage of the ether linkage. The intact fenazaquin has been oxidized on the quinazoline ring to yield an alcohol, or on the *tert*-butyl group to yield a carboxylic acid.



1. Fenazaquin
2. Fenazaquin Dimer, formed via photolysis. Major degradate found in stover.
3. 4-Hydroxyquinazoline
4. Fenazaquin Acid
5. 2-Oxy-fenazaquin
6. 4-*tert*-Butylphenethyl Alcohol

Freezer storage stability in plant matrices				**PMRA# 2962427, 2962751, 2962752, 2962753, 2962754, 2962756, 2962757, 2962758, 3165148, 3165149**	
Tested matrices	**Analyte**	**Tested intervals (days)**	**Temperature (°C)**	**Demonstrated stability (days)**	**Category**
Whole apple	Fenazaquin	0, 65, 147, 197, 352 and 435	≤-15	435	High-water

Whole apple	Fenazaquin	1, 104, 178, 245 and 798	-20	798	
Whole pear	Fenazaquin	0, 237, 411, 414 and 1034	-20	1034	
Corn forage	Fenazaquin	0, 91, 183, 268, 353, 515 and 764	-25 to -10	353	
Whole tomato	Fenazaquin	0, 45, 105, 197, 282, 367, 529 and 778	-25 to -10	778	
Field corn grain	Fenazaquin	0, 45, 105, 197, 281, 367, 529 and 756	-25 to -10	756	High-starch
Almond nutmeat	Fenazaquin	0, 105, 197, 281, 367, 529 and 756	-25 to -10	No discernible trend	High-oil
Mint leaves	Fenazaquin	0, 105, 197, 281, 367, 529 and 756	-25 to -10	756	
Orange pulp	Fenazaquin	0, 77 and 399	-27 to -15	399	High-acid
Field corn stover	Fenazaquin	0, 105, 197, 282, 367, 529 and 756	-25 to -10	778	Not classified
Orange peel	Fenazaquin	0, 89 and 371	-27 to -15	371	Not classified

Crop field trials and residue decline on fruting vegetables Crop Group 8-09 – Representative commodities are tomato (standard size and one cultivar of small size); bell pepper and one cultivar of nonbell pepper; and one cultivar of small nonbell pepper	**PMRA# 2962797**

Crop field trials were conducted in 2008. For tomatoes (fresh, processing and cherry varieties), trials were conducted in North American growing regions 1 (1 trial), 2 (1 trial), 3 (2 trials), 5 (1 trial) and 10 (7 trials including 1 small cultivar and 1 processing variety) for a total of 12 trials. For peppers, trials were conducted in North American growing regions 2 (1 trial; bell pepper), 3 (1 trial; bell pepper), 5 (1 trial; bell pepper), 6 (1 trial; bell pepper), 8 (1 trial; chilli pepper) and 10 (4 trials; 2 bell pepper and 2 chilli pepper) for a total of 9 trials (6 bell and 3 non-bell). GWN-1708, a suspension concentrate formulation of fenazaquin, was applied once as foliar spray at a rate of 493–594 g a.i./ha. Tomato and pepper samples were harvested at maturity 2-3 days after treatment. In order to assess residue decline, additional samples were collected 0-, 7- and 14-DAT (days after treatment).

A non-ionic surfactant was used at all field trial sites. Foliar applications were made using ground equipment with concentrate spray volumes. A sufficient number of trials were conducted with fenazaquin in North America in the principal growing regions for fruiting vegetables. Independence of trials was assessed for each representative crop. Residue decline data show that residues of fenazaquin decreased in tomatoes with increasing preharvest intervals (PHIs). For peppers (bell), the residue decline data were relatively constant over the sampling period. Adequate storage stability data are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total application rate (g ai/ha)	PHI (days)	Analyte	Residue levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Tomato [Standard + cherry]	504-594	3	Fenazaquin	12[1]	0.027	0.186[2]	0.049	0.058	0.043
Bell pepper	493-515	2-3	Fenazaquin	6	0.017	0.118	0.056	0.063	0.033
Nonbell pepper [Chilli pepper]	504	3	Fenazaquin	3	0.082	0.186	0.124	0.131	0.052
Bell + nonbell peppers	493-515	2-3	Fenazaquin	9	0.017	0.186	0.079	0.086	0.050

n = number of independent trials. LAFT = Lowest average field trial. HAFT = Highest average field trial. SDEV = Standard deviation.

[1] Includes 11 trials with standard tomato varieties and one trial with cherry tomatoes.

[2] The HAFT was from the cherry tomato field trial.

Crop field trials and residue decline on cucurbit vegetables Crop Group 9 – Representative commodities are cucumber, muskmelon and summer squash	**PMRA# 2962782**

Crop field trials were conducted in 2008. For zucchini, trials were conducted in North American growing regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (1 trial) and 10 (1 trial) for a total of 5 trials. For cantaloupe, trials were conducted in North American growing regions 2 (1 trial), 5 (1 trial), 6 (1 trial) and 10 (3 trials) for a total of 6 trials. For cucumber, trials were conducted in North American growing regions 2 (2 trials), 3 (1 trial), 5 (2 trials), 6 (1 trial) for a total of 6 trials. GWN-1708, a suspension concentrate formulation of fenazaquin, was applied once as foliar spray at a rate of 493–519 g a.i./ha. Cantaloupe, cucumber and zucchini were harvested at maturity 3 days after treatment at all sites.

A non-ionic surfactant was used at all field trial sites. Foliar applications were made using ground equipment with concentrate spray volumes. A sufficient number of trials were conducted with fenazaquin in North America in the principal growing regions for cucurbit vegetables. Independence of trials was assessed for each representative crop. Adequate storage stability data are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total application rate (g ai/ha)	PHI (days)	Analyte	Residue levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Cantaloupe	493-509	3	Fenazaquin	6	0.020	0.145	0.060	0.071	0.043
Cucumber	498-519	3	Fenazaquin	6	0.030	0.165	0.053	0.067	0.050
Zucchini	504-511	3	Fenazaquin	5	0.040	0.130	0.075	0.076	0.034

n = number of independent trials. LAFT = Lowest average field trial. HAFT = Highest average field trial. SDEV = Standard deviation.

Crop field trials and residue decline on pome fruits Crop Group 11-09 – Representative commodities apple and pear	**PMRA# 2962779**

Crop field trials were conducted in 2008. For apples, trials were conducted in North American growing regions 1 (3 trials), 2 (1 trial), 5 (2 trials), 9 (1 trial), 10 (1 trial) and 11 (4 trials) for a total of 12 trials. For pears, trials were conducted in North American growing regions 1 (1 trial), 10 (2 trials) and 11 (3 trials) for a total of 6 trials. GWN-1708, a suspension concentrate formulation of fenazaquin, was applied once as foliar spray at a rate of 495–528 g a.i./ha. Samples of pear and apple were harvested at maturity 7 days after treatment. In order to assess residue decline, additional apple samples were collected 0-, 3-, 9/10- and 14-DAT.

A non-ionic surfactant was used at all field trial sites. Foliar applications were made using ground equipment with dilute and concentrate spray volumes. A sufficient number of trials were conducted with fenazaquin in North America in the principal growing regions for pome fruits. Independence of trials was assessed for each representative crop. Residue decline data show that residues of fenazaquin generally decreased in apples with increasing PHIs.

Adequate storage stability data are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total application rate (g ai/ha)	PHI (days)	Analyte	Residue levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Apple	495–528 [Concentrate and dilute sprays]	7	Fenazaquin	12	<0.01	0.15	0.070	0.072	0.045
Pear	504–513 [Concentrate and dilute sprays]	7	Fenazaquin	6	0.12	0.28	0.190	0.192	0.064

n = number of independent trials. LAFT = Lowest average field trial. HAFT = Highest average field trial. SDEV = Standard deviation. N/A = Not applicable. For computation of the LAFT, HAFT, median, mean and standard deviation, values <LOQ are assumed to be LOQ.

Crop field trials and residue decline on stone fruits
Crop Group 12-09 – Representative commodities – sweet or tart cherry, peach and plum or prune

PMRA# 2962799

Crop field trials were conducted in 2008 and 2009. For cherries (sweet and tart), trials were conducted in North American growing regions 5 (3 trials; 2 tart and 1 sweet), 10 (1 trial; sweet) and 11 (2 trials; sweet and tart) for a total of 6 trials (4 sweet; 2 tart). For peaches, trials were conducted in North American growing regions 1 (1 trial), 2 (3 trials), 5 (1 trial), 6 (1 trial), 10 (3 trials) for a total of 9 trials. For plums, trials were conducted in North American growing regions 5 (1 trial), 10 (4 trials, including one trial with a plum prune variety) and 12 (1 trial) for a total of 6 trials. GWN-1708, a suspension concentrate formulation of fenazaquin, was applied once as foliar spray at a rate of 482–526 g a.i./ha. Samples of cherries, peaches and plums were harvested at maturity 3 days after treatment. In order to assess residue decline, additional cherry, peach and plum samples were collected 0-, 7- and 12 to 14-DAT.

A non-ionic surfactant was used at all field trial sites. Foliar applications were made using ground equipment with dilute and concentrate spray volumes. A sufficient number of trials were conducted with fenazaquin in North America in the principal growing regions for stone fruits. Independence of trials was assessed for each representative crop. Residue decline data show that residues of fenazaquin decreased in cherries, peach and plums with increasing PHIs. Adequate storage stability data are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total application rate (g ai/ha)	PHI (days)	Analyte	Residue levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Cherry	504 [Concentrate and dilute sprays]	3	Fenazaquin	6	0.255	0.914	0.522	0.587	0.246
Peach	482-560 [Concentrate and dilute sprays]	3	Fenazaquin	9	0.203	0.885	0.378	0.408	0.230
Plum	504-526 [Concentrate and dilute sprays]	3	Fenazaquin	6	<0.01	0.235	0.140	0.121	0.094

n = number of independent trials. LAFT = Lowest average field trial. HAFT = Highest average field trial. SDEV = Standard deviation.
For computation of the LAFT, HAFT, median, mean and standard deviation, values <LOQ are assumed to be LOQ.

Crop field trials and residue decline on fruting berries and small fruits **Crop subgroup 13-07A Caneberries – Representative commodity raspberry** **Crop subgroup 13-07B Bushberries – Representative commodity highbush blueberry** **Crop subgroup 13-07F Small fruits vine climbing, except fuzzy kiwifruit - Representative commodity grape** **Crop subgroup 13-07F Low growing berries – Representative commodity strawberry**	**PMRA# 2962772 (or 2962781), 2962773, 2962777**

Crop field trials were conducted in 2008 and 2009. For blueberries, trials were conducted in North American growing regions 1 (1 trial), 2 (2 trials), 5 (2 trials) and 12 (1 trial) for a total of 6 trials. For raspberries, trials were conducted in North American growing regions 1 (1 trial), 5 (1 trial) and 12 (3 trials) for a total of 5 trials. For strawberries, trials were conducted in North American growing regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (1 trial), 10 (3 trials) and 12 (1 trial) for a total of 8 trials. For grapes, trials were conducted in North American growing regions 1 (2 trials), 10 (8 trials) and 11 (2 trials) for a total of 12 trials. GWN-1708, a suspension concentrate formulation of fenazaquin, was applied once as foliar spray at a rate of 493-526 g a.i./ha. Samples were harvested at maturity at 6–7 days after treatment for raspberries, blueberries and grapes, and 1 day after treatment for strawberries. In order to assess residue decline, additional blueberry and raspberry samples were collected 0-, 10-, and 14-DAT, and additional strawberry samples were collected 0-, 7- and 10-DAT.

A non-ionic surfactant was used at all field trial sites. Foliar applications were made using ground equipment with dilute and concentrate spray volumes. The number and geographic distribution of trials were generally in accordance with Health Canada's DIR98-02. Independence of trials was assessed for each representative crop. Residue decline data show that residues of fenazaquin decreased in blueberries, raspberries and strawberries with increasing PHIs. Adequate storage stability data are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total application rate (g ai/ha)	PHI (days)	Analyte	Residue levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Raspberry	504–526 [Concentrate and dilute sprays]	7	Fenazaquin	5	0.178	0.362	0.184	0.230	0.078
Blueberry	504–515 [Concentrate and dilute sprays]	6-7	Fenazaquin	6	0.171	0.411	0.248	0.270	0.083
Strawberry	493–515 [Concentrate spray]	1	Fenazaquin	8	0.078	1.165	0.488	0.524	0.311
Grape	497–514 [Concentrate]	7	Fenazaquin	12	0.045	0.33	0.19	0.191	0.107

n = number of independent trials. LAFT = Lowest average field trial. HAFT = Highest average field trial. SDEV = Standard deviation.

Crop field trials and residue decline on citrus fruits
Crop Group 10 (Revised)
Representative commodities – Orange, lemon and grapefruit

PMRA# 2962423

Crop field trials were conducted in 2008 and 2009. For oranges, trials were conducted in North American growing regions 3 (8 trials), 6 (1 trial) and 10 (3 trials) for a total of 12 trials. For lemons, trials were conducted in North American growing regions 3 (1 trial) and 10 (4 trials) for a total of 5 trials. For grapefruits, trials were conducted in North American growing regions 3 (3 trials), 6 (1 trial) and 10 (2 trials) for a total of 6 trials. GWN-1708, a suspension concentrate formulation of fenazaquin, was applied once as foliar spray at a rate of 500–533 g a.i./ha. Samples of citrus fruits were harvested at maturity 7-8 days after treatment. In order to assess residue decline, additional orange samples were collected 1, 3, 10 and 14-DAT.

A non-ionic surfactant or crop oil concentrate was used at all field trial sites. Foliar applications were made using ground equipment with dilute and concentrate spray volumes. The number and geographic distribution of trials were in accordance with current regulatory guidelines in the United States. Independence of trials was assessed for each representative crop. Residue decline data show that residues of fenazaquin generally decreased in oranges

with increasing PHIs. Adequate storage stability data are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Note: Residues of fenazaquin in samples of flesh from each of the citrus fruits trials were <LOQ (<0.01 ppm). As such, only the data from analysis of the whole fruit are included in the table below.

Crop	Total application rate (g ai/ha)	PHI (days)	Analyte	Residue levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Whole orange	500-533 [Concentrate and dilute spray volumes]	7–8	Fenazaquin	12	0.07	0.23	0.125	0.134	0.048
Whole lemon	500-513 [Concentrate and dilute spray volumes]	7	Fenazaquin	5	0.02	0.12	0.080	0.074	0.043
Whole grapefruit	502-513 [Concentrate and dilute spray volumes]	7	Fenazaquin	6	0.03	0.14	0.055	0.072	0.045

n = number of independent trials. LAFT = Lowest average field trial. HAFT = Highest average field trial. SDEV = Standard deviation.

Processed food and feed - Apple — **PMRA# 2962796, 2962809, 2962810, 2962811, 2962812, 2962813, 2962814, 2962815**

A processing study was conducted in the United Kingdom using the end-use product EF 1127 SC, a suspension concentrate formulation of fenazaquin, at 300 g ai/ha in/on apples. Adequate storage stability data are available on diverse crop types to support the storage intervals of the processed food and feed. Samples were analyzed using a validated analytical method.

RAC	Processed fractions	HAFT[RAC] (ppm)	Median processing factor	Anticipated residues of fenazaquin (ppm)
Apple	Puree	0.15	0.67×	0.10
	Pomace		2×	0.30
	Juice		0.33×	0.05

Processed food and feed - Orange — **PMRA# 2962423**

A processing study was conducted in a representative North American growing region using GWN-1708, a suspension concentrate formulation of fenazaquin, at 2.53 kg ai/ha in/on oranges. Adequate storage stability data are available on diverse crop types to support the storage intervals of the processed food and feed. Samples were analyzed using a validated analytical method.

RAC	Processed Fractions	HAFT[RAC] (ppm)	Median processing factor	Anticipated residues of fenazaquin (ppm)
Orange	Juice	0.23	<0.01×	<0.01
	Dried pulp		0.18	0.041
	Oil		79×	18.2

Processed food and feed - Plum **PMRA# 2962799**

A processing study was conducted in a representative North American growing region using GWN-1708, suspension concentrate formulation of fenazaquin, at 2.50 kg ai/ha in/on plums. Adequate storage stability data are available on diverse crop types to support the storage intervals of the processed food and feed. Samples were analyzed using a validated analytical method.

RAC	Processed fractions	HAFT[RAC] (ppm)	Median processing factor	Anticipated residues of fenazaquin (ppm)
Plum	Prunes	0.235	4.8×	1.1

Processed food and feed - Grape **PMRA# 2962795**

A processing study was conducted in France using Magister 200SC, a suspension concentrate formulation of fenazaquin, at 0.995–1.04 kg ai/ha in/on grapes. Adequate storage stability data are available on diverse crop types to support the storage intervals of the processed food and feed. Samples were analyzed using a validated analytical method.

