Proposed Re-evaluation Decision PRVD2020-01

Fenhexamid and Its Associated End-use Products

Consultation Document

(publié aussi en français)

7 January 2020

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6607 D
Ottawa, Ontario K1A 0K9

Internet: canada.ca/pesticides
hc.pmra.publications-arla.sc@canada.ca
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
hc.pmra.info-arla.sc@canada.ca

Canada

ISSN: 1925-0959 (print)
1925-0967 (online)

Catalogue number: H113-27/2020-01E (print)
H113-27/2020-01E-PDF (PDF version)

Table of Contents

Proposed Re-evaluation Decision

Under the authority of the *Pest Control Products Act*, all registered pesticides must be regularly re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they continue to meet current health and environmental standards and continue to have value. The re-evaluation considers data and information from pesticide manufacturers, published scientific reports, and other regulatory agencies. Health Canada applies internationally accepted risk assessment methods as well as current risk management approaches and policies.

Fenhexamid is a foliar fungicide registered for use on greenhouse vegetables and ornamentals, as well as outdoor fruit trees, berries, ginseng, grapes, stone fruits and ornamentals. Currently registered products containing fenhexamid can be found in Appendix I.

This document presents the proposed regulatory decision for the re-evaluation of fenhexamid including the proposed risk mitigation measures to further protect human health and the environment, as well as the science evaluation on which the proposed decision was based. All products containing fenhexamid registered in Canada are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period, during which the public including the pesticide manufacturers and stakeholders may submit written comments and additional information to PMRA Publications. The final re-evaluation decision will be published taking into consideration the comments and information received.

Outcome of Science Evaluation

Fenhexamid controls gray mold on a wide variety of crops and ornamentals. It is an important rotational fungicide as it is the only Group 17 mode of action registered on several agricultural commodities for managing *Botrytis cinerea*, which is susceptible to developing fungicide resistance.

With respect to human health, risks have been shown to be acceptable with mitigation measures required for greenhouse and outdoor ornamentals grown for cut flowers. Exposure from the remaining uses is unlikely to affect human health when used according to the proposed label directions.

Fenhexamid enters the environment when used to control molds in a variety of agricultural food and feed crops and outdoor ornamentals or when it is present in discharge water from use in greenhouses. Based on available scientific information, potential risks to the environment have been shown to be acceptable when fenhexamid is used according to the proposed label directions.

Proposed Regulatory Decision for Fenhexamid

Under the authority of the *Pest Control Products Act*, and based on the evaluation of currently available scientific information, Health Canada is proposing that products containing fenhexamid are acceptable for continued registration in Canada, provided that the additional proposed risk mitigation measures are in place.

Proposed Risk Mitigation Measures

Registered pesticide product labels include specific directions for use. Directions include risk mitigation measures to protect human health and the environment and must be followed by law. As a result of the re-evaluation of fenhexamid, further risk mitigation measures, as summarized below, are being proposed for product labels. Refer to Appendix IX for details.

Human Health

To protect mixer/loader/applicators:

- Require that workers wear a minimum level of protective clothing, including chemical-resistant gloves;
- Require that workers wear additional personal protective equipment (PPE) when applying using handheld air blast/mistblower equipment.

To protect workers entering treated sites:

- Increase the minimum restricted entry interval (REI) from 4 to 12 hours;
- Increase the REIs for some postapplication activities in some crops;
- Reduce the number of applications for greenhouse and outdoor ornamentals grown for cut flower production

To protect bystanders from spray drift:

- Require a statement on end-use product labels to promote best management practices to minimize human exposure from spray drift or spray residues resulting from drift.

Environment

To protect the environment:

- Standard label statements to inform users of the potential toxic effect of fenhexamid to small mammals, fish and amphibians;
- Spray buffer zones up to 20 m to protect sensitive aquatic habitats;
- Precautionary label statements for sites with characteristics that may be conducive to runoff and when heavy rain is forecasted to reduce the potential for runoff of fenhexamid into adjacent aquatic habitats;
- A label statement directing users not to discharge fenhexamid-contaminated effluent from greenhouses into aquatic environments.

International Context

Fenhexamid is currently acceptable for use in other Organisation for Economic Co-operation and Development (OECD) member countries, including the United States, the EU, and Australia. No decision by an OECD member country to prohibit all uses of fenhexamid for health or environmental reasons has been identified.

Next Steps

The public including the registrants and stakeholders are encouraged to submit additional information that could be used to refine risk assessments during the 90-day public consultation period[1] upon publication of this proposed re-evaluation decision.

All comments received during the 90-day public consultation period will be taken into consideration in preparation of re-evaluation decision document[2], which could result in revised risk mitigation measures. The re-evaluation decision document will include the final re-evaluation decision, the reasons for it and a summary of comments received on the proposed re-evaluation decision with Health Canada's responses.

Additional Scientific Information

No additional data are required at this time.

For the uses where changes to the use pattern are proposed as mitigation measures, Health Canada is asking stakeholders if these measures are considered to be agronomically feasible for the management of the pest in the production of the crop across Canada. Stakeholders are specifically asked to provide comment regarding the feasibility of the proposed new 3-day restricted-entry interval for fruit thinning by hand in stone fruit (cherries, peaches and nectarines).

Stakeholders should also note that for the control of *Botrytis*, the registrant has requested to reduce the number of applications from 3 to 1 for grapes, and from 3 to 2 per crop cycle for greenhouse tomatoes and greenhouse peppers.

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

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

Science Evaluation

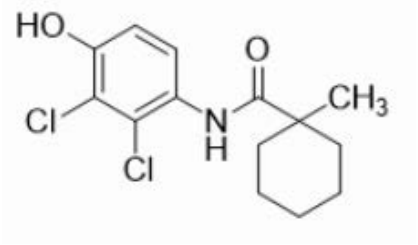
1.0 Introduction

Fenhexamid is a foliar fungicide registered for use on greenhouse vegetables, greenhouse ornamentals, berries, ginseng, grape, stone fruits and outdoor ornamentals for the control of *Botrytis* and *Monilinia* (on stone fruit only).