RAC	Processed fractions	HAFT[RAC] (ppm)	Median processing factor	Anticipated residues of fenazaquin (ppm)
Grapes	Wine	0.33	<0.02×	<0.01
	Juice		0.14×	0.046
	Raisins		2.3×	0.759

Processed food and feed - Tomato **PMRA# 2962797**

A processing study was conducted in a North American growing region using GWN-1708, a suspension concentrate formulation of fenazaquin, at 2.54 kg ai/ha in/on tomatoes. Adequate storage stability data are available on diverse crop types to support the storage intervals of the processed food and feed. Samples were analyzed using a validated analytical method.

RAC	Processed fractions	HAFT[RAC] (ppm)	Median processing factor	Anticipated residues of fenazaquin (ppm)
Tomatoes	Sauce	0.186	0.49×	0.091
	Paste		1.0×	0.186

Confined accumulation in rotational crops – Lettuce, radish and wheat **PMRA# 2962532**

Radiolabel Position	[^{14}C-quinazoline] (specific activity as supplied: 0.144 mCi/mg, 3.20 × 10^8 dpm/mg; isotopically diluted to 1.5 × 10^8 dpm/mg; 2.5 MBq/mg); [^{14}C-*tert*-butyl-phenyl] (specific activity as supplied: 0.165 mCi/mg, 3.66 × 10^8 dpm/mg; isotopically diluted to 1.5 × 10^8 dpm/mg; 2.5 MBq/mg).		
Treatment			
Test Site	Outdoors in above-ground wooden boxes filled with soil. The boxes had a surface area of 0.5 m^2 and a soil column depth of approximately 15 cm.		
Soil Type	Sandy loam		
Treatment	Bare soil was treated at a target rate of 505 g ai/ha, and aged for 30, 120 and 365 days. The actual rates ranged from 550-554 g a.i./ha		
Formulation	Liquid formulation		
Extraction solvents	All three PBIs of the wheat straw and grain were allowed to soak for 17–22 hours in water (refrigerated) prior to initiation of the extraction procedures, except for the 365-day straw. Acetonitrile:water (1:1; v/v) and acetonitrile; partition with dichloromethane		
Matrices	**PBI (days)**	**[^{14}C-quinazoline] TRR (ppm)**	**[^{14}C-phenyl] TRR (ppm)**
Immature lettuce	30	0.050	0.055
	120	0.043	0.035
	365	0.004	0.007
Mature lettuce	30	0.056	0.067
	120	0.044	0.034
	365	0.012	0.008
Radish roots	30	0.104	0.095
	120	0.047	0.055
	365	0.008	0.011
Radish tops	30	0.030	0.028
	120	0.020	0.021
	365	0.007	0.016
Wheat forage	30	0.037	0.044
	120	0.067	0.029
	365	0.009	0.129
Wheat hay	30	0.125	0.185
	120	0.100	0.079
	365	0.013	0.189
Wheat straw	30	0.116	0.243
	120	0.128	0.104

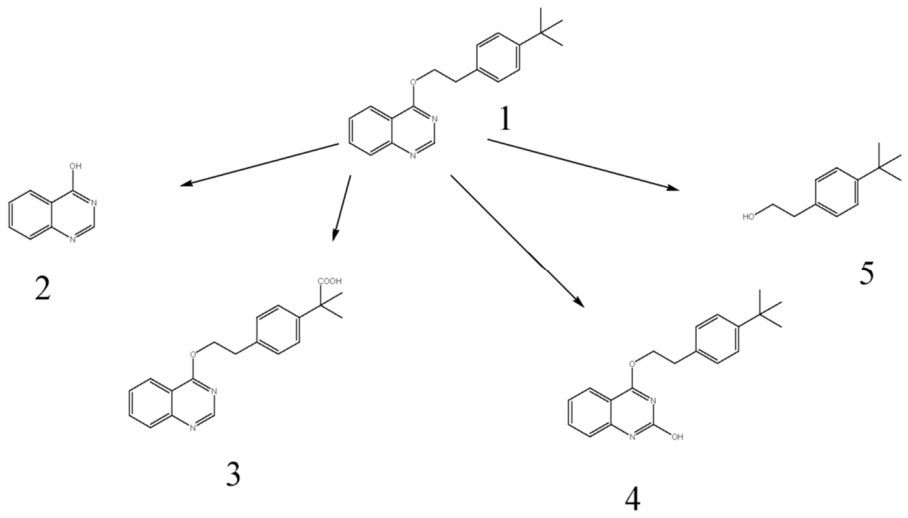
	365	0.025	0.187
Wheat grain	30	0.047	0.069
	120	0.045	0.039
	365	0.010	0.017

Summary of major identified metabolites in rotated crops

Plantback Intervals (PBI)	1st Rotation (30-day PBI)		2nd Rotation (120-day PBI)		3rd Rotation (365-day PBI)	
Radiolabel Position	[^{14}C-quinazoline]	[^{14}C-phenyl]	[^{14}C-quinazoline]	[^{14}C-phenyl]	[^{14}C-quinazoline]	[^{14}C-phenyl]
Immature lettuce	None	None	None	None	None	None
Mature lettuce	None	None	None	None	None	None
Radish roots	Fenazaquin	Fenazaquin	Fenazaquin; 4-hydroxyquinazoline	Fenazaquin	None	None
Radish tops	None	None	None	None	None	None
Wheat forage	None	None	4-hydroxyquinazoline	None	None	None
Wheat hay	None	None	4-hydroxyquinazoline	None	None	None
Wheat straw	None	None	None	None	None	None
Wheat grain	None	None	None	None	None	None

Proposed metabolic scheme in rotational crops

Fenazaquin can be cleaved at the oxygen bridge of the *tert*-butyl phenyl and quinazoline rings to form the two alcohols 4-hydroxyquinazoline and 2,4-TBPE. Fenazaquin can also be oxidized on the *tert*-butyl group to give fenazaquin acid or on the quinazoline ring to give 2-oxyfenazaquin. The large percentages of radioactive residue extracted in the aqueous phases and shown to consist of multiple components, each of which has low concentration, indicated extensive degradation of fenazaquin when applied to the soil and taken up by succeeding crops.



1. Fenazaquin
2. 4-Hydroxyquinazoline
3. Fenazaquin Acid
4. 2-Oxy Fenazaquin
5. 4-*tert*-Butylphenyl alcohol

Table 18 Food residue chemistry overview of metabolism studies and risk assessment

Plant studies	
Residue definition for enforcement **Primary crops (list crops)** **Rotational crops**	Fenazaquin
Residue definition for risk assessment **Primary crops** **Rotational crops**	Fenazaquin
Metabolic profile in diverse crops	The profile in diverse crops cannot be determined because only fruit and cereal crops were investigated.

Dietary risk from food and drinking water			
	Population	**Estimated risk % of acute reference dose (ARfD)**	
		Food alone	**Food and drinking water**
Refined (intermediate level) acute dietary exposure analysis, 95th percentile **ARfD = 0.02 mg/kg bw** **Estimated acute drinking water concentration = 0.0093 ppm**	All infants <1 year	44.4	45.9
	Children 1–2 years	56.3	57.4
	Children 3–5 years	41.1	41.9
	Children 6–12 years	23.1	23.9
	Youth 13–19 years	12.6	13.7
	Adults 20–49 years	21.7	22.8
	Adults 50+ years	17.1	18.3
	Females 13–49 years	15.8	16.8
	Total population	22.3	23.6

	Population	**Estimated risk % of acceptable daily intake (ADI)**	
		Food alone	**Food and drinking water**
Refined (intermediate level) chronic (non-cancer and cancer) dietary exposure analysis **ADI = 0.02 mg/kg bw/day** **Estimated chronic drinking water concentration = 0.0045 ppm**	All infants <1 year	5.3	7.0
	Children 1–2 years	9.3	9.9
	Children 3–5 years	6.5	7.0
	Children 6–12 years	3.2	3.6
	Youth 13–19 years	2.0	2.3
	Adults 20–49 years	4.0	4.5
	Adults 50+ years	3.3	3.8
	Females 13–49 years	2.6	3.0
	Total population	3.8	4.2

Table 19 Major chemical fate inputs for water modelling

Parameter	Fenazaquin	4-quinazolinol[1]	2,4-TBPE[1]	2-oxy-fenazaquin[1]	Fenazaquin propionic acid[1]
Molecular weight (g/mol)	306.4	146.15	178.28	322.41	338.41
Vapour pressure (mm Hg) at 25°C	1.42×10^{-9}	1.43×10^{-4}	3.35×10^{-4}	1.84×10^{-9}	4.46×10^{-10}
Solubility (mg/L) in water at pH 7	0.102	1.24×10^{4}	195.3	0.567	5.23
Henry's law constant (unitless)	2.29×10^{-7}	9.06×10^{-8}	1.64×10^{-5}	5.63×10^{-8}	1.55×10^{-9}
Photolysis at 40°N latitude (days)	48[2]	Stable	Stable	Stable[3]	Stable[3]
Hydrolysis at pH 7 at 20°C (days)	168[2]	Stable	71.1	Stable[3]	Stable[3]
Aerobic aquatic half-life at 20°C (days)	5.5, 173[2]	10	Stable[3]	104	Stable
Anaerobic aquatic half-life	Stable[3]	Stable[3]	Stable[3]	Stable[3]	Stable[3]
Aerobic soil half-life at 20°C (days)	33.4-251[2]	0.08[4]	0.16[4]	22.9-205	12.2-19.2
K_{oc} (L/kg)	25964[2]	190[4]	141[4]	72430[4]	814.9

[1] Part of residue definition for drinking water only. Residue definition for environmental risk assessment was parent fenazaquin only.
[2] Photolysis: longer of two values; hydrolysis: only one value; aerobic aquatic half-life: longer of two values used for environmental risk assessment, both values used for drinking water modelling; aerobic soil half-life: 90th percentile confidence bound on the mean of five values; K_{oc}: 20th percentile of four values
[3] Assumed stable due to lack of data
[4] Taken from EFSA review (PMRA# 3074403)

Table 20 Level 1 EECs for the Combined Residue of Fenazaquin, 4-Quinazolinol, 2,4 TBPE, 2-Oxy-fenazaquin, and Fenazaquin Propionic Acid in Potential Sources of Drinking Water, Reported as Parent Equivalent

Use pattern	Groundwater (µg a.i./L)		Surface water (µg a.i./L)		
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]	Overall[5]
One application of 539.15 g a.i./ha	2×10^{-5}	2×10^{-5}	9.3	4.5	3.8

[1] 90th percentile of daily concentrations
[2] 90th percentile of 365-day moving average concentrations
[3] 90th percentile of the highest 1-day average concentration from each year
[4] 90th percentile of yearly average concentrations
[5] Average of all yearly average concentrations

Table 21 Fate and behaviour of fenazaquin in the environment

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
Abiotic transformation					
Hydrolysis	Fenazaquin (quinazoline-^{14}C-labelled) pH 5, 7, and 9 at 25°C Study duration: 3 days (pH 5) or 34 days (pH 7, 9)	pH 5 DT_{50} = 9.6 days (SFO) pH 7 DT_{50} = 120 days (SFO) pH 9 DT_{50} = 217 days (SFO)	**Major:** • **4-quinazolinol** • **2,4-TBPE**	Hydrolysis is not expected to be an important route of dissipation for fenazaquin in the environment; however, there is a potential for hydrolysis in more acidic environments.	2962540
	Fenazaquin (unlabelled) pH 5, 7, and 9 at 25, 50 and 70°C Study duration: up to 17 days (pH 5); up to 30 days (pH 7, 9)	**25°C** pH 5 DT_{50} = 6.4 days (SFO) pH 7 DT_{50} = Not determined (stable) pH 9 DT_{50} = Not determined (stable) **50°C** pH 5 DT_{50} = 0.98 days	Not analyzed	Hydrolysis of fenazaquin is both temperature and pH dependant.	3045442

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
		(SFO) pH 7 DT_{50} = 25 days (SFO) pH 9 DT_{50} = 25 days (SFO) **70°C** pH 5 DT_{50} = 0.29 days (SFO) pH 7 DT_{50} = 6.73 days (SFO) pH 9 DT_{50} = 2.36 days (SFO)			
	Fenazaquin (unlabelled) Sterilized and un-sterilized natural water from Florida (FL) (pH 6.7) and Indiana (IN) (pH 7.9), and distilled water control. 25°C Study duration: 30 days	Distilled DT_{50} = 65.4 days (SFO) Sterilized FL DT_{50} = 110 days (SFO) Sterilized IN DT_{50} = Not determined Non-sterilized FL DT_{50} = 82.5 days (SFO) Non-sterilized IN DT_{50} = 187 days (SFO)	Not analyzed	The effect of microbial degradation on the rate of hydrolysis is minimal.	3039016
Phototransformation on soil	Fenazaquin (quinazoline-^{14}C and phenyl-^{14}C-labelled) 25°C	Phototransformation half-life of 26 days in summer sunlight at 40°N latitude.	**Major:** • **4-quinazolinol** • **2,4-TBPE** **Minor:** • **4-*tert*-**	Phototransformation on soil can be an important route of dissipation for fenazaquin in the environment.	3039020

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
	Study duration: 30 days		**butylphenylacetic acid** • **4-*tert*-butylstyrene** • **CO_2**		
Phototransformation in water	Fenazaquin (quinazoline-2-^{14}C-labelled) Buffered solutions at pH 7 and 23°C Study duration: 15 days	Phototransformation half-life of 48 days in summer sunlight at 30–50°N latitude.	**Major:** • **4-quinazolinol** **Minor:** • **CO_2**	Phototransformation in water can be an important route of dissipation for fenazaquin in the environment.	2962541
	Fenazaquin (quinazoline-^{14}C and phenyl-^{14}C-labelled) Distilled water at pH 7.6 and 25°C Study duration: Up to 32 days	Phototransformation half-life of 28 days in summer sunlight at 40°N latitude.	**Major:** • **4-quinazolinol** • **2,4-TBPE** **Minor:** • **4-*tert*-butylstyrene**		2962542
	Various non-guideline studies were conducted with radiolabelled fenazaquin and the transformation product, 4-*tert*-butylstyrene,	In water samples (no sediment), there was a loss of radioactivity observed for the ^{14}C-phenyl irradiated samples which was not observed in the ^{14}C-quinazoline irradiated samples or dark controls. This loss of radioactivity was attributed to the formation of a volatile transformation product; however, no radioactivity was detected in the traps. It was assumed that 4-*tert*-butylstyrene volatilised from the surface water. In the water/sediment systems, fenazaquin partitioned strongly to the sediment phase in both irradiated and			3039019

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
	in natural water and water/sediment systems to investigate whether 4-*tert*-butylstyrene is only formed by photolytic degradation or under conditions where sorption, hydrolysis, photolysis and microbial degradation may be competing.	dark samples. Characterization of the radioactivity in the systems showed only the transformation products, 4-quinazolinol and 2,4-TBPE. No quantitation of compounds was conducted, and the presence of 4-*tert*-butylstyrene in surface water could not be confirmed. The presence of sediment likely reduced the rate of formation of 4-*tert*-butylstyrene due to the extensive partitioning of fenazaquin into the sediment, thus reducing the amount of fenazaquin available in solution for photolysis. In an additional study, fenazaquin was applied to water in a closed system. After 7 days irradiation, 4-*tert*-butylstyrene was present in very low amounts (<1 µg/L). Water samples were also spiked directly with 4-*tert*-butylstyrene to determine its rate of volatilisation. 4-*tert*-butylstyrene was found to have a half-life of approximately 1 hour in water.			
Phototransformation in air	Fenazaquin is not expected to be volatile under field conditions based on its vapour pressure and Henry's law constant. A volatile transformation product of fenazaquin, 4-*tert*-butylstyrene, was detected in laboratory transformation studies, but is expected to be present at very low levels. A phototransformation study in air is not required.				
Biotransformation					
Biotransformation in aerobic soil	Fenazaquin (quinazoline-^{14}C and phenyl-^{14}C-labelled) 1 sandy loam soil (Indiana); pH 7.7; organic matter 1.5%; Study duration: 365 days at 22-	DT_{50} = 60 days (IORE, t_R = 138 days)	Twelve transformation products were identified; however, they were not quantified at each sampling interval (refer to Table 1-6 for their names and chemical structures). NER and CO_2	Fenazaquin is moderately persistent. Biotransformation in aerobic soil can be an important route of dissipation for fenazaquin.	2962543

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
	23°C		up to 25% and 21% AR, respectively.		
	Fenazaquin (phenyl-^{14}C-labelled) 4 soils: • **LUFA Speyer loamy sand (Germany; pH 6.3; 2.3% OC)** • **Marcham sandy clay loam (UK; pH 7.4, 4.3% OC)** • **Jülich clayey silt (Germany; pH 7.0; 1.2% OC)** • **Neustadt silty sand (Germany; pH 6.5; 0.6% OC)** Study duration: 180 days at 20°C	LUFA: DT_{50} = 84 days (SFO) Marcham: DT_{50} = 46 days (IORE, t_R = 66 days) Jülich: DT_{50} = 51 days (IORE, t_R = 89) Neustadt: DT_{50} = 119 days (SFO)	**Major:** none **Minor:** • **2-oxy-fenazaquin** • **fenazaquin propionic acid** • **2-[4-(carboxymethyl)phenyl]-2-methylpropanoic acid** • **2-(4-*tert*-butylphenyl)ethyl 2-(forrnylamino)benzoate** NER and CO_2 up to 27% and 38% AR, respectively.	Fenazaquin is moderately persistent. Biotransformation in aerobic soil can be an important route of dissipation for fenazaquin.	2962544
Biotransformation in anaerobic soil	Fenazaquin (quinazoline-^{14}C and phenyl-^{14}C-labelled) 1 sandy loam soil (Indiana); pH 7.7; organic	DT_{50} = 155 days (SFO)	**Major:** none **Minor:** Up to seventeen compounds could be separated by thin layer chromatography, none exceeding	Fenazaquin is moderately persistent. Biotransformation in anaerobic soil can be an important route of dissipation for fenazaquin.	3039018

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
	matter 1.5% Study duration: 60 days at 22-23°C		7% AR. NER and CO_2 up to 24% and 2% AR, respectively.		
	Fenazaquin (quinazoline-^{14}C and phenyl-^{14}C-labelled) 1 soil (LUFA 2.2 sandy loam; Germany; pH 5.7; 2.2% OC) Study duration: 120 days at 20°C	**Quinazoline label** DT_{50} = 264 days (SFO) **Phenyl label** DT_{50} = 320 days (SFO)	**Major:** • **2,4-TBPE** **Minor:** • **4-quinazolinol** NER and CO_2 up to 13% and 6% AR, respectively.	Fenazaquin is persistent. Biotransformation in anaerobic soil is not an important route of dissipation for fenazaquin.	2962548 and 2962549
Biotransformation in aerobic water systems	Fenazaquin (quinazoline-^{14}C and phenyl-^{14}C-labelled) 2 Test systems: Brown Carrick sandy loam and Auchingilsie clay loam Study duration: 100 days at 20°C	Brown Carrick: DT_{50} = 26 days (DFOP, t_R = 149 days) Auchingilsie: DT_{50} = 144 days (DFOP, t_R = 173 days) Note: All values are for the whole system	**Major:** • **2-oxy-fenazaquin** • **fenazaquin propionic acid** **Minor:** • **4-quinazolinol** • **2-[4-(carboxymethyl)phenyl]-2-methylpropanoic acid** NER and CO_2 up to 16% and 21% AR, respectively.	Fenazaquin is slightly to moderately persistent. Biotransformation in aerobic water systems can be an important route of dissipation for fenazaquin.	2962547

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
Biotransformation in anaerobic water systems	No biotransformation study in anaerobic water systems with fenazaquin was submitted.				
Mobility					
Adsorption / desorption	Fenazaquin (quinazoline-^{14}C-labelled) Values obtained in 4 soils from Texas and Indiana.	K_{oc} ranging from 16 027 to 82 507 L/kg	N/A	Fenazaquin is classified as immobile in soil.	2962551
	EPI Suite estimates for major transformation products	4-Quinazolinol K_{oc}: 102 – 512 L/kg 2,4-TBPE K_{oc}: 268 – 274 L/kg 2-Oxy-fenazaquin K_{oc}: 3422 – 146 200 L/kg Fenazaquin propionic acid K_{OC}: 7388–427 800 L/kg	N/A	Major transformation products of fenazaquin can range from a potential for high mobility to immobile.	N/A – USEPA EPI Suite version 4.1
Soil leaching	Fenazaquin (quinazoline-^{14}C and phenyl-^{14}C-labelled) 3 German aged and unaged soils Study duration: 60	More than 93% AR remained in the upper soil layer (0–5 cm) and radioactivity in the leachate did not exceed 0.3% AR in each soil column. After aging periods	**Major:** none **Minor:** Up to 5 compounds were observed, with only 2-hydroxy-fenazaquin identified, none exceeding 7% AR.	These results indicate that fenazaquin and its transformation products, including soil bound residues, can be considered virtually immobile in the soil column.	2962552

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
	days	of 30 and 60 days, more than 68% AR remained in the upper soil layer (0–5 cm), and radioactivity in the leachate did not exceed 0.5% in each soil column.	NER and CO_2 up to 27% and 31% AR, respectively.		
	Fenazaquin (quinazoline-^{14}C and phenyl-^{14}C-labelled) 2 aged soils from Texas and Indiana Study duration: 30 days	More than 74% AR remained in the upper soil layer (0–6 cm) and radioactivity in the leachate did not exceed 2.45% AR in any soil column. Smaller amounts of radioactivity were detected in lower column segments, with the amount of radioactivity decreasing with increasing depth. Radioactivity in the leachate did not exceed 2.5% in each soil column.	**Major:** none **Minor:** Various compounds were observed, with only 2-hydroxy-fenazaquin and 4-quinazolinol identified, none exceeding 8% AR. NER and CO_2 up to 13% and 7% AR, respectively.		2962553
Volatilization	A volatilization study was not submitted nor required for the review of fenazaquin. Fenazaquin is not expected to be volatile under field conditions based on its vapour pressure (1.9×10^{-7} Pa at 25°C) and Henry's law constant (5.7×10^{-4} Pa·m^3/mol at 25°C). AEROWIN				2962550

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
	predicts that 77 to 95% of fenazaquin in the atmosphere is expected to be sorbed to atmospheric particles. The sorbed fraction may be resistant to atmospheric oxidation. Given the large fraction of fenazaquin expected to be sorbed to atmospheric particles, the AOPWIN program (version 1.90) was not suitable for predicting the atmospheric half-life of fenazaquin, and therefore long range transport potential in the atmosphere could also not be determined.				
Field studies					
Field leaching	Fenazaquin (quinazoline-^{14}C and phenyl-^{14}C-labelled) formulated as an emulsifiable concentrate (EC) Location: Two bare ground sites in Indiana Rate: Broadcast spray of 224 g a.i./ha Study duration: 112 days	Site 1: DT_{50} = 37.7 days (SFO) Site 2: DT_{50} = 33.8 days (SFO) The majority of radioactivity was recovered in the in the upper soil layer (0–7.6 cm), with the amount of radioactivity decreasing with increasing depth (<25% AR in lower segments at any time point).	Transformation products were not analyzed. NER reached up to 79% in the top soil segment (0–7.6 cm). Additional extractions did not substantially increase the extracted radioactivity; however, extraction methods were not exhaustive.	At the sites tested, fenazaquin did not appear to be inherently susceptible to leaching.	2962545
Terrestrial field dissipation	End-use product, GWN-1708, 200 g/L SC Location: Bare ground site in Washington Rate:	Washington: DT_{50} = 14.1 days (SFO) Mean residues of fenazaquin and its transformation products were for the most part not	**Major:** none **Minor:** 2-oxy-fenazaquin and 4-quinazolinol	Fenazaquin is unlikely to accumulate in soil and carry over to the next growing season under the conditions of these studies. Fenazaquin did not appear to be	2962831

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
	Broadcast spray of 560 g a.i./ha Study duration: 270 days	detected below the 15 cm soil depth, or detected at levels below the LOQ (0.01 mg/kg).		inherently susceptible to leaching.	
	End-use product, EF-1127, 200 g/L SC Location: Two bare ground sites in Germany Rate: Broadcast spray of 150 g a.i./ha Study duration: 215-216 days	Site 1 - Nordssheim Westfahlen, Silt loam: DT_{50} = 55.0 days (SFO) Site 2 - Bayern, Sandy loam: DT_{50} = 41.0 days (SFO) Fenazaquin was not detected in soil below the 0-5 cm soil depth at Site 1. At Site 2, fenazaquin was detected at levels below the LOQ (0.005 mg/kg) in the 5-10 cm depth, at each of the last three sampling intervals (92, 155, and 215 days post-treatment).	Transformation products were not analyzed.		2962832
	End-use product, EF-	Site 1 - Lauter, Loamy silt:	Transformation products were		2962835

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
	1127, 200 g/L SC Location: Two bare ground sites in Germany Rate: Broadcast spray of 150 g a.i./ha Study duration: 215-216 days	DT_{50} = 20.7 days (SFO) Site 2 - Landsberg, Silty loam: DT_{50} = <30 days (SFO) Fenazaquin was not detected in soil below the 0–5 cm soil depth at either of the sites.	not analyzed.		
	End-use product, EF-1127, 200 g/L SC Location: Two bare ground sites in Italy Rate: Broadcast spray of 200 g a.i./ha Study duration: 215-216 days	Site 1 - Parma, Loam: DT_{50} = 44.4 days (SFO) Site 2 - Parma, Clay: DT_{50} = 11.0 days (SFO) Fenazaquin was not detected in soil below the 0–10 cm soil depth at Site 1. At Site 2, fenazaquin was detected above the LOQ (0.005 mg/kg) once in the 10–20 cm soil depth, at a mean concentration of 0.011 mg/kg	Transformation products were not analyzed.		2962834

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
		at 13 days and was either not detected or detected at <LOQ at all other sampling times.			
Aquatic field dissipation	No aquatic field dissipation study with fenazaquin was submitted and none is required.				
Bioconcentration / Bioaccumulation					
Bioconcentration in fish	Fenazaquin (quinazoline-^{14}C-labelled) Rainbow trout (*Oncorhynchus mykiss*), were exposed to fenazaquin under flow-through conditions at nominal concentrations of 0.2 and 1.0 µg a.i./L for an uptake period of 28 days, followed by a depuration period of 14 days.	**Low dose:** Maximum BCF = 1073 for whole fish (14 days) Depuration $t_{1/2}$ rate = 0.7 days. **High dose:** Maximum BCF = 1354 for whole fish (7 days) Depuration $t_{1/2}$ rate = 1.4 days Elimination of fenazaquin after 14 days was >98% for both low and high dose.	Transformation products were not measured.	Fenazaquin does not readily bioconcentrate in fish tissue under the conditions of the study.	2962601

[1] DT_{50} and DT_{90} values for each fit are the times the fitted curve reaches 50% and 90%, respectively, of the fitted initial concentration. These values are used for descriptive characterization and persistence classification for soil (Goring *et al.*, 1975) and natural waters (McEwen and Stephenson, 1979). The representative half-life (t_R), is the half-life of an exponential curve that is considered to be a conservative approximation of the measured concentration decline, and is used for exposure modelling. The DT_{50} for the SFO (single first-order) model is t_R if the SFO model is deemed acceptable. The t_R value from DFOP (double first-order in parallel) is a half-life determined from the slow degradation rate from the DFOP model. The t_R value from IORE (indeterminate order rate equation) is the half-life of an exponential curve passing through the

Study type	Test material/test system	Value[1]	Transformation products	Comments	PMRA#
DT_{90} of the IORE model fit. NER: Non-extracted Residues AR: Applied Radioactivity					

Table 22 Toxicity to non-target terrestrial organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Invertebrates					
Earthworm, *Lumbricus terrestris*	14-d Acute	Fenazaquin (technical grade active ingredient, purity 98%)	LC_{50} = 1.93 mg a.i./kg ww soil (mortality) EC_{50} = 0.98 mg a.i./kg ww soil (body weight) NOAEC = 0.044 mg a.i./kg ww soil (mortality)	N/A	2962554
Earthworm, *Eisenia foetida*	14-d Acute	Fenazaquin (technical grade active ingredient, purity 100.2%)	LC_{50} = 25.2 mg a.i./kg dw soil (mortality) EC_{50} > 30 mg a.i./kg dw soil (body weight) NOAEC = 10 mg a.i./kg dw soil (mortality)	N/A	2962555
	14-d Acute	End-use product, EF-1127 200 g/L SC (210 g a.i./L)	LC_{50} = 21.8 mg a.i./kg dw soil or 113 mg EP/kg dw soil (mortality) NOAEC <12.1 mg a.i./kg dw soil or <62.5 mg EP/kg dw soil (body weight)	N/A	2962568
	56-d Chronic	End-use product, Magister 200 SC (208 g a.i./L)	NOAER = 312 g a.i./ha or 1500 mL EP/ha (reproduction rate) LOAER = 624 g a.i./ha or 3000 mL	N/A	2962570

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			EP/ha (reproduction rate) No statistically significant effects on survival or reduction in body weight. There was a statistically significant reduction in reproduction rate (34% less juveniles compared to control) at the highest treatment level of 3000 mL EP/ha (624 g a.i./ha).		
Collembola, *Folsomia candida*	28-d Chronic	End-use product, Pride 200 SC (205 g a.i./L)	NOAEC = 23.0 mg a.i./kg dw soil or 125 mg EP/kg dw soil (mortality) There was a statistically significant effect on mortality at the three highest treatment levels (250, 500, 1000 mg EP/kg dw soil, in other words, 47.0, 94.0, and 188.0 mg a.i./kg dw soil), and a statistically significant reduction in reproduction rate at the highest treatment level.	N/A	2962569
Honey bee, *Apis mellifera*	**Acute laboratory studies**				
	48-h Oral, adults	Fenazaquin (technical grade active ingredient, purity 98.6%)	LD_{50} = 7.3 µg a.i./bee NOAEL = 2.5 µg a.i./bee (mortality)	Moderately toxic	2962556
	48-h Contact, adults		LD_{50} = 8.1 µg a.i./bee	Moderately toxic	

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			NOAEL = 2.5 µg a.i./bee (mortality)		
	48-h Oral, adults	Fenazaquin (technical grade active ingredient, purity 98%)	LD_{50} = 5.8 µg a.i./bee NOAEL = 0.31 µg a.i./bee (mortality)	Moderately toxic	2962558
	48-h Contact, adults	Fenazaquin (technical grade active ingredient, purity 98.4%)	LD_{50} = 1.1 µg a.i./bee NOAEL = 0.375 µg a.i./bee (mortality)	Highly toxic	2962557
	24- to 72-h Exposure of adult bees by vapour, residues on treated filter paper, direct spraying and oral intake (non-guideline)	End-use product, EL-436 SC (200 g a.i./L)	Oral 72-h LD_{50} >100 µg EP/bee (>20 µg a.i./bee) Direct spray contact, filter paper contact, and vapor inhalation 72-h LD_{50} >0.1% formulated product.	N/A	2962559
	72-h Oral, larva	Fenazaquin (technical grade active ingredient, purity 99.9%)	LD_{50} = 0.35 µg a.i./larva (10.7 mg a.i./kg diet) NOAEL = 0.22 µg a.i./larva (6.8 mg a.i./kg diet; mortality)	Highly toxic	2962560
	CHRONIC LABORATORY STUDIES				
	10-d Chronic, adults	Fenazaquin (technical grade active ingredient, purity 99.9%)	LD_{50} = 0.87 µg a.i./bee/day NOAEL <0.69 µg a.i./bee/day (mortality) There was a statistically significant effect on mortality in all five test item treatment	N/A	2962561

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			groups (37% in lowest treatment group and 90–100% in all other treatment groups). No sub-lethal effects were observed in the lowest treatment group. Various sub-lethal effects were observed in the higher treatment groups (lethargy, frantic, and spasmodic body movements) prior to eventual mortality.		
	TOXICITY OF RESIDUES ON FOLIAGE STUDIES				
	24-h Foliar residue test, alfalfa treated at 504 g a.i./ha	End-use product, GWN-1708 SC (202 g a.i./L)	Honey bees showed no treatment-related mortality when exposed for 24 hours to treated alfalfa foliage collected at 3, 24 and 48 hours after application of fenazaquin. The residual toxicity time required for weathered residues to cause mortality to 25% of the bees (in other words, the RT_{25} value) was <3 hours for adult honey bees under the conditions tested.	N/A	2962582
	Semi-field studies				
	3- to 4-d semi-field study (Germany) to determine	EP, DOE 56200 A (201 g a.i./L)	Directly after application a repellent effect was observed; however, half an hour after	N/A	2962581

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
	effects on honey bees. *Phacelia tanacetifolia* in full bloom were exposed by foliar application from a plot sprayer to 300 g a.i./ha (~ half of max proposed Canadian field application rate), while bees were actively foraging.		application the flight activity returned to the same level observed before treatment. Except on the afternoon of the 3rd day, when the bees showed lower foraging activity than those in the control, no abnormal behaviour was observed. The mortality of the test item group was slightly higher compared to the control; however, mortality in the test item group was also higher than the control on the two days before application. In both trials no abnormal decrease in brood development was observed after application of the test substance. Under the conditions of this study, acute intoxication was not evident up to an application rate of 300 g a.i./ha.		
	3-d semi-field study (Germany) to determine effects on honey bees. *Phacelia*	EP, DOE 56200 A (201 g a.i./L)	Flight density was clearly reduced until half an hour after application and then reached a similar level as the control. Treatment mortality	N/A	2962578

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
	tanacetifolia in full bloom were exposed by foliar application from a portable sprayer to 80 g a.i./ha (~15% of max proposed Canadian field application rate), while bees were actively foraging.		was greater than the negative control in the first test. In the second test, mortality was greater in the treatment group; however, it was not greater than the control after accounting for mortality prior to treatment. All developmental stages of bee brood were found in all colonies before and after application. Under the conditions of this study, acute intoxication was not evident up to an application rate of 80 g a.i./ha.		
Predatory arthropod, *Typhlodromus pyri* (mite)	7-d Contact, glass plates	EP, EL-436 200 g/L SC (200 g a.i./L)	LR_{50} <2 g a.i./ha (mortality) There was 100% mortality in all treatment groups (2, 20, and 40 g a.i./ha). Analysis of the reproduction capacity was not possible due to the high mortality.	N/A	2962562
	48-h Contact, leaf discs	EP, EL-436 200 g/L SC (200 g a.i./L)	LR_{50} = 58.8 g a.i./ha (mortality) Note: This study included both *Typhlodromus pyri* and the pest,	N/A	2962577