All uses were supported by the registrants at the time of re-evaluation initiation and were therefore considered in the health and environmental risk assessments of fenhexamid. However, the registrant has requested to reduce the number of applications for grapes from 3 to 1 and for greenhouse tomatoes and greenhouse peppers from 3 to 2 (Appendix II).

2.0 Technical Grade Active Ingredient

2.1 Identity

Common name		Fenhexamid
Function		Fungicide
Chemical Family		Anilide
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	2′,3′-dichloro-4′-hydroxy-1-methylcyclohexanecarboxanilide
2	**Chemical Abstracts Service (CAS)**	*N*-(2,3-dichloro-4-hydroxyphenyl)-1-methylcyclohexanecarboxamide
CAS Registry Number		126833-17-8
Molecular Formula		$C_{14}H_{17}Cl_2NO_2$
Structural Formula		
Molecular Weight		302.2
Purity of the Technical Grade Active Ingredient		98.6%
Registration Number		25899

2.2 Physical and Chemical Properties

Property	Result
Vapour pressure at 20°C	0.0004 mPa
Ultraviolet (UV) / visible spectrum	Not expected to absorb at λ >300 nm
Solubility in water at 20-25°C	24.0 mg/L (pH 5–7)
n-Octanol/water partition coefficient	Log K_{ow} = 3.51 (pH 7)
Dissociation constant	pK_a = 7.3

3.0 Human Health Assessment

3.1 Toxicology Summary

A detailed review of the toxicological database for fenhexamid, an anilide fungicide, was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The core studies were carried out in accordance with accepted international testing protocols and Good Laboratory Practices. The toxicology assessment also considered information from the published scientific literature. The scientific quality of the data is acceptable and the database is considered adequate to characterize the potential health hazards associated with fenhexamid.

In rats, radiolabelled fenhexamid was rapidly and completely absorbed by the gastrointestinal (GI) tract, distributed, metabolized and almost completely excreted within 48 hours following single or repeated gavage low doses. Following high-dose administration, a sub-proportional increase in plasma levels was observed, indicating possible saturation of absorption. Peak plasma levels were detected within 5–10 minutes after single and repeated low-dose administration, and 40-90 minutes postdosing after administration of a high dose.

Essentially, all the administered dose (AD) was excreted via the urine and faeces, with the majority being eliminated within 48 hours postdosing in the faeces. Elimination via expired air was negligible. Slight sex-related differences in elimination were noted following oral low-dose administration, with higher renal excretion observed in females. This difference was not apparent following high-dose administration and did not significantly impact the half-life, which was approximately 10 hours.

In both sexes, renal excretion was significantly higher after administration of a single low dose as compared to a single high dose. In bile cannulation experiments with a single low dose, more than 90% of the AD was recovered in the bile, with minor amounts being excreted in the feces and urine.

For all dosing regimens, tissue residues declined rapidly and total residual radioactivity in the body 48 hours postdosing, excluding the GI tract, was less than 0.3% of the AD. The highest tissue concentrations, 48 hours after dosing, were detected in the GI tract, liver and kidneys.

Unchanged fenhexamid accounted for the majority of the AD in excreta, regardless of sex or dosing regimen. The faeces contained almost exclusively unchanged fenhexamid, while urine contained fenhexamid and its glucuronide conjugate as a major metabolite. Additional metabolites formed by hydroxylation of the cyclohexyl ring, as well as glucuronide, and sulphate conjugates of these metabolites were present in minor amounts in the urine. The bile contained mostly the glucuronide conjugate of fenhexamid, which was indicative of a pronounced first pass effect and enterohepatic recirculation. The importance of enterohepatic recirculation and pronounced liver clearance observed with this compound was further corroborated by the results of a supplemental dietary 8-week plasma kinetic study in rats in which fenhexamid plasma concentrations were below the level of detection after 3 or 4 weeks of treatment.

Fenhexamid was of low acute oral and inhalation toxicity in rats and of low acute dermal toxicity in rats and mice. It was non-irritating to the rabbit eye and skin and it was not a dermal sensitizer to guinea pigs following testing by either the Buehler or Maximization method.

Short-term dermal exposure in rabbits did not result in systemic effects or dermal irritation at the limit dose of testing. Short-term nose-only inhalation exposure to fenhexamid in rats caused decreased bodyweight in males, as well as increased lung weight, histopathological changes in the lungs and lung-associated lymph nodes, and decreased landing foot splay in both sexes at the highest dose level.

Short-term dietary administration in mice and rats resulted in increased food consumption, decreased food efficiency and histopathological findings in the kidneys and liver. Dogs exhibited a different toxicity profile than rodents following repeated oral dosing and were the most sensitive species to the toxicological effects of fenhexamid. Hematological changes such as decreased erythrocyte, haemoglobin and haematocrit, as well as increased Heinz bodies, were observed in the 90-day and one-year dog dietary toxicity studies. Other notable findings in the one-year dog dietary toxicity study included increased intracytoplasmic vacuoles in the adrenal cortex in females and decreased ovarian and uterine weights in females at the high-dose level. Observed changes in ovarian and uterine weights were considered secondary to the effects of stress and negative energy balance, as suggested by the thin appearance and accompanying bodyweight decrease observed in these animals.

Long-term dietary administration of fenhexamid in mice resulted in decreased kidney weight and histopathological changes in the kidneys of males. At the highest dose level, which was above the limit dose of testing, decreased bodyweight and body-weight gain in males, as well as increased water consumption and evidence of kidney toxicity were observed in both sexes. In rats, decreased bodyweights, increased cecal mucosal hyperplasia, increased splenic extramedullary hematopoiesis, and bone marrow hyperplasia were observed following chronic dietary exposure. There was evidence of increased toxicity with increased duration of dosing. In mice, increased duration of dosing resulted in more pronounced histological changes in the kidney, while effects on bodyweight in rats and hematological changes in dogs were observed at lower dose levels in long-term studies than in the short-term studies.