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			Panonychus ulmi, with the intent of demonstrating the selectivity of fenazaquin. The LR_{50} for *P. ulmi* was 1.28 g a.i./ha.		
	40-d Field study in France, backpack spray application in apple orchard at 150 and 225 g a.i./ha	EP, EF-1127 200 g/L SC (210 g a.i./L)	This study included both *T. pyri* and the pest, *P. ulmi*. At both treatment rates there was significantly higher mortality of *T. pyri* compared to the control up to the end of the study (~80–90% mortality at 4 DAT and 50% mortality by 40 DAT); however, there was a consistent increase of nymphs in plots treated with fenazaquin, indicating that these treatments were not harmful to eggs, and gradual recovery of the mites was evident by 14 DAT. The results did not demonstrate a full recovery of *T. pyri* but were much better compared to the pest mite, *P. ulmi*. Additionally, aged residue tests were performed with adult *T. pyri* exposed for 48 hours to treated apple leaves	N/A	2962563

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			collected 1 and 15 DAT. The bioassays showed that residual toxicity to *T. pyri* was of short duration as higher mortality compared to the control was only observed 1 DAT and not 15 DAT.		
	90-d Field study in four Switzerland locations, backpack spray application in apple orchard at 117-500 g a.i./ha	EP, DE-436 200 g/L SC (200 g a.i./L)	At all treatment rates and trial locations there was significantly higher mortality of *T. pyri* compared to the control at all time points (appeared dose-responsive). On average, recovery of *T. pyri* was observed after 2–3 months.	N/A	2962564
	46-d Field study in Hungary, backpack spray application in vineyard at 100 g a.i./ha	EP, Magister 200 SC (200 g a.i./L)	There was an initial significant reduction of *T. pyri* (up to approximately 90% mortality at 7 DAT). 28 DAT the population reached nearly 50% of the control population and by 35 DAT, mite populations approached a similar level to the control.	N/A	2962573
Parasitic arthropod, *Aphidius rhopalosiphi* (wasp)	48-h Contact, glass plates	EP, Fenazaquin 200 SC (205 g a.i./L)	LR_{50} = 187.3 g a.i./ha (mortality) The reproduction of surviving parasitoids was not statistically significantly affected at all rates tested, in other words, up to	N/A	2962567

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			and including 75.0 g a.i./ha.		
Ladybird, *Coccinella septempunctata*	56-d Contact, glass plates	EP, EAF-618 200 g/L SC (200 g a.i./L)	LR_{50} <21.9 g a.i./ha (mortality) There was 67.5% mortality (corrected for 24.5% control mortality) in the only treatment group of 21.9 g a.i./ha. The assessment of the reproduction rate also indicated a decrease of 22.2% in the treatment group compared to the control.	N/A	2962571
	21-d Extended laboratory, dried residues on apple leaves at 150 g a.i./ha	EP, Matador 200 SC (209 g a.i./L)	LR_{50} >150 g a.i./ha (mortality) Mortality was 14% (corrected for 10% control mortality). No adverse effects on reproductive capacity (# of eggs or % egg hatch) were observed.	N/A	2962576
Predatory arthropod, *Zetzellia mali* (mite)	80-d Field study in Hungary, spray gun application in vineyard at 100 g a.i./ha	EP, Magister 200 SC (200 g a.i./L)	The population density of the treated group was comparable to the control up to 14 DAT. The population density in the treated group 28, 42, and 80 DAT was slightly lower than the control; however, it is unlikely to be due to treatment application.	N/A	2962572

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Predatory arthropods, *Amblyseius californicus, Phytoseiulus persimilis*, and *Metaseiulus occidentalis* (all mites)	72-h, Contact, leaf discs Additionally, eggs of *P. persimilis* and *M. occidentalis* were sprayed with the test item and evaluated for hatching success after 72 hours of exposure	EP, XDE-436 1.5 EC (guarantee not indicated, unknown formulation)	*A. californicus* was the least sensitive species with an LR_{50} = 36 g a.i./ha (average, adult mortality) *P. persimilis* and *M. occidentalis* were comparably sensitive with an LR_{50} = 3 g a.i./ha (average, adult mortality). Three pest species were also tested and appeared to be comparably sensitive with an LR_{50} = 2 g a.i./ha (average, adult mortality). The egg stage of tested species appeared to be 10 times less sensitive to the test item than the corresponding mobile forms.	N/A	2962566
Non-target arthropods, *Bembidion lampros* (ground-dwelling beetle), *Pardosa spp.* (ground-dwelling spider), and *Aphidius colemani* (parasitoid)	5-d Study in UK and Belgium, beetles and spiders in trays/pots were placed under apple trees while spraying at 111 and 252 g a.i./ha. Parasitoids were also exposed in lab to	EP, Matador 200 SC (209 g a.i./L)	LR_{50} >252 g a.i./ha for all three species (mortality) The corrected mortality for all groups of test organisms did not exceed 28% at all test rates. Though the feeding activity of *B. lampros* was reduced at the lower treatment rate, it was not affected at the higher treatment rate.	N/A	3087652

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
	foliated twigs removed from the treated apple trees.		Reproduction of *A. colemani* was not affected at any rate.		
Birds					
Zebra finch, *Poephila guttata*	14-d Acute Oral	Fenazaquin (TGAI, purity 99.92%)	LD_{50} = 1592 mg a.i./kg bw (mortality) Sublethal effects (lethargy, loss of coordination, prostate posture, etc.) were observed at ≥432 mg a.i./kg bw.	Slightly toxic	2962590
Bobwhite quail, *Colinus virginianus*	19-d Acute Oral	Fenazaquin (TGAI, purity 98.4%)	LD_{50} = 1747 mg a.i./kg bw Sublethal effects (body weight, loose feces, ataxia) were observed at ≥1000 mg a.i./kg bw.	Slightly toxic	2962602
	5d-Dietary	Fenazaquin (TGAI, purity 98.4%)	LC_{50} >5204 mg a.i./kg diet LD_{50} >1169 mg a.i./kg bw/day Sublethal effects (body weight, ataxia) were observed at 5204 mg a.i./kg diet.	Practically nontoxic	2962605
	22-w Reproduction	Fenazaquin (TGAI, purity 98.0%)	NOAEC = 287 mg a.i./kg diet NOAEL = 23.6 mg a.i./kg bw/day Parental NOAEC/NOAEL, based on slight decrease in mean body weight of males.	N/A	2962606

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			There were no treatment-related effects on any reproductive parameter, therefore the reproductive endpoints are: NOAEC = 953 mg a.i./kg diet NOAEL = 80.3 mg a.i./kg bw/day (highest treatment level)		
Mallard duck, *Anas platyrhynchos*	14-d Acute Oral	Fenazaquin (TGAI, purity 98%)	LD_{50} >2000 mg a.i./kg bw Mortality (8–17%) occurred at ≥1000 mg a.i./kg bw. Sublethal effects (food consumption, ataxia) were observed at 2000 mg a.i./kg bw.	Practically nontoxic	2962603
	5-d Dietary	Fenazaquin (TGAI, purity 98.4%)	LC_{50} >5030 mg a.i./kg diet LD_{50} >1452 mg a.i./kg bw/day Sublethal effects (body weight) were observed at ≥837 mg a.i./kg diet.	Practically nontoxic	2962604
	20-w Reproduction	Fenazaquin (TGAI, purity 99.92%)	NOAEC = 1000 mg a.i./kg diet NOAEL = 152.2 mg a.i./kg bw/day There were no treatment-related effects on any adult, reproductive, or offspring parameter.	N/A	2962607

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Mammals					
Rat (Fischer or Sprague Dawley)	Acute oral	Fenazaquin (TGAI, purity 97.28%)	LD_{50} (male/female) = 134/138 mg a.i./kg bw	Moderately toxic	2962479
	Acute oral	EP, Fenazaquin 200 AS (18.9% a.i.)	LD_{50} (male/female) >56.7/>37.8 mg a.i./kg bw or >300/>200 mg EP/kg bw LD_{50} values were considered "greater than" values as the mortality pattern did not follow a clear dose-response. Male mortality in the dose groups was: 200 mg EP/kg bw (0/10, 0%), 300 mg EP/kg bw (1/5, 20%), 365 mg EP/kg bw (4/5, 80%), 500 mg EP/kg bw (2/5, 40%), 600 mg EP/kg bw (3/5, 60%), 650 mg EP/kg bw (0/5, 0%), 700 mg EP/kg bw (1/5, 20%), 1200 mg EP/kg bw (1/5, 20%), or 2000 mg EP/kg bw (6/10, 60%). Female mortality in the dose groups was: 200 mg EP/kg bw (1/10, 10%), 300 mg EP/kg bw (3/5, 60%), 365 mg EP/kg bw (0/5, 0%), 500 mg EP/kg bw (4/5,	The end-use product is moderately (males) or highly (females) toxic to practically non-toxic (non-definitive endpoint)	2962734

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			80%), 600 mg EP/kg bw (5/5, 100%), 650 mg EP/kg bw (4/5, 80%), 700 mg EP/kg bw (2/5, 40%), 1200 mg EP/kg bw (5/5, 100%), or 2000 mg EP/kg bw (9/10, 90%).		
	2-Generation Reproduction	Fenazaquin (TGAI, purity 98.4%)	Parental NOAEL = 5 mg a.i./kg bw/day (decreased body weight, body weight gain, and feed consumption) Reproductive NOAEL = 25 mg a.i./kg bw/day (no treatment-related reproductive toxicity findings)	N/A	2962505 and 2962504
Vascular plants					
Monocot and dicot crop species (corn, rice, sorghum, wheat, cabbage, cotton, cucumber, radish, soybean and sunflower)	6-d Seedling germination	Fenazaquin (TGAI, purity 98.0%)	NOAER = 224 g a.i./ha for all species tested ER_{25} >224 g a.i./ha for all species tested	N/A	3045443
	21-d Seedling emergence	Fenazaquin (TGAI, purity 98.0%)	NOAER = 897 g a.i./ha for all species tested ER_{25} >897 g a.i./ha for all species tested	N/A	2962615
	21-d Vegetative vigour	Fenazaquin (TGAI, purity 98.0%)	NOAER = 897 g a.i./ha for all species tested ER_{25} >897 g a.i./ha for all species tested Very slight, temporary injury was	N/A	2962616

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			observed with one monocot and with several dicots (slight stunting or slightly burned, crinkled or cupped leaves) at ≥448 g a.i./ha.		
[1] Atkins *et al.* (1981) for bees and USEPA classification for others, where applicable					

Table 23 Toxicity to non-target aquatic organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
Freshwater species					
Daphnia magna	48-h Acute	Fenazaquin (TGAI, purity 98%)	EC_{50} = 5.6 µg a.i./L (immobilization) NOAEC = 0.8 µg a.i./L Hypoactivity or prostration was observed at the ≥3.0 µg a.i./L exposure levels in 100% of the remaining daphnids.	Very highly toxic	2962583
	48-h Acute (natural water with and without sediment)	Fenazaquin (TGAI, purity 98%)	**Without sediment** EC_{50} = 5.7 µg a.i./L (immobilization) NOAEC = 3.0 µg a.i./L **With sediment** EC_{50} = 12.7 µg a.i./L (immobilization) NOAEC = 10.0 µg a.i./L Hypoactivity	Very highly toxic	3096457

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
			was observed in all but the lowest test concentrations in both studies.		
	48-h Acute	Fenazaquin propionic acid (TP, purity 89.7%)	EC_{50} = 2.3 × 10^3 µg/L (immobilization) NOAEC = 0.5 × 10^3 µg/L	Moderately toxic	3096455
	48-h Acute	2,4-TBPE (TP, purity 88.9%)	EC_{50} = 3.86 × 10^3 µg/L (immobilization) NOAEC = 1.0 × 10^3 µg/L	Moderately toxic	3102692
	48-h Acute (microcosm study)	EP, EL-436 EC, 18%	EC_{50} >2.87 µg a.i./L or >15.9 µg EP/L NOAEC = 2.87 µg a.i./L or 15.9 µg EP/L No adverse effects on aquatic organisms were observed after a direct spray and simulated run-off event under the conditions of this microcosm study.	No signs of toxicity at the tested concentration	2962546
	21-d Chronic	Fenazaquin (TGAI, purity 98%)	NOAEC = 0.52 µg a.i./L LOAEC = 0.78 µg a.i./L (number of offspring/female) No treatment-related effects on	N/A	2962584

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
			survival, time to first brood, or growth.		
	21-d Chronic	Fenazaquin (TGAI, purity 99.92%)	NOAEC = 1.3 µg a.i./L LOAEC >1.3 µg a.i./L No treatment-related effects on any measured endpoint (survival, time to first brood, offspring production, or growth).	N/A	2962585
	21-d Chronic	EP, EF-1127 200 g/L SC (210 g a.i./L)	NOAEC = 0.20 µg a.i./L or 1.0 µg EP/L LOAEC = 0.64 µg a.i./L or 3.2 µg EP/L (immobilization) No treatment-related effects on reproduction. Survival was 28% at the highest treatment concentration of 0.64 µg a.i./L.	N/A	2962586
Midge, *Chironomus riparius*	28-d Chronic, spiked water	Fenazaquin (TGAI, purity >98%)	NOAEC = 0.67 µg a.i./L LOAEC = 2.6 µg a.i./L Based on mean-measured time-weighted average overlying water concentrations	N/A	2962591

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
			and significant effects on development rate observed at higher treatment levels.		
Rainbow trout, *Oncorhynchus mykiss*	96-h Acute, flow-through	Fenazaquin (TGAI, purity 98%)	LC_{50} = 3.9 µg a.i./L NOAEC = 3.0 µg a.i./L Sublethal effects (in other words, sluggishness, hypoactivity, or prostration) were only observed in surviving fish from the 4.4 µg a.i./L level from 24 to 48 hours.	Very highly toxic	2962594
	96-h Acute, semi-static	Fenazaquin (TGAI, purity 98%)	Natural water with suspended sediment: LC_{50} = 11.4 µg a.i./L NOAEC = 9.6 µg a.i./L Well water: LC_{50} = 6.0 µg a.i./L NOAEC = 3.8 µg a.i./L Sublethal effects including hypoactivity, sluggishness, impaired swimming, and prostrate positioning, were observed in all	Very highly toxic	2962593

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
			levels treated with fenazaquin, regardless of the presence of suspended sediment. Effects were noted up to 72 hours in some fish, leading to either death or continued effects by 96 hours (in other words, no fish recovered). The presence of suspended sediment may very slightly attenuate the toxic effects of fenazaquin.		
	96-h Acute, semi-static	Fenazaquin propionic acid (TP, purity 89.7%)	LC_{50} = 735 µg/L NOAEC = 214 µg/L Sublethal effects (in other words, lethargy, hyperventilation, slowed respiration rate, darkened pigmentation, and immobility) were observed in the three highest treatment groups. However, with the exception of aggressive behavior in one fish, no sublethal	Highly toxic	2962595

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
			effects were observed in surviving fish at test termination.		
	96-h Acute, semi-static	2,4-TBPE (TP, purity 88.9%)	LC_{50} = 13.3 × 10^3 µg a.i./L NOAEC = 4.48 × 10^3 µg a.i./L Sublethal effects (in other words, darkened pigmentation, vertically oriented, immobilization, and loss of coordination) were observed in several fish in the three highest treatment levels and persisted until test termination or death.	Slightly toxic	2962596
	96-h Acute, flow-through	EP, EF-1127 200 g/L SC (203 g a.i./L)	LC_{50} = 41 µg a.i./L (equivalent to 202 µg EP/L) NOAEC = 6.5 µg a.i./L (equivalent to 32 µg EP/L) Sublethal effects were observed in surviving fish at all but the lowest treatment level (10, 30, 38 and 100% effects in the 11, 20, 37 and 65 µg a.i./L groups,	The active ingredient is very highly toxic. The formulation is highly toxic.	2962592

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
			respectively) and included loss of equilibrium, increased pigmentation, lethargy, on the tank base, exophthalmia, and moribund behaviour.		
	96-h Acute (microcosm study)	EP, EL-436 EC, 18%	EC_{50} >2.87 µg a.i./L or >15.9 µg EP/L NOAEC = 2.87 µg a.i./L or 15.9 µg EP/L No adverse effects on aquatic organisms were observed after a direct spray and simulated run-off event under the conditions of this microcosm study.	No signs of toxicity at the tested concentration.	2962546
	63-d ELS, flow-through	Fenazaquin (TGAI, purity 98%)	NOAEC = 0.95 µg a.i./L LOAEC = 1.97 µg a.i./L Decreases in post-hatch larval survival, increases in behavioral abnormalities, and decreases in growth (length and wet weight) were observed at the two highest	N/A	2962600