There was no evidence of oncogenicity in rats or mice in chronic toxicity/oncogenicity studies. Fenhexamid was not genotoxic in a battery of in vitro genotoxicity studies that included a bacterial gene mutation assay, a chromosome aberration assay in Chinese hamster ovary cells, a mammalian gene mutation assay in hamster lung V79 cells, and an unscheduled DNA synthesis assay in rat hepatocytes. An in vivo mouse micronucleus test was also negative for genotoxicity.

In a dietary two-generation reproductive toxicity study in rats, decreased bodyweight and body-weight gain, as well as increased food consumption were noted in the parental generations at the mid-dose level. At the highest dose level, which was well above the limit dose of testing, increased mortality was noted postweaning in F_1 animals that had been retained to produce F_2 progeny (F_1 parents). Effects in offspring during lactation were limited to decreases in bodyweight at maternally toxic dose levels. The effect on bodyweight in offspring was greater than in parental animals, possibly as a result of either increased test material intake due to exposure via both milk and feed during late lactation, or metabolic saturation. Decreased uridine diphosphate (UDP)-glucuronyl transferase enzymatic activity is a normally occurring phenomenon in rat pups and may result in a decreased capacity of pups to metabolize fenhexamid, particularly at higher doses, given that glucuronide conjugation was the major detoxification pathway for this compound. Metabolic saturation in neonates may have also led to the observed bodyweight decrements noted from postnatal day (PND) 4 onwards at the highest dose level. The small size of F_1 pups at weaning was considered the principal causal factor for the increased mortality observed in F_1 offspring postweaning (F_1 parents). Reproductive toxicity in this study was observed at the highest dose level only, and consisted of a slight decrease in litter size at birth in both generations.

In rat gavage developmental toxicity studies, no adverse effects were noted in developing fetuses up to the limit dose of testing. In adult animals, decreased bodyweight gain and food consumption were noted at the limit dose. In a rabbit gavage developmental toxicity study, clinical signs of toxicity along with decreased placental weights were noted in maternal animals. At the high dose level, which was also the limit dose of testing, increased resorption and decreased bodyweight gain and food consumption were also observed in these animals. Foetal effects occurred only at the high dose level and consisted of ossification delays as well as a marginal decrease in male foetal weight.

The potential for fenhexamid to produce neurotoxic effects following acute exposure was investigated in rats. In a gavage acute neurotoxicity study, no evidence of selective neurotoxicity or systemic toxicity was observed up to the limit dose of testing. Functional observational batteries included in supplemental 90-day dietary studies in rats and mice did not identify any evidence of selective neurotoxicity.

Several studies conducted with fenhexamid were available in the published literature. Most of these studies examined the the potential effect of fenhexamid on the endocrine system in vitro. Specifically, these studies indicated that fenhexamid had an effect on the oestrogen receptor (ER) and androgen receptor (AR) signalling pathways. In general, fenhexamid was an ER agonist and an AR antagonist. Overall, the results from these studies cannot be quantitatively factored into the risk assessment given that these were conducted in vitro.

There were no specific endocrine-related in vivo toxicity studies available in the fenhexamid toxicology database and sexual maturation was not evaluated in the available reproductive toxicity study. However, potential concerns for endocrine-mediated effects are alleviated by the absence of effects on endocrine sensitive tissues in the core toxicology database.

The toxicology reference values used for human health risk assessment are summarized in Appendix III, Table 1. The results of toxicology studies conducted in laboratory animals with fenhexamid are summarized in Appendix III, Table 2.

3.1.1 *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 standard complement of required studies for risk assessment were available for fenhexamid, including gavage developmental toxicity studies in rats and rabbits and a two-generation dietary reproductive toxicity study in rats.

With respect to potential prenatal and postnatal toxicity, there were no effects on fetuses up to or beyond the limit dose of testing in the rat developmental toxicity studies. In the rabbit developmental toxicity study, minor developmental effects consisting of ossification delays and decreased fetal weight, as well as total litter resorption were observed at a maternally-toxic dose level, which was also the limit dose of testing. In the two-generation rat reproductive toxicity study, postnatal decreases in bodyweight and body-weight gain in offspring were observed in the presence of maternal toxicity. At the highest dose level, well beyond the limit dose of testing, a significant reduction in pup bodyweight resulted in increased mortality of F_1 offspring postweaning (F_1 parents). Concern for the serious endpoints noted in the rabbit developmental toxicity study and two generation rat reproductive toxicity are offset by the establishment of more conservative points of departure for these studies as well as the consideration that these findings occurred at the limit dose of testing.

Overall, the database is adequate for determining the sensitivity of the young. Although serious effects in the young (mortality and total litter resorption) were noted in the presence of maternal toxicity in the rat two-generation reproductive toxicity study and in the rabbit developmental toxicity study, the toxicological reference values selected for risk assessment are protective of these effects. Accordingly, the *Pest Control Products Act* factor (PCPA factor) was reduced to onefold.

3.2 Dietary Exposure and Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Dietary exposure assessments are age-specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when exposure exceeds 100% of the reference dose. The PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides in Food, A User's Guide*, presents detailed chronic risk assessment procedures. For cancer risk, the PMRA is concerned when the exposure estimates exceed the cancer risk estimate exceeds 1×10^{-6} (one-in-a-million).

Sufficient information was available to adequately assess the dietary exposure and risk from fenhexamid. Residues in all other agricultural commodities, including those approved for treatment in Canada but without specific MRLs, are regulated under Subsection B.15.002 (1) of the Food and Drugs Regulations, which requires that residues do not exceed 0.1 ppm. A complete list of MRLs specified in Canada can be found on the PMRA's MRL Database, an online query application that allows users to search for specified MRLs, regulated under the *Pest Control Products Act*, both for pesticides or food commodities.