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
			treatment levels of 1.97 and 3.90 µg a.i./L.		
	21-d Chronic	EP, EF-1127 200 g/L SC (203 g a.i./L)	NOAEC = 5.7 µg a.i./L or 28 µg EP/L LOAEC =18.3 µg a.i./L or 90 µg EP/L Mortality was 20 and 100% in the two highest treatment groups of 90 and 290 µg formulation/L, respectively. Sublethal effects were observed throughout the study in the two highest treatment levels and included lethargy, increased pigmentation, loss of equilibrium, and moribund behaviour.	N/A	2962599
Bluegill sunfish, *Lepomis macrochirus*	96-h Acute, flow-through	Fenazaquin (TGAI, purity 98%)	LC_{50} = 34.1 µg a.i./L NOAEC = 20.4 µg a.i./L (mortality and sublethal effects) Sublethal effects (in other words, sluggishness, hypoactivity, impaired swimming, or	Very highly toxic	2962598

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
			prostration) were observed in surviving fish from the two highest treatment levels of 30.6 and 33.0 µg a.i./L until test termination.		
	96-h Acute (microcosm study)	EP, EL-436 EC, 18%	EC_{50} >2.87 µg a.i./L or >15.9 µg EP/L NOAEC = 2.87 µg a.i./L or 15.9 µg EP/L	No signs of toxicity at the tested concentration	2962546
Diatom, *Navicula pelliculosa*	96-h Acute	Fenazaquin (TGAI, purity 99.92%)	EC_{50} >45.4 µg a.i./L There were no effects on cell density, yield, or growth rate, resulting in a NOAEC of 45.4 µg a.i./L (highest concentration tested).	Indeterminate	2962609
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute	Fenazaquin (TGAI, purity 97.9%)	EC_{50} >208 µg a.i./L There were no effects on cell density, yield, or growth rate, resulting in a NOAEC of 208 µg a.i./L (highest concentration tested).	Indeterminate	2962608
	72-h Acute	Fenazaquin propionic acid (TP, purity	$EC_{50} = 7.6 \times 10^3$ µg a.i./L (cell density)	Moderately toxic	2962612

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
		89.7%)	There were statistically significant, dose responsive effects on cell density and other measures of algal growth (in other words, biomass, growth rate, and area under the curve), resulting in a NOAEC of 483 µg a.i./L.		
Blue-green algae, *Anabaena flos-aquae*	96-h Acute	Fenazaquin (TGAI, purity 99.92%)	EC_{50} >78.8 µg a.i./L There were no effects on cell density, yield, or growth rate, resulting in a NOAEC of 78.8 µg a.i./L (highest concentration tested).	Indeterminate	2962610
Green algae, *Scenedesmus subspicatus*	96-h Acute	EP, EF-1127 200 g/L SC (203 g a.i./L)	$EC_{50} = 7.2 \times 10^3$ µg a.i./L (cell density) or 35.5×10^3 µg EP/L There were statistically significant, dose responsive effects on cell density and other measures of algal growth (in other words, biomass and growth rate), resulting in a	Moderately toxic	2962611

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
			NOAEC of 1.01 × 10^3 µg a.i./L (4.98 × 10^3 µg EP/L)		
Vascular plant, duckweed, *Lemna gibba*	7-d Acute	Fenazaquin (TGAI, purity 99.92%)	EC_{50} >75.1 µg a.i./L There were no effects on frond density, yield, or growth rate, resulting in a NOAEC of 75.1 µg a.i./L (highest concentration tested).	Indeterminate	2962617
Marine species					
Mollusc, Eastern oyster, *Crassostrea virginica*	96-h Acute	Fenazaquin (TGAI, purity 97.48%)	EC_{50} = 3.9 µg a.i./L (shell deposition) NOAEC <3.1 µg a.i./L A 38% reduction in shell deposition was observed at the lowest treatment level of 3.1 µg a.i./L to 75% at the highest treatment levels of 64 and 210 µg a.i./L	Very highly toxic	2962587
Crustacean, brown shrimp, *Crangon crangon*	96-h Acute	Fenazaquin (TGAI, purity 99.3%)	LC_{50} = 21 µg a.i./L NOAEC = 10 µg a.i./L (mortality and sublethal effects)	Very highly toxic	2962588
Crustacean, mysid shrimp, *Americamysis*	96-h Acute	Fenazaquin (TGAI, purity	LC_{50} = 5.0 µg a.i./L NOAEC = 3.5	Very highly toxic	2962589

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA #
bahia		99.92%)	µg a.i./L (mortality and sublethal effects)		
Marine diatom, *Skeletonema costatum*	96-h Acute	Fenazaquin (TGAI, purity 99.92%)	EC_{50} = 0.84 µg a.i./L (yield) There were statistically significant, dose responsive effects on cell density and other measures of algal growth (in other words, yield and growth rate), resulting in a NOAEC of 0.017 µg a.i./L.	Very highly toxic	2962613
Sheepshead minnow, *Cyprinodon variegatus*	96-h Acute, static	Fenazaquin (TGAI, purity 99.2%)	LC_{50} = 43.2 µg a.i./L NOAEC = 30.1 µg a.i./L Sublethal effects (in other words, loss of equilibrium and lying on the bottom of the test chamber) were observed in the highest treatment level of 62.0 µg a.i./L until test termination or death.	Very highly toxic	2962597
[1] USEPA classification, where applicable					

Table 24 Endpoints used in the environmental risk assessment

Organism	Exposure / Test substance	Endpoint	Value	Uncertainty factor[1]	Level of Concern
Terrestrial species					
Earthworm	Acute – a.i.	14-d LC_{50}	1.93 mg a.i./kg ww soil	2	1
	Acute – EP, 200 g/L SC	14-d LC_{50}	21.8 mg a.i./kg dw soil	2	1
	Reproduction – EP, 200 g/L SC	56-d NOAER	312 g a.i./ha	1	1
Collembola, *Folsomia candida*	Reproduction – EP, 200 g/L SC	28-d NOAEC	23.0 mg a.i./kg dw soil	1	1
Honey bee, *Apis mellifera*	Acute oral, adults – a.i.	48-h LD_{50}	5.8 µg a.i./bee	1	0.4
	Acute oral, adults – EP, 200 g/L SC	72-h LD_{50}	>20 µg a.i./bee	1	0.4
	Acute contact, adults – a.i.	48-h LD_{50}	1.1 µg a.i./bee	1	0.4
	Acute oral, larvae – a.i.	72-h LD_{50}	0.35 µg a.i./bee	1	0.4
	Chronic oral, adults – a.i.	10-d NOAEL	<0.69 µg a.i./bee/day[2]	1	1
Predatory mite, *Typhlodromus pyri*	Contact, glass plates – EP, 200 g/L SC	7-d LR_{50}	<2 g a.i./ha[3]	1	2
	Contact, leaf discs – EP, 200 g/L SC	48-h LR_{50}	58.8 g a.i./ha	1	1
Parasitoid wasp, *Aphidius rhopalosiphi*	Contact, glass plates – EP, 200 g/L SC	48-h LR_{50}	187.3 g a.i./ha	1	2
Ladybird, *Coccinella septempunctata*	Contact, glass plates – EP, 200 g/L SC	56-d LR_{50} and NOAER	<21.9 g a.i./ha[4]	1	1
Zebra finch, *Poephila guttata*	Acute oral – a.i.	14-d LD_{50}	1592 mg a.i./kg bw/d	10	1
Bobwhite quail, *Colinus virginianus*	Acute oral – a.i.	14-d LD_{50}	1747 mg a.i./kg bw/d	10	1
	Acute dietary – a.i.	5-d LD_{50}	>1169 mg a.i./kg bw/d	10	1
	Reproduction – a.i.	22-w NOAEL	80.3 mg a.i./kg bw/d[5]	1	1

Organism	Exposure / Test substance	Endpoint	Value	Uncertainty factor[1]	Level of Concern
Mallard duck, *Anas platyrhynchos*	Acute oral – a.i.	14-d LD_{50}	>2000 mg a.i./kg bw/d	10	1
	Acute dietary – a.i.	5-d LD_{50}	>1452 mg a.i./kg bw/d	10	1
	Reproduction – a.i.	20-w NOAEL	152.2 mg a.i./kg bw/d	1	1
Rat (Fischer or Sprague Dawley)	Acute oral – a.i.	LD_{50}	134 mg a.i./kg bw	10	1
	Acute oral – EP, 200 g/L AS	LD_{50}	>37.8 mg a.i./kg bw[6]	10	1
	Reproduction – a.i.	NOAEL	25 mg a.i./kg bw/d[7]	1	1
Terrestrial vascular plants	Seedling germination	6-d ER_{25}	>224 g a.i./ha	1	1
	Seedling emergence and vegetative vigour	21-d ER_{25}	>897 g a.i./ha	1	1
Freshwater species					
Invertebrate, *Daphnia magna*	Acute – a.i.	48-h EC_{50}	5.6 µg a.i./L	2	1
	Acute – TP	48-h EC_{50}	2.3×10^3 µg/L	2	1
	Acute – TP	48-h EC_{50}	3.86×10^3 µg/L	2	1
	Chronic – a.i.	21-d NOAEC	0.52 µg a.i./L	1	1
	Chronic – EP, 200 g/L SC	21-d NOAEC	0.20 µg a.i./L	1	1
Midge, *Chironomus riparius*	Chronic – a.i. (spiked water)	28-d NOAEC	0.67 µg a.i./L (overlying water)	1	1
Rainbow trout, *Oncorhynchus mykiss*	Acute – a.i.	96-h LC_{50}	3.9 µg a.i./L	10	1
	Acute – EP, 200 g/L SC	96-h LC_{50}	41 µg a.i./L	10	1
	Acute – TP	96-h LC_{50}	735 µg/L	10	1
	Acute – TP	96-h LC_{50}	13.3×10^3 µg/L	10	1
	Chronic – EP, 200 g/L SC	21-d NOAEC	5.7 µg a.i./L	1	1

Organism	Exposure / Test substance	Endpoint	Value	Uncertainty factor[1]	Level of Concern
	ELS – a.i.	63-d NOAEC	0.95 µg a.i./L	1	1
Bluegill sunfish, *Lepomis macrochirus*	Acute – a.i.	96-h LC_{50}	34.1 µg a.i./L	10	1
Amphibians (using fish data as a surrogate)	Acute	96-h LC_{50}	3.9 µg a.i./L	10	1
	Chronic	63-d NOAEC	0.95 µg a.i./L	1	1
Diatom, *Navicula pelliculosa*	Acute – a.i.	96-h EC_{50}	>45.4 µg a.i./L	2	1
Green algae, *Pseudokirchneriella subcapitata*	Acute – a.i.	96-h EC_{50}	>208 µg a.i./L	2	1
	Acute – TP	72-h EC_{50}	7.6×10^3 µg/L	2	1
Green algae, *Scenedesmus subspicatus*	Acute – EP, 200 g/L SC	96-h EC_{50}	7.2×10^3 µg a.i./L	2	1
Blue-green algae, *Anabaena flos-aquae*	Acute – a.i.	96-h EC_{50}	>78.8 µg a.i./L	2	1
Aquatic vascular plants, *Lemna gibba*	Acute – a.i.	7-d EC_{50}	>75.1 µg a.i./L	2	1
Marine species					
Mollusc, Eastern oyster, *Crassostrea virginica*	Acute – a.i.	96-h EC_{50}	3.9 µg a.i./L	2	1
Crustacean, brown shrimp, *Crangon crangon*	Acute – a.i.	96-h LC_{50}	21 µg a.i./L	2	1
Crustacean, mysid shrimp, *Americamysis bahia*	Acute – a.i.	96-h LC_{50}	5.0 µg a.i./L	2	1
Marine diatom, *Skeletonema costatum*	Acute – a.i.	96-h EC_{50}	0.84 µg a.i./L	2	1
Sheepshead minnow, *Cyprinodon variegatus*	Acute – a.i.	96-h LC_{50}	43.2 µg a.i./L	10	1

[1] As per the PMRA environmental risk assessment Guidance Manual.

Organism	Exposure / Test substance	Endpoint	Value	Uncertainty factor[1]	Level of Concern

[2] Due to statistically significant mortality (37%) at the lowest treatment level (0.69 µg a.i./bee/day), the study resulted in a non-definitive NOAEL. 90-100% mortality was observed in all other treatment groups. Despite the mortality in the lowest treatment level, the endpoint is considered adequate for use in the risk assessment.
[3] There was 100% mortality in all treatment groups (2, 20, and 40 g a.i./ha), resulting in an LR_{50} <2 g a.i./ha.
[4] There was 67.5% mortality (corrected for 24.5% control mortality) in the only treatment group of 21.9 g a.i./ha, resulting in a non-definitive NOAEL and an LR_{50} <21.9 g a.i./ha. The assessment of the reproduction rate also indicated a decrease of 22.2% in the treatment group compared to the control.
[5] The parental NOAEL in this bobwhite quail study was 23.6 mg a.i./kg bw/day and is based on slight decrease in the mean body weight of males. As there were no treatment-related effects on any reproductive parameter, the reproductive NOAEL = 80.3 mg a.i./kg bw/day (highest treatment level tested). The reproductive NOAEL was considered appropriate for use in the screening level assessment as it is considered adequately conservative and representative of potential effects on birds. It is noted that this is consistent with the mallard duck reproductive study, where no treatment-related effects on any adult, reproductive, or offspring parameter were observed, resulting in a NOAEL = 152.2 mg a.i./kg bw/day (highest treatment level).
[6] LD_{50} values were considered greater than values as the mortality pattern did not follow a clear dose-response.
[7] In this 2-generation reproduction study there were significant, albeit slight, treatment-related decreases in parental body weight, body weight gain, and feed consumption at the highest treatment level (25 mg/kg bw/day), resulting in a parental NOAEL of 5 mg/kg bw/day. There were no treatment-related reproductive toxicity findings, resulting in a reproductive NOAEL of 25 mg/kg bw/day. The reproductive NOAEL was used in the screening level risk assessment, as the reductions in body weight and weight gain were not considered biologically significant.

Table 25 Screening level risk assessment for non-target terrestrial species other than birds and mammals

Organism	Exposure	Endpoint value	EEC	RQ	Level of Concern[1]
Invertebrates					
Earthworm	Acute – a.i.	LC_{50}/2: 0.965 mg a.i./kg soil	0.24 mg a.i./kg soil[2]	0.2	Not exceeded
	Acute – EP, 200 g/L SC	LC_{50}/2: 10.9 mg a.i./kg soil	0.24 mg a.i./kg soil[2]	<0.1	Not exceeded
	Reproduction – EP, 200 g/L SC	NOAER: 312 g a.i./ha	539.15 g a.i./ha[3]	**1.7**	**Exceeded**
		LOAER: 624 g a.i./ha	539.15 g a.i./ha[3]	0.9	Not exceeded
Collembola, *Folsomia candida*	Reproduction – EP, 200 g/L SC	NOAEC: 23.0 mg a.i./kg soil	0.24 mg a.i./kg soil[2]	<0.1	Not exceeded
Honey bee, *Apis mellifera*	Acute oral, adults – a.i.	LD_{50}: 5.8 µg a.i./bee	15.43 µg a.i./bee[4]	**2.5**	**Exceeded**
	Acute oral, adults – EP, 200 g/L SC	LD_{50}: >20 µg a.i./bee	15.43 µg a.i./bee[4]	**<0.8**	**Exceeded**
	Acute contact, adults – a.i.	LD_{50}: 1.1 µg a.i./bee	1.29 µg a.i./bee[4]	**1.2**	**Exceeded**
	Acute oral, larvae – a.i.	LD_{50}: 0.35 µg a.i./bee	6.6 µg a.i./larva[4]	**18.7**	**Exceeded**

	Chronic oral, adults – a.i.	NOAEL: <0.69 µg a.i./bee/day	15.43 µg a.i./bee[4]	**>22.4**	**Exceeded**
Predatory mite, *Typhlodromus pyri*	Contact, glass plates – EP, 200 g/L SC	LR_{50}: <2 g a.i./ha	In-field: 539.15 g a.i./ha[5]	**>269.6**	**Exceeded**
			Off-field: 398.97 g a.i./ha[5]	**>199.5**	**Exceeded**
	Contact, leaf discs – EP, 200 g/L SC	LR_{50}: 58.8 g a.i./ha	In-field: 539.15 g a.i./ha[5]	**9.2**	**Exceeded**
			Off-field: 398.97 g a.i./ha[5]	**6.8**	**Exceeded**
Parasitoid wasp, *Aphidius rhopalosiphi*	Contact, glass plates – EP, 200 g/L SC	LR_{50}: 187.3 g a.i./ha	In-field: 539.15 g a.i./ha[5]	**2.9**	**Exceeded**
			Off-field: 398.97 g a.i./ha[5]	**2.1**	**Exceeded**
Ladybird, *Coccinella septempunctata*	Contact, glass plates – EP, 200 g/L SC	LR_{50}: <21.9 g a.i./ha	In-field: 539.15 g a.i./ha[5]	**>24.6**	**Exceeded**
			Off-field: 398.97 g a.i./ha[5]	**18.2**	**Exceeded**
Vascular plants					
Vascular plant	Seedling germination – a.i.	ER_{25}: >224 g a.i./ha	539.15 g a.i./ha[3]	**<2.4**	**Exceeded**
	Seedling emergence – a.i.	ER_{25}: >897 g a.i./ha	539.15 g a.i./ha[3]	<0.6	Not exceeded
	Vegetative vigour – a.i.	ER_{25}: >897 g a.i./ha	539.15 g a.i./ha[3]	<0.6	Not exceeded

[1] Level of concern (LOC) = 1 for most species; 0.4 for acute risk to pollinators; 1 for chronic risk to pollinators; and 2 for glass plate studies using the standard beneficial arthropod test species, *Typhlodromus pyri* and *Aphidius rhopalosiphi.*
[2] EEC in soil in mg a.i./kg soil based on direct overspray of maximum Canadian rate of one single application of 539.15 g a.i./ha, mixed homogenously in the top 15 cm of soil with a bulk density of 1.5 g/cm^3.
[3] EEC on plant surfaces assumes direct spray at the maximum Canadian rate of one single application of 539.15 g a.i./ha.
[4] Contact exposure EEC = application rate (kg a.i./ha) × adjustment factor (2.4 µg a.i./bee per kg a.i./ha); adult oral exposure EEC = single application rate (kg a.i./ha) × adjustment factor (28.6 µg a.i./bee per kg a.i./ha); brood exposure EEC = application rate (kg a.i./ha) × adjustment factor (12.15 µg a.i./bee per kg a.i./ha). All EECs calculations based on USEPA and PMRA Guidance for Assessing Pesticide Risks to Bees (2014) and maximum Canadian rate of one single application of 539.15 g a.i./ha.
[5] In-field EEC on plant surfaces assumes direct spray at the maximum Canadian rate of one single application of 539.15 g a.i./ha. Off-field EEC is calculated by adjusting the in-field EEC by a drift factor of 74% (the most for any application method permitted for fenazaquin EPs).