Chronic dietary exposure and risk assessments for fenhexamid was conducted using the Dietary Exposure Evaluation Model – Food Commodity Intake Database™ (DEEM-FCID™, Version 4.02, 05-10-c) program, which incorporates consumption data from the National Health and Nutrition Examination Survey/What We Eat in America (NHANES/WWEIA) for the year 2005-2010 available through the Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics (NCHS). Further details on the consumption data are available in the PMRA's Science Policy Note (SPN 2014-01), *General Exposure Factor Inputs for Dietary, Occupational and Residential Exposure Assessments.* For more information on the dietary risk estimates or the residue chemistry information used in the dietary assessment, see Appendix IV and Appendix V.

3.2.1 Determination of Acute Reference Dose

No endpoint of concern attributable to an acute exposure was identified in the toxicology database; therefore, an acute reference dose (ARfD) was not established and an acute dietary risk assessment was not required.

3.2.2 Determination of Acceptable Daily Intake

To estimate risk from repeated dietary exposure, the dietary one-year dog toxicity study with a NOAEL of 17 mg/kg bw/day was selected for risk assessment. At the LOAEL of 124 mg/kg bw/day, hematological changes (decreased erythrocytes, hematocrit, and hemoglobin and increased Heinz bodies) were observed in both sexes, as well as increased adrenal weight and an increased incidence of adrenocortical intracytoplasmic vacuoles in females. This study provides the lowest NOAEL in the database. 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 onefold. Thus, the composite assessment factor (CAF) is 100.

The acceptable daily intake (ADI) is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{17 \text{ mg/kg bw/day}}{100} = 0.2 \text{ mg/kg bw/day of fenhexamid}$$

The ADI provides a margin of >2000 to the NOAEL for the offspring mortality observed postweaning in the rat two-generation reproductive toxicity study and a margin of 1500 to the NOAEL for total litter resorption noted in the rabbit developmental toxicity study.

3.2.3 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated using average consumption of different food residue values. The estimated exposure was then compared to the ADI, which is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no harmful effects. When the estimated exposure is less than the ADI, the chronic dietary exposure is acceptable.

The chronic dietary assessment was conducted using residue estimates from Canadian MRLs/American Tolerances and processing factors (theoretical and experimental) into DEEM, and all crops were assumed to have been 100% treated.

The chronic risk for all populations from food-only sources are <15% of the ADI and the chronic risk for all populations from food and water sources are <16% of the ADI for the general population and all other subpopulations. Results from both exposure assessments are not of concern.

3.2.4 Cancer Assessment

There was no evidence of oncogenicity and therefore, no separate cancer risk assessment is necessary.

3.3 Exposure from Drinking Water

Residues of fenhexamid in potential drinking water sources were estimated from water modelling.

3.3.1 Concentrations in Drinking Water

For the human health assessment, estimated environmental concentrations (EECs) in potential drinking water sources are calculated for both groundwater and surface water.

For surface water, the Pesticide in Water Calculator (PWC) calculated the amount of pesticide entering the water body by runoff and drift, and the subsequent degradation of the pesticide in the water system. EECs are calculated by modelling a total land area of 173 ha draining into a 5.3 ha reservoir with a depth of 2.7 m. Groundwater EECs are calculated by simulating leaching through a layered soil profile and reporting the average concentration in the top 1m of a water table.

Drinking water modelling follows a tiered approach consisting of progressive levels of refinement. Level 1 EECs are conservative values intended to screen out pesticides that are not expected to pose any concern related to drinking water. These are calculated using conservative inputs with respect to application rate, application timing, and geographic scenario. Level 2 EECs are based on a narrower range application timing, methods, and geographic scenarios, and are not considered conservative values that cover all regions of Canada.

Modelling was performed at Level 1. EECs for surface water were calculated based on a single standard scenario. EECs in groundwater were calculated for several scenarios representing different regions of Canada; only the highest EECs from across these scenarios are reported. All scenarios were run for 50 years.

Level 1 EECs, expressed as parent equivalent, are reported in Table 1 below.

Table 1 EECs (in µg a.i./L) for the drinking water risk assessment of fenhexamid.

Use pattern	Groundwater (µg a.i./L)		Surface Water (µg a.i./L)	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
4 applications of 850 g a.i./ha at a 7-day interval	98	97	108	32

[1] 90th percentile of daily average concentrations
[2] 90th percentile of 365-day moving average concentrations
[3] 90th percentile of the peak concentrations from each year
[4] 90th percentile of yearly average concentrations

3.3.2 Drinking Water Exposure and Risk Assessment

Drinking water exposure estimates were combined with food exposure estimates, with EEC values incorporated directly in the dietary (food and drinking water) assessments. Please refer to Sections 3.2.3 for additional details.

3.4 Occupational and Non-Occupational Exposure and Risk Assessment

Occupational and non-occupational (residential) risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

3.4.1 Toxicology Endpoint Selection for Residential and Occupational Exposure

Short- and Intermediate-term Dermal

The available 21-day dermal toxicity study in rabbits was not considered appropriate for risk assessment as the dog was the most sensitive species to the hematological changes induced by fenhexamid following repeated oral dosing. Furthermore, the toxicity studies conducted in rabbits indicated that this species was not sensitive to the hematological effects of fenhexamid. For short- and intermediate-term occupational exposures via the dermal route, the NOAEL of 34 mg/kg bw/day from the 90-day dog dietary toxicity study, supported by the findings noted at 90 days in the one-year dog dietary toxicity study, was selected for risk assessment. In the 90-day study, at the LOAEL of 239 mg/kg bw/day, increased Heinz bodies and liver weight were observed in both sexes and increased alkaline phosphatase activity was noted in females. In the one-year study, after 90 days, decreased erythrocytes, hematocrit and haemoglobin and increased Heinz bodies were observed in both sexes at 124 mg/kg bw/day.

Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied resulting in a target MOE of 100. The selection of this study and MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

Long-term Dermal

For the long-term dermal risk assessment, the NOAEL of 17 mg/kg bw/day from the one-year dog dietary toxicity study was selected based on decreased erythrocytes, haematocrit, and haemoglobin as well as increased Heinz bodies in both sexes and increased adrenal weights and intracytoplasmic vacuoles in the adrenal cortex in females. No long-term dermal toxicity studies were available.

Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied resulting in a target MOE of 100. The selection of this study and MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

Short- and Intermediate-term Inhalation

For short- and intermediate-term occupational exposures via the inhalation route, the NOAEC of 0.069 mg/L (≈19 mg/kg bw/day) from the 28-day inhalation toxicity study in rats was selected. At the LOAEC of 0.487 mg/L (≈132 mg/kg bw/day), decreased bodyweight in males, increased lung weight, histopathological findings in the lungs and lung-associated lymph nodes and decreased landing foot splay were observed in both sexes.

Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied resulting in a target MOE of 100. The selection of this study and MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

Cancer Assessment

See Section 3.2.4 above.

Dermal Absorption

A dermal absorption value of 20% was determined for fenhexamid based on a rat in vivo study.

3.4.2 Non-Occupational Exposure and Risk Assessment

Non-occupational (residential) risk assessment involves estimating risks to the general population, including youth and children, during or after pesticide application.

Since there are no registered domestic-class products containing fenhexamid, a residential handler assessment was not required. Also, postapplication exposure to residents was assumed not to occur, since commercial-class products are not registered for use in residential areas. The commercial-class product labels will be updated to reflect current wording for this statement.

3.4.2.1 Bystander Exposure and Risk Assessment

Monitoring data from France and Spain reported detectable residues of fenhexamid in the air in rural and urban areas situated close to agricultural settings during the spray season. Information regarding the use of fenhexamid during these monitoring times was not reported in the literature studies. As part of a conservative (in other words, upper bound) Tier 1 assessment, it was assumed that the use in Europe is similar to that in Canada, and the highest air concentration from the available data would be present during the entire Canadian spray season (intermediate-term; several months). Calculated MOEs ranged from 1 100 000 000 to 5 300 000 000 for adults, youth (11<16 years old), and toddlers (6<12 months old) and, therefore, risks were shown to be acceptable.

3.4.3 Occupational Exposure and Risk Assessment

There is potential for exposure to fenhexamid in occupational scenarios from workers handling fenhexamid products during mixing/loading and application activities, and from workers entering treated areas.

3.4.3.1 Mixer, Loader, and Applicator Exposure and Risk Assessment

For potential exposures to mixers, loaders, and applicators, the following scenarios were assessed:

- Mixing/loading water dispersible granules (WDG)
- Groundboom application
- Air blast application
- Handheld air blast/mistblower application
- Mixing, loading, and applying by backpack sprayer
- Mixing, loading, and applying by manually-pressurised hand wand (ManPHW)
- Mixing, loading, and applying by mechanically-pressurised hand gun (MechPHG)

The exposure estimates for mixer/loaders and applicators are based on different levels of personal protective equipment (PPE) and engineering controls:

- Baseline PPE: Long pants, long-sleeved shirt and chemical-resistant gloves.
- Maximum PPE: Chemical-resistant coveralls over long pants, long-sleeved shirt, and chemical-resistant gloves.
- Chemical-Resistant Headgear. Chemical-resistant headgear that covers the neck (for example, Sou'Wester hat, rain hat).
- Respirator: a respirator with NIOSH-approved organic-vapour removing cartridge with a prefilter approved for pesticides.

Exposure Durations:

Based on the number of applications and the timing of application, workers applying fenhexamid would generally have a short- to intermediate-term (<6 months) duration of exposure.

Exposure Data:

No appropriate chemical-specific handler exposure data were available for fenhexamid. Therefore, dermal and inhalation exposure for field and greenhouse applications were estimated using data from the Pesticide Handlers Exposure Database (PHED), the Agricultural Handler Exposure Task Force (AHETF), and worker exposure studies.

The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of PPE. The open cab air blast, open cab groundboom, and open mix/load dry flowable (used as surrogate for WDG)

studies from AHETF were also used. For applicators using handheld air blast/mistblowers application equipment, unit exposures were determined from two worker exposure studies. While there are limitations in the use of generic data, these exposure data represent the most reliable information currently available.

For other handheld equipment, only PHED data were available. The data were considered to be limited in terms of number of replicates (less than 15 per body part) or study quality (for example, low or missing field recovery). Furthermore, since exposure studies were not available for mixing/loading and applying WDG using handheld equipment, an estimate for these scenarios was made by using unit exposure values for open mix/load for dry flowable plus open mix/load/apply of liquids by backpack sprayer, manually-pressurized handheld sprayer, or mechanically-pressurised hand gun, respectively. This would result in an overestimate of exposure; however, it is the best available data at this time.

Risk Assessment Outcomes:

Route specific MOEs for mixer/loader and applicators are outlined in Appendix VI, Table 1. Calculated dermal and inhalation MOEs for mixer/loaders and applicators of fenhexamid exceeded target MOEs for all scenarios and were therefore shown to be acceptable. Exposure for the dermal and inhalation routes of exposure did not need to be combined as they did not contribute to the same adverse toxicological endpoint.

For application to fruit trees, the updated risk assessment resulted in less PPE than is currently required on the label. As the current label PPE was not required by the risk assessment nor by the product hazard classification, the PPE can be reduced to align with the results of the risk assessment.

3.4.3.2 Postapplication Worker Exposure and Risk Assessment

The postapplication occupational risk assessment considered exposures to workers who enter treated sites to conduct agronomic activities involving foliar contact (for example, hand harvesting). For outdoor agricultural crops, there is potential for short- to intermediate-term (<6 months) postapplication exposure for workers based on the use pattern. For greenhouse crops, there is potential for long-term (>6 months) postapplication exposure, as there is potential for multiple crop cycles per year.

Based on the vapour pressure of fenhexamid, inhalation exposure is not likely to be of concern provided that the minimum 12 hour restricted-entry interval is followed. This rationale is supported by a greenhouse air monitoring study where air concentrations of fenhexamid decreased to below the quantitation limit by 12 hours after application to greenhouse tomatoes. Thus, exposure would be predominantly via the dermal route for workers performing postapplication activities in crops treated with a foliar spray.

Potential dermal exposure for postapplication workers was estimated using updated activity-specific transfer coefficients (TCs), and dislodgeable foliar residue (DFR), chemical-specific data or default values for scenarios where chemical-specific DFR data were not available (see below).

The DFR refers to the amount of residue that can be dislodged or transferred from a surface, such as leaves of a plant. The TC is a measure of the relationship between exposure and DFR for individuals engaged in a specific activity and is calculated from data generated in field exposure studies. The TCs are specific to a given crop and activity combination (for example, hand harvesting apples, scouting late season corn) and reflect standard agricultural work clothing worn by adult workers. Activity-specific TCs from the Agricultural Re-Entry Task Force (ARTF) were used. For more information about estimating worker postapplication exposure refer to the PMRA's Regulatory Proposal PRO2014-02, *Updated Agricultural Transfer Coefficients for Assessing Occupational Exposure to Pesticides*.

A chemical-specific DFR study conducted on grapes was available and used to calculate DFR for grapes, blackberries, raspberries, high bush blueberries, and other crops with similar morphology. As the use pattern in this study did not reflect the registered use pattern for these crops, the peak DFR after the first application (20% of the application rate) and predicted "daily dissipation" rate of 2.4% per day were used. The predicted daily dissipation rate was calculated from the linear equation of plotting the natural logarithm (ln) of DFR versus dissipation time (postapplication interval) following the final application. Multiple application scenarios were modelled by summing residues from a single application. For all other outdoor crops, the default peak DFR value of 25% of the application rate was used along with the daily dissipation rate of 2.4% per day from the grape DFR study. For greenhouse crops, the default peak value of 25% of the application rate was used along with the default dissipation rates of 2.3% per day for ornamentals and 0% for vegetables. For further information on these default values, refer to the PMRA's Science Policy Note SPN2014-02, *Estimating Dislodgeable Foliar Residues and Turf Transferrable Residues in Occupational and Residential Postapplication Exposure Assessments.*

For workers entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely enter after application. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE.

Appendix VII, Table 1 lists the REIs determined for each crop and activity combination. Risks are shown to be acceptable provided that the proposed REIs are followed. REIs range from 12 hours to 40 days and are considered to be agronomically feasible for most crops, including a 3-day REI for thinning stone fruit by hand and a 40-day REI for girdling and turning grapes. REIs were not considered to be agronomically feasible for the uses listed below.

- Greenhouse cut flowers: 44 day REI for for disbudding, hand harvesting, hand pruning
- Outdoor cut flowers: 9 day REI for for disbudding, hand harvesting, hand pruning;

To mitigate these risks, it is proposed to reduce the number of applications for greenhouse and outdoor cut flowers. Cancellation is otherwise proposed where REIs or other mitigation options are not considered to be agronomically feasible. As outlined in Appendix VII, Table 1, in the number of applications would be reduced from 6 to 1 per crop cycle for greenhouse cut flowers and from 6 to 4 per year for outdoor cut flowers.

3.5 Aggregate Exposure and Risk Assessment

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). For fenhexamid, the aggregate assessment consisted of combining food and water exposure only (see Section 3.2.3), since residential exposure is not expected to occur. The aggregate risk for bystanders was considered to be acceptable as the contribution to the total aggregate exposure (diet and drinking water) would be minimal.

3.6 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. Fenhexamid is an anilide fungicide. Other Canadian registered anilide fungicides include sedaxane, metalaxyl-M and penflufen. For the current re-evaluation, the PMRA did not identify information indicating that fenhexamid shares a common mechanism of toxicity with other pest control products in this class and it does not appear to produce a toxic metabolite produced by other pest control products. Therefore, a cumulative risk assessment is not required at this time.

3.7 Incident Reports

As of 26 September 2019, no human or domestic animal incidents involving fenhexamid have been submitted to the PMRA.

4.0 Environmental Assessment

4.1 Fate and Behaviour in the Environment

A summary of terrestrial environmental data for fenhexamid is presented in Appendix VIII, Table 1.

Based on its physical-chemical properties, fenhexamid is soluble and does not have the potential to volatilize from moist soil. Soil photolysis is not a major route of transformation and fenhexamid is considered to be stable to this process. No information on photolysis in air is available. Predictive modelling indicates that airborne fenhexamid will sorb to airborne particles which could be transported long distances via atmospheric currents; however, no information on detections of fenhexamid in remote areas was found.

Laboratory biotransformation studies (terrestrial and aquatic) demonstrate that a significant proportion of fenhexamid residues become bound to soil or sediment and are non-extractable (for example, in soil, non-extractable residues reached a maximum of 57–67% of applied radioactive as parent).

However, because study extraction methods did not employ solvents with varying polarities (as recommended by USEPA (2014)), there is some uncertainty as to whether residues remaining in the non-extractable phase are truly bound. As a conservative measure, the PMRA has determined half-lives from biotransformation studies based on parent fenhexamid as well as fenhexamid combined with non-extractable residues.

In aerobic soils fenhexamid dissipated quickly with DT_{50}s of 0.09–1.4 days; however, this is primarily due to formation of non-extractable residues. When non-extractable residues are combined with fenhexamid, the DT_{50}s range from 311–1248 days. According to the classification system of Goring et al. (1975), fenhexamid is classified as being non-persistent in aerobic soil; while fenhexamid combined with non-extractable residues is classified as persistent in aerobic soil. No major transformation products were formed in aerobic soil studies.

Under anaerobic soil conditions, fenhexamid is shown to be moderately persistent (DT_{50} = 76 days). Parent fenhexamid combined with non-extractable residues is considered persistent under anaerobic soil conditions (DT_{50} = 645 days). No major transformation products were formed in anaerobic soil studies.