Table 26 Screening level risk assessment for birds and mammals

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)[1]	RQ	Level of Concern[2]
Small Bird (0.02 kg)					
Acute	159.2	Insectivore	43.88	0.28	Not exceeded
Reproduction	80.3	Insectivore	43.88	0.55	Not exceeded
Medium Sized Bird (0.1 kg)					
Acute	159.2	Insectivore	34.25	0.22	Not exceeded
Reproduction	80.3	Insectivore	34.25	0.43	Not exceeded
Large Sized Bird (1 kg)					
Acute	159.2	Herbivore (short grass)	22.12	0.14	Not exceeded
Reproduction	80.3	Herbivore (short grass)	22.12	0.28	Not exceeded
Small Mammal (0.015 kg)					
Acute	>3.78	Insectivore	25.24	**<6.68**	**Exceeded**
Reproduction	25.0	Insectivore	25.24	**1.01**	**Exceeded**
Medium Sized Mammal (0.035 kg)					
Acute	>3.78	Herbivore (short grass)	48.95	**<12.95**	**Exceeded**
Reproduction	25.0	Herbivore (short grass)	48.95	**1.96**	**Exceeded**
Large Sized Mammal (1 kg)					
Acute	>3.78	Herbivore (short grass)	26.16	**<6.92**	**Exceeded**
Reproduction	25.0	Herbivore (short grass)	26.16	**1.05**	**Exceeded**

[1] EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/bw) × EEC, where:
FIR: Food Ingestion Rate (Nagy, 1987)
For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used:
Passerine Equation (body weight < or = 200 g): FIR (g dry weight/day) = $0.398(\text{bw in g})^{0.850}$
For generic birds with body weight greater than 200 g, the "all birds" equation was used:
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = $0.648(\text{bw in g})^{0.651}$
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = $0.235(\text{bw in g})^{0.822}$
bw: Generic Body Weight
EEC: Concentration of pesticide on food item based on Hoerger and Kenaga (1972) and Kenaga (1973) and modified according to Fletcher *et al*. (1994), using most conservative Canadian rate of one single application of 539.15 g a.i./ha. At the screening level, relevant food items representing the most conservative EEC for each feeding guild are used.
[2] Level of concern (LOC) = 1 for birds and mammals

Table 27 Refined risk assessment for mammals

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off-field[3]		On-field		Off-field[3]	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)[1]	RQ[2]	EDE (mg a.i./kg bw)[1]	RQ[2]	EDE (mg a.i./kg bw)[1]	RQ[2]	EDE (mg a.i./kg bw)[1]	RQ[2]
Small Mammal (0.015 kg)										
Acute	13.4	Insectivore	25.24	**1.88**	18.68	**1.39**	17.43	**1.30**	12.90	0.96
	13.4	Granivore (grain and seeds)	3.91	0.29	2.89	0.22	1.86	0.14	1.38	0.10
	13.4	Frugivore (fruit)	7.81	0.58	5.78	0.43	3.73	0.28	2.76	0.21
Reproduction	25.0	Insectivore	25.24	**1.01**	18.68	0.75	17.43	0.70	12.90	0.52
	25.0	Granivore (grain and seeds)	3.91	0.16	2.89	0.12	1.86	0.07	1.38	0.06
	25.0	Frugivore (fruit)	7.81	0.31	5.78	0.23	3.73	0.15	2.76	0.11
Medium Sized Mammal (0.035 kg)										
Acute	13.4	Insectivore	22.13	**1.65**	16.37	**1.22**	15.28	**1.14**	11.31	0.84
	13.4	Granivore (grain and seeds)	3.42	0.26	2.53	0.19	1.63	0.12	1.21	0.09
	13.4	Frugivore (fruit)	6.85	0.51	5.07	0.38	3.27	0.24	2.42	0.18
	13.4	Herbivore (short grass)	48.95	**3.65**	36.23	**2.70**	17.39	**1.30**	12.87	0.96
	13.4	Herbivore (long grass)	29.89	**2.23**	22.12	**1.65**	9.76	0.73	7.22	0.54
	13.4	Herbivore (forage crops)	45.29	**3.38**	33.52	**2.50**	14.97	**1.12**	11.08	0.83
Reproduction	25.0	Insectivore	22.13	0.89	16.37	0.65	15.28	0.61	11.31	0.45
	25.0	Granivore (grain and seeds)	3.42	0.14	2.53	0.10	1.63	0.07	1.21	0.05
	25.0	Frugivore (fruit)	6.85	0.27	5.07	0.20	3.27	0.13	2.42	0.10
	25.0	Herbivore (short	48.95	**1.9**	36.23	**1.4**	17.3	0.7	12.8	0.5

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off-field[3]		On-field		Off-field[3]	
	Toxicity (mg a.i./kg bw/d)	**Food Guild (food item)**	**EDE (mg a.i./kg bw)[1]**	**RQ[2]**	**EDE (mg a.i./kg bw)[1]**	**RQ[2]**	**EDE (mg a.i./kg bw)[1]**	**RQ[2]**	**EDE (mg a.i./kg bw)[1]**	**RQ[2]**
		grass)		**6**		**5**	9	0	7	1
	25.0	Herbivore (long grass)	29.89	**1.20**	22.12	0.88	9.76	0.39	7.22	0.29
	25.0	Herbivore (Broadleaf plants)	45.29	**1.81**	33.52	**1.34**	14.97	0.60	11.08	0.44
Large Sized Mammal (1 kg)										
Acute	13.4	Insectivore	11.82	0.88	8.75	0.65	8.16	0.61	6.04	0.45
	13.4	Granivore (grain and seeds)	1.83	0.14	1.35	0.10	0.87	0.07	0.65	0.05
	13.4	Frugivore (fruit)	3.66	0.27	2.71	0.20	1.75	0.13	1.29	0.10
	13.4	Herbivore (short grass)	26.16	**1.95**	19.36	**1.44**	9.29	0.69	6.87	0.51
	13.4	Herbivore (long grass)	15.97	**1.19**	11.82	0.88	5.22	0.39	3.86	0.29
	13.4	Herbivore (Broadleaf plants)	24.20	**1.81**	17.91	**1.34**	8.00	0.60	5.92	0.44
Reproduction	25.0	Insectivore	11.82	0.47	8.75	0.35	8.16	0.33	6.04	0.24
	25.0	Granivore (grain and seeds)	1.83	0.07	1.35	0.05	0.87	0.03	0.65	0.03
	25.0	Frugivore (fruit)	3.66	0.15	2.71	0.11	1.75	0.07	1.29	0.05
	25.0	Herbivore (short grass)	26.16	**1.05**	19.36	0.77	9.29	0.37	6.87	0.27
	25.0	Herbivore (long grass)	15.97	0.64	11.82	0.47	5.22	0.21	3.86	0.15
	25.0	Herbivore (Broadleaf plants)	24.20	0.97	17.91	0.72	8.00	0.32	5.92	0.24

[1] EDE calculation as per footnote in screening level table.
[2] RQs exceeding the level of concern are in bold.
[3] Off-field EECs are calculated by adjusting the in-field EECs by a drift factor of 74% for early airblast application (the most for any application method permitted for fenazaquin EPs).

Table 28 Screening level risk assessment for non-target aquatic organisms

Organism	Exposure	Endpoint value (mg a.i./L)	EEC[1] (mg a.i./L)	RQ	Level of Concern[2]
Freshwater species					
Invertebrate, *Daphnia magna*	Acute – a.i.	EC_{50}/2: 0.0028	0.067	**24.1**	**Exceeded**
	Acute – Fenazaquin propionic acid (TP)	EC_{50}/2: 1.15	0.074	0.06	Not exceeded
	Acute – 2,4-TBPE (TP)	EC_{50}/2: 1.93	0.039	0.02	Not exceeded
	Chronic – a.i.	NOAEC: 0.00052	0.067	**129.6**	**Exceeded**
	Chronic – EP, 200 g/L SC	NOAEC: 0.00020	0.067	**337.0**	**Exceeded**
Midge, *Chironomus riparius*	Chronic – a.i. (spiked water)	NOEC: 0.00067	0.067	**100.6**	**Exceeded**
Rainbow trout, *Oncorhynchus mykiss*	Acute – a.i.	LC_{50}/10: 0.00039	0.067	**172.8**	**Exceeded**
	Acute – EP, 200 g/L SC	LC_{50}/10: 0.0041	0.067	**16.4**	**Exceeded**
	Acute – Fenazaquin propionic acid (TP)	LC_{50}/10: 0.0735	0.074	1.0	Not exceeded
	Acute – 2,4-TBPE (TP)	LC_{50}/10: 1.33	0.039	0.03	Not exceeded
	Chronic – EP, 200 g/L SC	NOAEC: 0.0057	0.067	**11.8**	**Exceeded**
	ELS – a.i.	NOAEC: 0.00095	0.067	**70.9**	**Exceeded**
Bluegill sunfish, *Lepomis macrochirus*	Acute – a.i.	LC_{50}/10: 0.00341	0.067	**19.8**	**Exceeded**
Amphibians (using fish data as a surrogate)	Acute – a.i.	LC_{50}/10: 0.00039	0.36	**921.6**	**Exceeded**
	ELS – a.i.	NOAEC: 0.00095	0.36	**378.4**	**Exceeded**
Diatom, *Navicula pelliculosa*	Acute – a.i.	EC_{50}/2: >0.0227	0.067	**<3.0**	**Exceeded**
Green algae, *Pseudokirchneriella subcapitata*	Acute – a.i.	EC_{50}/2: >0.104	0.067	<0.6	Not exceeded
	Acute – Fenazaquin propionic acid (TP)	EC_{50}/2: 3.8	0.074	0.02	Not exceeded

Organism	Exposure	Endpoint value (mg a.i./L)	EEC[1] (mg a.i./L)	RQ	Level of Concern[2]
Green algae, *Scenedesmus subspicatus*	Acute – EP, 200 g/L SC	EC_{50}/2: 3.6	0.067	0.02	Not exceeded
Blue-green algae, *Anabaena flos-aquae*	Acute – a.i.	EC_{50}/2: >0.0394	0.067	**<1.7**	**Exceeded**
Aquatic vascular plants, *Lemna gibba*	Acute – a.i.	EC_{50}/2: >0.03755	0.067	**<1.8**	**Exceeded**
Marine species					
Mollusc, Eastern oyster, *Crassostrea virginica*	Acute – a.i.	EC_{50}/2: 0.00195	0.067	**34.6**	**Exceeded**
Crustacean, brown shrimp, *Crangon crangon*	Acute – a.i.	LC_{50}/2: 0.0105	0.067	**6.4**	**Exceeded**
Crustacean, mysid shrimp, *Americamysis bahia*	Acute – a.i.	LC_{50}/2: 0.0025	0.067	**27.0**	**Exceeded**
Marine diatom, *Skeletonema costatum*	Acute – a.i.	EC_{50}/2: 0.00042	0.067	**160.5**	**Exceeded**
Sheepshead minnow, *Cyprinodon variegatus*	Acute – a.i.	LC_{50}/10: 0.00432	0.067	**15.6**	**Exceeded**

[1] EEC calculated assuming direct overspray at the maximum Canadian rate of one application of 539.15 g a.i./ha, and complete mixing in a water body of 15-cm depth for amphibians, and 80-cm depth for all other organisms. EECs for transformation products were calculated assuming 100% conversion of the parent fenazaquin, and were the parent EEC multiplied by the molar ratio between the transformation product and parent fenazaquin (178.28/306.4 for 2,4-TBPE and 338.41/306.4 for fenazaquin propionic acid).
[2] Level of Concern = 1

Table 29 Risk assessment for aquatic organisms exposed to cranberry floodwater

Organism (exposure)	Endpoint (mg a.i./L)	RQ[1]	Level of Concern[2]
Freshwater species			

Organism (exposure)	Endpoint (mg a.i./L)	RQ[1]	Level of Concern[2]
Invertebrate, *Daphnia magna* (acute; 48 hours; technical fenazaquin)	EC_{50}/2: 0.0028	0.11	Not exceeded
Invertebrate, *Daphnia magna* (chronic; 21 days; technical fenazaquin)	NOAEC: 0.00052	0.60	Not exceeded
Invertebrate, *Daphnia magna* (chronic; 21 days; EP, 200 g/L SC)	NOAEC: 0.0002	**1.55**	**Exceeded**
Invertebrate, *Chironomus riparius* (chronic spiked water; 28 days; technical fenazaquin)	NOEC: 0.00067	0.46	Not exceeded
Fish, *Oncorhynchus mykiss* (acute; 96 hours; technical fenazaquin)	LC_{50}/10: 0.00039	0.79	Not exceeded
Fish, *Oncorhynchus mykiss* (acute; 96 hours; EP, 200 g/L SC)	LC_{50}/10: 0.0041	0.08	Not exceeded
Fish, *Oncorhynchus mykiss* (chronic; 21 days; EP, 200 g/L SC)	NOAEC: 0.0057	0.05	Not exceeded
Fish, *Oncorhynchus mykiss* (ELS; 63 days; technical fenazaquin)	NOAEC: 0.00095	0.33	Not exceeded
Fish, *Lepomis macrochirus* (acute; 96 hours; technical fenazaquin)	LC_{50}/10: 0.00341	0.09	Not exceeded
Amphibians (acute; 96 hours; technical fenazaquin)[3]	LC_{50}/10: 0.00039	0.79	Not exceeded
Amphibians (chronic; 63 days; technical fenazaquin)[3]	NOAEC: 0.00095	0.33	Not exceeded
Algae, *Navicula pelliculosa* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: >0.0227	<0.01	Not exceeded
Algae, *Anabaena flos-aquae* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: >0.0394	<0.01	Not exceeded
Marine species			
Invertebrate, *Crassostrea virginica* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: 0.00195	0.16	Not exceeded

Organism (exposure)	Endpoint (mg a.i./L)	RQ[1]	Level of Concern[2]
Invertebrate, *Crangon crangon* (acute; 96 hours; technical fenazaquin)	LC_{50}/2: 0.0105	0.03	Not exceeded
Invertebrate, *Americamysis bahia* (acute; 96 hours; technical fenazaquin)	LC_{50}/2: 0.0025	0.12	Not exceeded
Algae, *Skeletonema costatum* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: 0.00042	0.74	Not exceeded
Fish, *Cyprinodon variegatus* (acute; 96 hours; technical fenazaquin)	LC_{50}/10: 0.00432	0.07	Not exceeded

[1] EEC: 0.00031 mg a.i./L, based on the maximum Canadian rate for cranberry, one application of 479.7 g a.i./ha and a cranberry field-floodwater model. The model simulates pesticide degradation in the soil of treated cranberry fields, pesticide movement from the soil to water following flooding, and mixing of flood water with water draining from the soil after the flood. The floodwater moves sequentially through a series of five model cranberry fields. The same chemical fate parameters were used as for runoff modelling. Further modelling details are available upon request.
[2] Level of Concern = 1
[3] Using fish data as a surrogate

Table 30 Refined risk assessment for aquatic organisms exposed to spray drift from early season airblast application

Organism (exposure)	Endpoint (mg a.i./L)	Refined EEC (mg a.i./L)[1]	RQ	Level of Concern[2]
Freshwater species				
Invertebrate, *Daphnia magna* (acute; 48 hours; technical fenazaquin)	EC_{50}/2: 0.0028	0.050	**17.8**	**Exceeded**
Invertebrate, *Daphnia magna* (chronic; 21 days; technical fenazaquin)	NOAEC: 0.00052	0.050	**95.9**	**Exceeded**
Invertebrate, *Daphnia magna* (chronic; 21 days; EP, 200 g/L SC)	NOAEC: 0.00020	0.050	**249.4**	**Exceeded**
Invertebrate, *Chironomus riparius* (chronic spiked water; 28 days; technical fenazaquin)	NOEC: 0.00067	0.050	**74.4**	**Exceeded**

Organism (exposure)	Endpoint (mg a.i./L)	Refined EEC (mg a.i./L)[1]	RQ	Level of Concern [2]
Fish, *Oncorhynchus mykiss* (acute; 96 hours; technical fenazaquin)	LC_{50}/10: 0.00039	0.050	**127.9**	**Exceeded**
Fish, *Oncorhynchus mykiss* (acute; 96 hours; EP, 200 g/L SC)	LC_{50}/10: 0.0041	0.050	**12.2**	**Exceeded**
Fish, *Oncorhynchus mykiss* (chronic; 21 days; EP, 200 g/L SC)	NOAEC: 0.0057	0.050	**8.7**	**Exceeded**
Fish, *Oncorhynchus mykiss* (ELS; 63 days; technical fenazaquin)	NOAEC: 0.00095	0.050	**52.5**	**Exceeded**
Fish, *Lepomis macrochirus* (acute; 96 hours; technical fenazaquin)	LC_{50}/10: 0.00341	0.050	**14.6**	**Exceeded**
Amphibians (acute; 96 hours; technical fenazaquin)[3]	LC_{50}/10: 0.00039	0.27	**682.0**	**Exceeded**
Amphibians (chronic; 63 days; technical fenazaquin)[3]	NOAEC: 0.00095	0.27	**280.0**	**Exceeded**
Algae, *Navicula pelliculosa* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: >0.0227	0.050	**<2.2**	**Exceeded**
Algae, *Anabaena flos-aquae* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: >0.0394	0.050	**<1.3**	**Exceeded**
Marine species				
Invertebrate, *Crassostrea virginica* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: 0.00195	0.050	**25.6**	**Exceeded**
Invertebrate, *Crangon crangon* (acute; 96 hours; technical fenazaquin)	LC_{50}/2: 0.0105	0.050	**4.7**	**Exceeded**
Invertebrate, *Americamysis bahia* (acute; 96 hours; technical fenazaquin)	LC_{50}/2: 0.0025	0.050	**19.9**	**Exceeded**
Algae, *Skeletonema costatum* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: 0.00042	0.050	**118.7**	**Exceeded**

Organism (exposure)	Endpoint (mg a.i./L)	Refined EEC (mg a.i./L)[1]	RQ	Level of Concern [2]
Fish, *Cyprinodon variegatus* (acute; 96 hours; technical fenazaquin)	LC_{50}/10: 0.00432	0.050	**11.5**	**Exceeded**

[1] Refined EECs adjust the screening level EECs by a drift factor of 74% for early airblast application (the most for any application method permitted for fenazaquin EPs).
[2] Level of Concern = 1
[3] Using fish data as a surrogate.

Table 31 Modelled EECs in water bodies resulting from input of surface runoff for the refined risk assessment for aquatic organisms

Use (g a.i./ha)	Water depth	Water column concentration (µg a.i./L)[1]				
		Peak	24-hour	96-hour	21-day	60-day
1 × 539.15	80-cm	8.6	6.7	5.4	4.9	4.8
	15-cm	28	9.5	7.5	7.1	7.1

[1] EECs were calculated with the Pesticide in Water Calculator model (version 1.52) which simulates runoff from a treated field into a small adjacent reservoir with a depth of either 15-cm (for amphibians) or 80-cm (for all other organisms), and fenazaquin partitioning and degradation in water and sediment. The maximum Canadian rate of one single application of 539.15 g a.i./ha was used in several model scenarios which represent different regions of Canada. Scenarios were run for 50 years each. The highest EECs of all model runs for various time periods of relevance for acute and chronic endpoints are selected for this table. Further details of water modelling inputs and calculations are available upon request.

Table 32 Refined risk assessment for aquatic organisms exposed to runoff

Organism (exposure)	Endpoint (mg a.i./L)	Refined EEC[1] (mg a.i./L)	RQ	Level of Concern[2]
Freshwater species				
Invertebrate, *Daphnia magna* (acute; 48 hours; technical fenazaquin)	EC_{50}/2: 0.0028	0.0067	**2.39**	**Exceeded**
Invertebrate, *Daphnia magna* (chronic; 21 days; technical fenazaquin)	NOAEC: 0.00052	0.0049	**9.42**	**Exceeded**
Invertebrate, *Daphnia magna* (chronic; 21 days; EP, 200 g/L SC)	NOAEC: 0.0002	0.0049	**24.5**	**Exceeded**
Invertebrate, *Chironomus riparius* (chronic spiked water; 28 days; technical fenazaquin)	NOEC: 0.00067	0.0049	**7.31**	**Exceeded**

Organism (exposure)	Endpoint (mg a.i./L)	Refined EEC[1] (mg a.i./L)	RQ	Level of Concern[2]
Fish, *Oncorhynchus mykiss* (acute; 96 hours; technical fenazaquin)	LC_{50}/10: 0.00039	0.0054	**13.8**	**Exceeded**
Fish, *Oncorhynchus mykiss* (acute; 96 hours; EP, 200 g/L SC)	LC_{50}/10: 0.0041	0.0054	**1.32**	**Exceeded**
Fish, *Oncorhynchus mykiss* (chronic; 21 days; EP, 200 g/L SC)	NOAEC: 0.0057	0.0049	0.86	Not exceeded
Fish, *Oncorhynchus mykiss* (ELS; 63 days; technical fenazaquin)	NOAEC: 0.00095	0.0048	**5.05**	**Exceeded**
Fish, *Lepomis macrochirus* (acute; 96 hours; technical fenazaquin)	LC_{50}/10: 0.00341	0.0054	**1.58**	**Exceeded**
Amphibians (acute; 96 hours; technical fenazaquin)[3]	LC_{50}/10: 0.00039	0.0075	**19.2**	**Exceeded**
Amphibians (chronic; 63 days; technical fenazaquin)[3]	NOAEC: 0.00095	0.0071	**7.47**	**Exceeded**
Algae, *Navicula pelliculosa* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: >0.0227	0.0054	<0.24	Not exceeded
Algae, *Anabaena flos-aquae* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: >0.0394	0.0054	<0.14	Not exceeded
Marine species				
Invertebrate, *Crassostrea virginica* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: 0.00195	0.0054	**2.77**	**Exceeded**
Invertebrate, *Crangon crangon* (acute; 96 hours; technical fenazaquin)	LC_{50}/2: 0.0105	0.0054	0.51	Not exceeded
Invertebrate, *Americamysis bahia* (acute; 96 hours; technical fenazaquin)	LC_{50}/2: 0.0025	0.0054	**2.16**	**Exceeded**
Algae, *Skeletonema costatum* (acute; 96 hours; technical fenazaquin)	EC_{50}/2: 0.00042	0.0054	**12.9**	**Exceeded**
Fish, *Cyprinodon variegatus* (acute; 96 hours; technical fenazaquin)	LC_{50}/10: 0.00432	0.0054	**1.25**	**Exceeded**

Organism (exposure)	Endpoint (mg a.i./L)	Refined EEC[1] (mg a.i./L)	RQ	Level of Concern[2]

[1] Using 24-h EECs for 48-h endpoints, 96-h EECs for 96-h endpoints, 21-d EECs for 21- and 28-d endpoints, and 60-d EECs for 63-d endpoints.
[2] Level of Concern = 1
[3] Using fish data as a surrogate.

Table 33 Toxic Substances Management Policy considerations – Comparisons to TSMP Track 1 criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Fenazaquin Endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]	Soil	Half-life ≥ 182 days	No: 46 days (laboratory, aerobic) Yes: 320 days (laboratory, anaerobic)
	Water	Half-life ≥ 182 days	No: 26 to 163 days (laboratory; total aerobic system)
	Sediment	Half-life ≥ 365 days	
	Air	Half-life ≥ 2 days or evidence of long range transport	Not determined. The AOPWIN model is not suited for predicting the atmospheric half-life of fenazaquin given the large fraction expected to be sorbed to airborne particles.
Bioaccumulation[4]	Log K_{OW} ≥ 5		Yes: 5.51 to 6.19
	BCF ≥ 5000		No: 1354
	BAF ≥ 5000		Not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No: does not meet all four TSMP Track 1 criteria.

[1] All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (in other words, all other TSMP criteria are met).

[2] The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.

TSMP Track 1 Criteria	TSMP Track 1 Criterion value	Fenazaquin Endpoints
[4] Field data (e.g., BAFs) are preferred over laboratory data (e.g., BCFs), which, in turn are preferred over chemical properties (e.g., log K_{OW}).		

Table 34 List of supported uses

All supported uses are for control of the listed pests with a maximum of one (outdoor) or two (indoor) foliar applications per year using conventional ground equipment. Indoor uses are for ornamentals only (greenhouse ornamentals, including fruit and nut tree seedlings, and indoor plants and plantscapes).

Crop or Site	Pest(s)	Application Rate(s) (volume of product)	Spray Volume
Supported Use Claims for Magister SC Miticide/Fungicide			
Bushberries (Crop Subgroup 13-07B)	Blueberry bud mite	1.75 L/ha	Minimum 500 L/ha
	Twospotted spider mite, European red mite, McDaniel spider mite, Pacific spider mite	1.75–2.34 L/ha	
Caneberries (Crop Subgroup 13-07A)	Twospotted spider mite, European red mite, McDaniel spider mite, Pacific spider mite	1.75–2.34 L/ha	Minimum 500 L/ha
Cucurbit Vegetables (Crop Group 9)	Twospotted spider mite, McDaniel spider mite, Pacific spider mite	1.75–2.34 L/ha	Minimum 250 L/ha
	Powdery mildew (*Golovinomyces cichoracearum* and *Podosphaera xanthii*)	1.75–2.63 L/ha	
Fruiting Vegetables (Crop Group 8-09)	Twospotted spider mite, McDaniel spider mite, Pacific spider mite	1.75–2.34 L/ha	Minimum 250 L/ha
Low Growing Berries (Crop Subgroup 13-07G)	Twospotted spider mite, McDaniel spider mite, Pacific spider mite	1.75–2.34 L/ha	Minimum 500 L/ha
Pome Fruits (Crop Group 11-09)	Apple rust mite, pear rust mite	1.75 L/ha	Minimum 500 L/ha
	European red mite,	1.75–2.34 L/ha	

Crop or Site	Pest(s)	Application Rate(s) (volume of product)	Spray Volume
	McDaniel spider mite, Pacific spider mite, twospotted spider mite		
	Pear psylla on pears only Powdery mildew (*Podosphaera leucotricha*)	1.75–2.63 L/ha	
Small Fruit Vine Climbing, Except Fuzzy Kiwifruit (Crop Subgroup 13-07F)	European red mite, McDaniel spider mite, Pacific spider mite, twospotted spider mite	1.75–2.34 L/ha	Minimum 500 L/ha
	Powdery mildew (*Erysiphe necator*) on Amur river grape and grape only	1.75–2.63 L/ha	
Stone Fruits (Crop Group 12-09)	European red mite, McDaniel spider mite, Pacific spider mite, twospotted spider mite	1.75–2.34 L/ha	Minimum 500 L/ha
	Powdery mildew (*Podosphaera clandestina*)	1.75–2.63 L/ha	
Supported Use Claims for both Magister SC Miticide/Fungicide and Magus SC Miticide			
Ornamental plants, including fruit and nut tree seedlings (greenhouse)	Twospotted spider mite, European red mite, McDaniel spider mite, Pacific spider mite	300-750 mL / 400 L spray volume	Maximum 1000 L/ha
	Sweetpotato whitefly	750-1000 mL / 400 L spray volume	
Ornamental plants, including non-bearing fruit and nut trees (field grown, outdoor nursery, shadehouse)	Twospotted spider mite, European red mite, McDaniel spider mite, Pacific spider mite	300-750 mL / 400 L spray volume	Maximum 1000 L/ha

Crop or Site	Pest(s)	Application Rate(s) (volume of product)	Spray Volume
Indoor ornamental plants and plantscapes	Twospotted spider mite, European red mite, McDaniel spider mite, Pacific spider mite	300-750 mL / 400 L spray volume	Maximum 1000 L/ha
	Sweetpotato whitefly	750-1000 mL / 400 L spray volume	
Established ornamental landscape plantings (outdoors)	Twospotted spider mite, European red mite, McDaniel spider mite, Pacific spider mite	300-750 mL / 400 L spray volume	Maximum 1000 L/ha

Appendix II Supplemental Maximum Residue Limit information—International situation and trade implications

Fenazaquin is an active ingredient that is currently being registered in Canada for foliar use on berries (caneberries, bushberries and low growing berries), cucurbit vegetables, fruiting vegetables, pome fruits, small vine climbing fruit (except fuzzy kiwifruit), and stone fruits. The MRLs proposed for fenazaquin in Canada, including imported citrus fruits are the same as corresponding tolerances established in the United States.

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data.

Table 1 compares the MRLs proposed for fenazaquin in Canada with corresponding American tolerances and Codex MRLs.[9] American tolerances are listed in the Electronic Code of Federal Regulations, 40 CFR Part 180, by pesticide. A listing of established Codex MRLs is available on the Codex Alimentarius Pesticide Index webpage, by pesticide or commodity.

Table 1 Comparison of proposed Canadian MRLs, American tolerances and Codex MRLs (where different)

Food Commodity	Canadian MRL (ppm)	American Tolerance (ppm)	Codex MRL (ppm)
Citrus oil	20	20	Not established
Stone Fruits Crop Group 12-09	2	2	2 [Cherries]
Low growing Berries Crop Subgroup 13-07G	2	2	Not established
Bushberries Crop Subgroup 13-07B	0.8	0.8	Not established
Raisins	0.8	0.8	Not established
Caneberries Crop Subgroup 13-07A	0.7	0.7	Not established

[9] The Codex Alimentarius Commission is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

Food Commodity	Canadian MRL (ppm)	American Tolerance (ppm)	Codex MRL (ppm)
Small fruit vine climbing, except fuzzy kiwifruit, Crop Subgroup 13-07F	0.7	0.7	Not established
Pome Fruits Crop Subgroup 11-09	0.6	0.6	Not established
Citrus Fruits (revised) Crop Group10	0.4	0.4	Not established
Fruiting Vegetables Crop Group 8-09	0.3	0.3	Not established
Cucurbit Vegetables Crop Group 9	0.3	0.3	Not established

References

A. List of studies/Information submitted by registrant

1.0 Chemistry

PMRA Document Number	Reference
3009917	2019, Fenazaquin process technology package, DACO: 2.11,2.13.3 CBI
2962727	2018, Group A: Product identity and composition, description of materials used to produce the product, description of production process, theoretical discussion of impurities, preliminary analysis, and enforcement analytical method for a new source of fenazaquin technical grade active ingredient., DACO: 3.4.1 CBI
3009918	1998, OPPTS 830.1620 Description of manufacturing process for fenazaquin technical: supplemental information for Argentina. Doc. No.: 121-001., DACO: 2.11,2.13.3 CBI
3009919	2007, 91/4141/EEC Review of fenazaquin five batch analysis and specification, DACO: 2.11,2.13.3 CBI
2962459	2018, Analysis of active ingredient and impurities in fenazaquin technical material under GLP-revised., DACO: 2.12.1,2.13.1,2.13.2,2.13.3 CBI
2962467	1999, Determination of physical state, colour and odour and estimation of photochemical oxidative degradation of fenazaquin; Dow AgroSciences Europe., DACO: 2.14,2.14.1,2.14.2,2.14.3,8.2.3,8.2.3.3,8.2.3.4.4 CBI
2962471	1992, XDE 436 (Technical): Determination of physico-chemical properties, DACO: 2.14,2.14.11,2.14.2,2.14.3,2.14.4,2.14.5,2.14.6,2.14.7 CBI
2962472	2006, Solubility of fenazaquin in various organic solvents, DACO: 2.14,2.14.8 CBI
2962468	1993, Determination of the dissociation constant of XDE 436 (technical), DACO: 2.14,2.14.10 CBI
2962473	1991, Vapor pressure of EL-436, DACO: 2.14,2.14.9 CBI
2962469	1989, Octanol/water partition coefficient of El 436, DACO: 2.14,2.14.11 CBI
2962476	2007, Physical properties of fenazaquin, DACO: 2.14,2.14.12,2.14.4,2.14.5 CBI
2962470	2011, Determination of stability to normal and elevated temperature, and corrosion characteristics of fenazaquin, DACO: 2.14,2.14.13 CBI
3157065	2020, Fenazaquin Technical: Physical and chemical characteristics: color, physical state, odor, stability to normal and elevated temperatures, ph, uv/visible absorption, melting point, bulk density, dissociation constant, partition coefficient, water solubility, and vapor pressure, DACO: 2.14.15,830.7000 CBI
2962726	2007, Production information for Fenazaquin 200 SC, DACO: 3.2,3.2.1,3.2.2,3.2.3,3.3.1 CBI
2962460	1992, Analytical method: XDE 436 SC Acaricide., DACO: 2.13,2.13.1 CBI
2962724	2009, SC formulation containing 200 g/L fenazaquin: storage stability, DACO: 3.0,3.5,3.5.10