According to soil K_{oc}s available for fenhexamid, it has low to moderate mobility in soil while its solubility in water indicates the potential for leaching. When taking into consideration the criteria of Cohen et al. (1984) and the groundwater ubiquity score (GUS), it was determined that fenhexamid was unlikely to leach. Laboratory soil column leaching studies were unavailable, but field lysimeter and field dissipation studies show that fenhexamid remained in the top 30 cm soil layer. Fenhexamid is non-persistent under field conditions (DT_{50}s ranged from <1 to 3.2 days). Based on the weight of evidence, parent fenhexamid is not expected to leach into groundwater or carry over into the following season. Fenhexamid combined with non-extractable residues could be a leacher when taking into consideration GUS scores and comparison to Cohen criteria; however, no empirical evidence is available from field data to support the GUS and Cohen conclusions.

A summary of aquatic environmental data for fenhexamid is presented in Appendix VIII, Table 2.

In aquatic habitats, aqueous hydrolysis is not a major route of transformation and fenhexamid is considered to be stable to this process. Aqueous photolysis can be a major route of transformation of fenhexamid.

In aerobic aquatic whole systems, fenhexamid dissipated with DT_{50} of 7.35–15.9 days but much of the dissipation is due to sorption to sediment as opposed to definitive biotransformation (non-extractable residues reached a maximum of 43–75% applied radioactivity [ARA] at termination of studies). According to the classification system of McEwen and Stephenson (1979), fenhexamid is classified as being non-persistent to slightly persistent in aerobic aquatic whole systems, however when non-extractable residues are considered along with fenhexamid, the DT_{50}s range from 110–1325 days, which classifies these combined residues as moderately persistent to persistent.

One major transformation product was formed in aerobic water/sediment systems (1-methylcyclohexane-1-carboxylic acid at a maximum of 14.2% ARA); however, it decreased to less than the limit of detection by study termination.

In anaerobic aquatic biotransformation studies, fenhexamid alone dissipated with DT_{50}s ranging from 60.7 to 115 days and is classified as being moderately persistent to persistent in anaerobic aquatic whole systems according to the classification system of McEwen and Stephenson (1979). Fenhexamid combined with non-extractable residues have DT_{50}s ranging from 58.4 to 1026 days. Major transformation products include 3-deschloro-fenhexamid and 1-methylcyclohexane-1-carboxylic acid. Non-extractable residues reached a maximum of 6–19% of ARA by study termination in one study but formed up to 73% ARA in another study.

Although the log K_{ow} ranges from 2.2–3.6 and indicates that there is a theoretical potential for bioaccumulation in fish, a bioconcentration study conducted with bluegill sunfish indicated that there was little bioaccumulation; the depuration half-life of <1 day precludes high bioaccumulation of fenhexamid.

Canadian surface water data was not available. Of the 1159 samples from the United States, the detection frequency was <2%. Due to the absence of Canadian ecological monitoring data, water modelling EECs will be relied on to assess the risk to aquatic organisms from runoff.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. 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 various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted using an uncertainty factor, 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 that are being evaluated (for example, 10 for fish, 2 for aquatic invertebrates). The difference in value of the uncertainty factors reflects, in part, the ability of certain 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.

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those 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 RQ is then compared to the level of concern (LOC). If the screening level RQ is below the LOC, the risk is considered negligible and no further risk characterization is necessary. If the screening level RQ is equal to or greater than the LOC, then 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.

The concentrations of fenhexamid were estimated for the aquatic environment and for food items consumed by birds and mammals (vegetation, seeds, and insects). The EECs, based on the use pattern are included in the risk assessment tables referenced below.

A summary of the terrestrial and aquatic toxicity endpoints selected for the risk assessment and the uncertainty factors applied is provided in Appendix VIII, Table 3.

4.2.1 Risks to Terrestrial Organisms

For the environmental risk assessment, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that may be exposed to fenhexamid. No acute or chronic risk is apparent for earthworms, terrestrial vascular plants and acute risks to bees, beneficial insects, birds or mammals (Appendix VIII, Table 4).

A chronic adult bee feeding study indicates an RQ of <7 which exceeds the LOC. However, there was no statistically significant difference in mortality between the controls and the treatment dose (there was only one treatment dose) and only one bee in each of two different replicate treatments showed any sublethal behavioural affects and these were resolved before study termination. The PMRA is concluding that it is unlikely that bees will be at risk due to chronic feeding on pollen or nectar containing residues of fenhexamid.

Chronic risk for beneficial arthropods (RQ of <1.72) is overestimated because the endpoint is ≥1.98 kg a.i./ha (the highest dose tested). At this rate, there were 0% mortalities; therefore, it is likely that the true endpoint is much greater than 1.98 kg a.i./ha. The chronic risk was also assessed using a cumulative application rate that did not take into consideration any dissipation between applications. Dissipation between applications would be expected and, therefore, the PMRA is concluding that beneficial arthropods will not be at a chronic risk from registered uses of fenhexamid.

The RQ for reproduction in small birds is 1.0 and considering that there were no effects observed at the endpoint used in the risk assessment, the PMRA is concluding that birds will not be at risk at registered application rates of fenhexamid (Appendix VIII, Table 4).

Reproductive risk to all size classes of mammals was found with a maximum RQ of 4.53 (Appendix VIII, Table 4). This was based on increased serum creatinine, increased liver weight and decreased kidney weight. It is unknown whether these effects would lead to effects on mortality, growth or reproduction, and the assessment is therefore considered to be highly conservative; however, as a precaution, a label statement to inform users of the potential for risk is proposed.

4.2.2 Risks to Aquatic Organisms

The PMRA has concluded that the transformation products of fenhexamid are not relevant to the aquatic risk assessment. However, as the non-extractable residues was not characterized in fate studies and could potentially contain parent fenhexamid, it was included in the residue of ecological concern.

Screening Level Risk Assessment

To assess the potential for effects from exposure to fenhexamid, screening level EECs in the aquatic environment were based on a direct application to water. This assessment identifies the taxonomic groups at risk. The calculated EECs were those determined in 15 cm body of water for amphibians and 80 cm body of water for all other aquatic organisms, at the highest cumulative application rate for agricultural uses (840 g a.i./ha × 4 applications at 7-day intervals) taking into consideration any dissipation between applications using the half-life of 222 days used for water modelling. For the screening level risk assessment for aquatic organisms, the laboratory endpoints were adjusted using uncertainty factors as described earlier.