PMRA Document Number	Reference
3168722	2013, Validation of the methods of determination of fenazaquin in a suspension concentrate formulation, in compliance with Good Laboratory Practice, DACO: 3.4.1 CBI
2962728	1990, Physical and chemical stability of Magister SC: EF 1127., DACO: 3.5, 3.5.1, 3.5.10, 3.5.13, 3.5.2, 3.5.3, 3.5.6, 3.5.7, 3.5.9 CBI
2962730	1996, Packaging storage stability trial for Fenazaquin 200 G/L SC Acaricide, EF-1127., DACO: 3.5.10, 3.5.13 CBI
2996843	2019, Chemistry requirements for the registration of manufacturing concentrates and end-use products formulated from registered technical grade of active ingredients or integrated system products., DACO: 3.0,3.1, 3.1.1, 3.1.2, 3.1.3, 3.1.4, 3.5.11, 3.5.12, 3.5.5 CBI
2962732	2003, Statement on the oxidizing properties of Magister 200 SC., DACO: 3.5.8 CBI
2962746	2010, Independent laboratory validation of enforcement method for the analysis of fenazaquin, 2-oxy-fenazaquin and 4-hydroxyquinazoline in soil., DACO: 171 - 4a,171 - 4c,171 - 4m,171-4a-4b,171-4c-4d,7.2,7.2.2,7.2.3A,860.1300,860.1340,860.1360,IIA 4.2.6,IIIA 5.3.1,b,d
3047643	2010, Analytical method report for the analysis of fenazaquin, 2-oxy-fenazaquin and 4-OHQ in soil, DACO: 8.2,8.2.2,8.2.2.1 CBI
3157069	2010, Terrestrial field dissipation of fenazaquin and its metabolites following one application of GWN-1708 to bare soil, DACO: 8.2.2.1
3168980	2009, 4-*Tert*-butylphenethyl alcohol (TBPE): degradation rate in three soils incubated under aerobic conditions, DACO: 8.2.2.1
2962538	2003, Fenazaquin: development and validation of the residue analytical method for fenazaquin in drinking, ground and surface water., DACO: 8.2.1,8.2.2,8.2.2.1,8.2.2.3
3168974	2007, Acute toxicity of 2-oxy-fenazaquin on *Chironomus riparius*, DACO: 8.2.2.3
3168976	2007, 4-Hydroxyquinazoline: Acute toxicity to *Daphnia Magna* in a 48-Hour immobilization test, DACO: 8.2.2.3
3168977	2007, 4-Hydroxyquinazoline: Acute toxicity to rainbow trout (*Oncorhynchus mykiss*) in a 96-hour static test, DACO: 8.2.2.3
2962595	1997, Fenazaquin propionic acid metabolite: acute toxicity to rainbow trout., DACO: 8.2.2.3,9.5,9.5.2,9.5.2.1
3168978	1997, Fenazaquin propionic acid metabolite: acute toxicity to *Daphnia Magna*, DACO: 8.2.2.3
2962596	1992, 2-(4-*Tert*-butylphenyl) ethanol: Acute toxicity to rainbow trout: final report., DACO: 8.2.2.3,9.5,9.5.2,9.5.2.1
3102692	1992, 2-(4-*Tert*-butylphenyl) ethanol: Acute toxicity to *Daphnia Magna*., DACO: 9.3,9.3.2

2.0 Human and Animal Health

PMRA Document Number	Reference
2962479	1990, The acute toxicity of Technical EL-436 (compound 193136) administered orally to Fischer 344 rats, DACO: 4.2,4.2.1
2962480	1990, The acute inhalation toxicity of EL-436 (Compound 193136) in the Fischer 344 rat, DACO: 4.2,4.2.3
2962481	1989, The acute ocular irritation of EL-436 (Compound 193136) in the New Zealand White rabbit, DACO: 4.2,4.2.4
2962482	1989, A guinea pig sensitization study of EL-436 (Compound 193136), DACO: 4.2,4.2.6
2962483	1994, Fenazaquin (Magister F): Magnusson & Kligman maximisation study in the guinea pig., DACO: 4.2,4.2.6
2962484	2009, GWN-1708: Dermal sensitization study in guinea pigs (Buehler method)., DACO: 4.2,4.2.6
2962485	1989, The acute dermal toxicity and primary dermal irritation of EL-436 (Compound 193136) in the New Zealand White rabbit, DACO: 4.2,4.2.2,4.2.5
2962486	1992, A subchronic toxicity study in fischer 344 rats given EL-436 (Compound 193136) in the diet for 3 months, DACO: 4.3,4.3.1
2962487	1992, A subchronic toxicity in syrian golden hamsters treated orally with EL-436 (Compound 193136) for 3 months, DACO: 4.3,4.3.1
2962488	1992, A subchronic toxicity study in Fischer 344 rats treated orally with EL-436 (Compound 193136) for 3 months followed by a 1-month reversibility period, DACO: 4.3,4.3.1
2962489	1992, XDE-436: 13-Week dietary toxicity study in beagle dogs; The Toxicology Research Laboratory, DACO: 4.3,4.3.2
2962490	1991, XDE-436: Palatability probe and two-week repeated dosing toxicity study in beagle dogs., DACO: 4.3,4.3.2
2962491	1993, XDE-436:1-year dietary toxicity study in beagle dogs., DACO: 4.3,4.3.2,4.4,4.4.1
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2962589	2010, Fenazaquin: A 96-hour static acute toxicity test with the saltwater mysid (*Americamysis bahia*): Final report., DACO: 9.4,9.4.2
2962590	2011, Fenazaquin: An acute oral toxicity study with the zebra finch (*Poephila guttata*)., DACO: 9.6,9.6.2,9.6.2.3
2962591	1998, Fenazaquin Technical: Toxicity to the sediment dwelling phase of the midge *Chironomus riparius*., DACO: 9.3.4
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2962593	1993, Influence of suspended sediment on the acute toxicity of EL-436 (Compound 193136) to rainbow trout (*Oncorhynchus mykiss*) in a static-renewal test system., DACO: 9.5,9.5.2,9.5.2.1
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2962596	1992, 2-(4-*Tert*-butylphenyl) ethanol: acute toxicity to rainbow trout: Final report., DACO: 9.5,9.5.2,9.5.2.1
2962597	2010, Fenazaquin: A 96-hour static acute toxicity test with the sheepshead minnow (*Cyprinodon variegatus*): Final report., DACO: 9.5,9.5.2,9.5.2.1
2962598	1990, The acute toxicity of EL-436 (Compound 193136) to bluegill (*Lepomis macrochirus*) in a flow-through test system., DACO: 9.5,9.5.2,9.5.2.2
2962599	1992, EF 1127: Prolonged toxicity to rainbow trout (*Oncorhynchus mykiss*)., DACO: 9.5,9.5.3,9.5.3.1
2962600	1992, The toxicity of EL-436 to rainbow trout (*Oncorhynchus mykiss*) in a 63-day early life-stage study., DACO: 9.5,9.5.3,9.5.3.1
2962601	1992, the assessment of bioaccumulation of c^{14}-fenazaquin in rainbow trout., DACO: 9.5.6
2962602	1989, The toxicity of EL-436 (Compound 193136) to bobwhite in a 19-day acute oral study: (GWN-1708 Miticide/Insecticide)., DACO: 9.6,9.6.2,9.6.2.1
2962603	1989, The toxicity of EL-436 (Compound 193136) to mallards in a 14-day acute oral study., DACO: 9.6,9.6.2,9.6.2.2
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2962609	2010, Fenazaquin: A 96-hour toxicity test with the freshwater diatom (*Navicula pelliculosa*): Final report., DACO: 9.8,9.8.2
2962610	2010, Fenazaquin: A 96-hour toxicity test with the freshwater alga (*Anabaena flos-aquae*): Final report., DACO: 9.8,9.8.2
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2962614	1989, Influence of EL-436 on the germination of seeds of ten crop plants: (GWN-1708 Miticide/Insecticide)., DACO: 9.8,9.8.4
2962615	1989, Influence of EL-436 preemergence spray on the seedling emergence and vegetative vigor of ten crop plants: (GWN-1708 Miticide/Insecticide)., DACO: 9.8,9.8.4
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3039017	1989, Influence of EL-436 on the germination of seeds of ten crop plants, DACO: 9.8,9.8.4
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3102692	1992, 2-(4-*tert*-butylphenyl) ethanol: Acute toxicity to *Daphnia Magna*., DACO: 9.3,9.3.2
3096455	1997, Fenazaquin propionic acid metabolite: Acute toxicity to *Daphnia magna*, DACO: 9.3.1,9.3.2
3096457	1993, Influence of suspended sediment on the acute toxicity of EL-436 (Compound 193136) to *Daphnia magna* in a static test system, DACO: 9.3.1,9.3.2
2962830	1993, Dissipation of [14 carbon] XDE-436 in soil exposed to natural environmental conditions: (GWN-1708 Miticide/Insecticide), DACO: 8.3,8.3.1,8.3.2
2962831	2010, Terrestrial field dissipation of fenazaquin and its metabolites following one application of GWN-1708 to bare soil: final report, DACO: 8.3,8.3.1,8.3.2
2962832	1994, The dissipation of fenazaquin in soil at intervals following application of EF 1127 - Germany 1993, DACO: 8.3,8.3.1,8.3.2

2962833	1996, The dissipation of fenazaquin in soil at intervals following a single application of Magister 200 SC formulation (EF-1127): Italy - 1994, DACO: 8.3,8.3.1,8.3.2
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4.0 Value

PMRA Document Number	Reference
2996753	2019, Value summary to register the new products, Magister SC Miticide / Fungicide and Magustm SC Miticide / Fungicide, both containing the active ingredient, fenazaquin, for broad-spectrum control of listed insect and mite pests and powdery mildew in cucurbit vegetables, fruiting vegetables, hops, legume vegetables, succulent and dried shelled peas and beans, berries, mint, pome fruits, grape, stone fruits, corn (field and sweet), ornamentals, and greenhouse vegetables in Canada, DACO: 10.1, 10.2, 10.2.1, 10.2.2, 10.2.3, 10.2.3.1, 10.3, 10.3.1, 10.3.2
2996758	2017, GWN-10396, GWN-10250/powdery mildew, DACO: 10.2.3.3(C)
2996767	2008, GWN-1708 - grapes 2008, DACO: 10.2.3.3(C)
2996769	2009, Determine the effectiveness of GWN 1708 applied on grapes to control web spinning mites, DACO: 10.2.3.3(C)
2996770	2010, Evaluate GWN 1708 applied on grapes to control spider mites, DACO: 10.2.3.3(C)
2996771	2013, GWN-10250 grape powdery mildew., DACO: 10.2.3.3(C)
2996772	2014, Efficacy of GWN-10250 on PM when combined with various adjuvants, DACO: 10.2.3.3(C)
2996773	2014, Evaluation of Gwn-10250 for powdery mildew control in table grapes, DACO: 10.2.3.3(C)
2996774	2014, What level of disease activity will GWN-10250 provide against powdery mildew in grapes, DACO: 10.2.3.3(C)
2996775	2019, Products for control of grape mildew, DACO: 10.2.3.3(C)
2996776	2018, Powdery mildew merlot wine grapes/ Magister/ Nexter, DACO: 10.2.3.3(C)
2996777	2009, Efficacy of miticides for control of twospotted spider mite in strawberry, DACO: 10.2.3.3(C)
2996778	2009, GWN-1708 for twospotted mite control in strawberry., DACO: 10.2.3.3(C)

2996779	2013, Efficacy of GWN-1708 for the control of two-spotted spider mites in eggplants, DACO: 10.2.3.3(C)
2996780	2008, Control of blueberry budmite, 2008., DACO: 10.2.3.3(C)
2996781	2009, Field Studies of onager and GWN-1708 application rates for control of pacific spider mite stages in cherries, DACO: 10.2.3.3(C)
2996783	2009, GWN-1708: Control of European red and spider mites in peach, DACO: 10.2.3.3(C)
2996784	2012, Evaluate GWN-1708 and combinations with other miticides compare to standards for control of twospotted spider mites?, DACO: 10.2.3.3(C)
2996785	2012, Field studies GWN-1708 application rates for control of two-spotted spider mite in sweet cherries, DACO: 10.2.3.3(C)
2996786	2012, Control of TSSM on tart cherries at NWHRS, 2012, DACO: 10.2.3.3(C)
2996787	2016, Control of TSSM on tart cherries, DACO: 10.2.3.3(C)
2996788	2013, Control of Powdery Mildew in Cherry, DACO: 10.2.3.3(C)
2996789	2015, Evaluate labeled rates for mite control and powdery mildew in Cherries and record the residual control of both pests., DACO: 10.2.3.3(C)
2996790	2016, Tree Fruit Disease Management Trials, DACO: 10.2.3.3(C)
2996791	2014, Efficacy of GWN-1708 for the control of two-spotted spider mites in eggplants, DACO: 10.2.3.3(C)
2996792	2008, Apple: *Malus domestica* Borkhausen 'delicious' European red mite (ERM): *Panonychus ulmi* (Koch) twospotted spider mite (TSSM): *Tetranychus urticae* Koch mite predator (AF): *Amblyseius fallacis* (Garman), DACO: 10.2.3.3(C)
2996793	2008, Control of twospotted spider mite in D'Anjou Pears, DACO: 10.2.3.3(C)
2996794	2009, How does GWN-1708 compare with local standards in controlling key target mite pests (TSSM)?, DACO: 10.2.3.3(C)
2996795	2009, How does GWN-1708 compare with local standards in controlling key target mite pests?, DACO: 10.2.3.3(C)
2996796	2010, GWN 1708 for control of key mite species on pear, DACO: 10.2.3.3(C)
2996797	2010, GWN-1708 apple mites, DACO: 10.2.3.3(C)
2996798	2018, GOW18I01, DACO: 10.2.3.3(C)
2996799	2018, GWN 101732 & GWN 10250 for use against mites in Apples, DACO: 10.2.3.3(C)
2996800	2008, Nexter efficacy on pear psylla, DACO: 10.2.3.3(C)
2996801	2010, Are new pyridaben SC formulations equal in efficacy to Nexter for control of key pear pests (psylla and mites) and safe to crop?, DACO: 10.2.3.3(C)
2996803	2017, Control of pear psylla with Magister, DACO: 10.2.3.3(C)
2996804	2017, Magister for pear psylla, DACO: 10.2.3.3(C)
2996805	2013, GWN-10250 / Powdery mildew / apple, DACO: 10.2.3.3(C)
2996813	2013, Summer squash powdery mildew screen, DACO: 10.2.3.3(C)
2996816	2009, Efficacy of GWN-1708 and Sanmite for control of spider mites (*Tetranichus urticae* Koch) and whitefly (*Bemisia tabaci*) on Verbena under greenhouse conditions., DACO: 10.2.3.3(C)

2996817	2011, Determine the performance of fenazaquin (Magus) against the two-spotted spider mite, *Tetranychus urticae* under greenhouse conditions, DACO: 10.2.3.3(C)
2996820	2010, Effects of GWN-1715 and GWN-1708 on mortality of adults, eggs, and nymphs of *Bemisia tabaci* biotype B ON hibiscus, DACO: 10.2.3.3(C)
2996821	2009, Efficacy of GWN-1708 for control of silverleaf whitefly in greenhouse ornamentals, DACO: 10.2.3.3(C)
2996822	2009, Efficacy of GWN-1708 for control of twospotted spider mite in ornamentals, DACO: 10.2.3.3(C)
2996823	2010, Control of twospotted spider mite on greenhouse and outdoor ornamentals with foliar and drench miticides, DACO: 10.2.3.3(C)
2996824	2013, Acorn squash powdery mildew screen, DACO: 10.2.3.3(C)
2996826	2019, Magus efficacy against TSSM (*Tetranychus uticae*) on ornamentals, DACO: 10.2.3.3(C)
2996835	2014, Control of powdery mildew in winter squash with GWN-10176 10EC, GWN-10250 20SC, and GWN-10389 20EC, DACO: 10.2.3.3(C)
2996842	2014, Powdery mildew control in cantaloupe 2014, DACO: 10.2.3.3(C)

B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

PMRA Document Number	Reference
2356215	Mullet, Steven J., and David A. Hinkle, 2011, DJ-1 Deficiency in astrocytes selectively enhances mitochondrial complex 1 inhibitor-induced neurotoxicity - Journal of Neurochemistry, Volume 117, Pages 375 to 387, DACO: 4.8
2356217	Sherer, Todd B. et al, 2006, Mechanism of toxicity of pesticides acting at complex 1: relevance to environmental etiologies of Parkinson's disease - Journal of Neurochemistry, Volume 100, Pages 1469 to 1479, DACO: 4.8
3217396	2014, USEPA, Fenazaquin: Summary of Hazard and Science Policy Council (HASPOC) Meeting of April 10, 2014: Recommendations on the need for subchronic inhalation, subchronic dermal, rabbit developmental, and neurotoxicity studies., DACO: 12.5.4