The LOC was exceeded for acute and chronic risk using the screening level aquatic EEC for 80 and 15 cm depths for freshwater fish and amphibians; a refined risk assessment taking into consideration drift and runoff is required for these biota. No other risks were identified in the screening level risk assessment (Appendix VIII, Table 5).

Refined Risk Assessment Due to Drift

The risk to aquatic organisms was further characterized by taking into consideration the concentrations of fenhexamid that could be deposited in off-field aquatic habitats that are downwind and directly adjacent to the treated field through drift of spray. The spray drift data of Wolf and Caldwell (2001) was used to determine the maximum spray deposit into an aquatic habitat located 1 metre downwind from a treated field. Drift from early season air blast applications results in 74% drift and freshwater fish and amphibians remain at risk (Appendix VIII, Table 6). Refined risk from ground boom and air blast applications are not discussed here, but were considered in the calculation of buffer zones. Spray buffer zones are required to protect sensitive aquatic habitats.

Refined Risk Assessment Due To Runoff

Aquatic organisms can also be exposed to fenhexamid from foliar applications as a result of runoff into a body of water. Estimated environmental concentrations (EECs) of fenhexamid in water were calculated for use in the ecological risk assessment using the Pesticide Water Calculator (PWC) version 1.52. The use pattern selected for the modelling was four applications of 850 g a.i./ha spaced seven days apart. Initial application dates between 1 April and 10 October were used for the modelling.

Acute and chronic RQ values were calculated using an EEC for the time frame which most closely matched the exposure time used to generate the endpoint (in other words, a 96-hour LC_{50} would use the 96-hour value generated by the model; a 96-day NOEC would use the 90-day EEC value).

The LOC is exceeded on an acute and chronic basis for both fish and amphibians (RQs from 1.7-8.3) (Appendix VIII, Table 7). Toxicity label statements to inform users of the potential toxicity and run-off label statements to protect aquatic habitats are required.

Sediment-Based Risk Assessment

Because fenhexamid sorbs to sediment quickly, concentrations of fenhexamid in pore-water were also modelled using PWC. There were two relevant endpoints for invertebrates, *C. dilutus* and *L. plumulousus*. The 21-d EEC in pore water was calculated to be 0.19 mg a.i./L; the RQs were all less than the LOC, which is 1 (Appendix VIII, Table 8). Fenhexamid is not expected to pose a risk to sediment-dwelling invertebrates due to exposure via pore-water.

4.2.3 Environmental Incident Reports

There was one incident involving tulips and one incident involving bees reported in the USEPA Ecological Incident Information System (USEPA EIIS). In 2002, six acres of tulips were treated directly with registered uses of fenhexamid, isoxaben, diclofop-methyl, iprodione, oryzalin and glyphosate at a nursery. Twisting of leaves occurred and the incident had a certainty classification of “possible” for all actives associated with this incident. Considering that fenhexamid shows very few toxic effects in terrestrial vascular plant studies and it is a fungicide, it seems unlikely that fenhexamid contributed to the plant damage. Glyphosate, oryzalin, diclofop-methyl and isoxaben are all herbicides and it is much more likely that these actives contributed to the plant damage than fenhexamid. The USEPA concluded that it was unlikely that fenhexamid contributed to the bee incident in the USEPA EIIS where 320 bee hives collapsed. Although fenhexamid was detected in some samples, carbaryl, coumaphous, fluvalinate and chlorpyrifos were also detected and more likely contributed to all hive collapses than fenhexamid.

Two bee incidents were reported to the PMRA in 2013, one from Ontario and one from Quebec. For both incidents, it was concluded to be unlikely that fenhexamid contributed to the effects observed due to its low toxicity to bees. In one incident, a large number of dead bees were reported which would not be expected from exposure to fenhexamid. In the other incident, dead bee samples were analyzed and several pesticides known to be toxic to bees were present.

5.0 Value Assessment

Fenhexamid is a foliar fungicide registered for use on greenhouse vegetables, greenhouse ornamentals, berries, ginseng, grape, stone fruits and outdoor ornamentals for the control of *Botrytis* and *Monilinia* (on stone fruit only). Fenhexamid is important for the control of gray mold (*Botrytis cinerea*) on greenhouse vegetables, as there are limited conventional alternatives available for rotation with fenhexamid. Fenhexamid is valuable to several sectors as it is the only product in the Group 17 mode of action and is therefore is important in resistance management.

6.0 Pest Control Product Policy Considerations

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, fenhexamid and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[3] and evaluated against the Track 1 criteria.

6.1 Toxic Substances Management Policy Considerations

In accordance with the PMRA Regulatory Directive DIR99-03,[4] the assessment of fenhexamid against Track 1 criteria of Toxic Substances Management Policy (TSMP) under *Canadian Environmental Protection Act* was conducted. Health Canada has reached the conclusions that:

- Fenhexamid does not meet all Track 1 criteria, and is not considered a Track 1 substance (refer to Appendix VIII, Table 9)
- Fenhexamid does not form any transformation products that meet all Track 1 criteria.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical grade active ingredient as well as formulants and contaminants in the end-use products are compared against the List of Pest control Product Formulants and Contaminants of Health or Environmental Concern maintained

[3] DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*.

[4] DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*.

in the *Canada Gazette*.[5] The list is used as described in the Health Canada Notice of Intent NOI2005-01[6] and is based on existing policies and regulations including DIR99-03 and DIR2006-02,[7] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). Health Canada has reached the following conclusions:

- Analysis of technical grade fenhexamid did not identify any Track 1 contaminants. Chromium, a Schedule 1 impurity, was found at levels comparable to other TGAIs with a similar use-pattern. The PMRA is managing the presence of these contaminants in accordance with the Agency's strategy to prevent or minimize releases, with the ultimate goal of virtual elimination as described in DIR99-03.

- The PMRA reached the conclusion that end-use products containing fenhexamid do not contain any other contaminants or formulants of environmental or health concern identified in the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.

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

7.0 Conclusion of Science Evaluation

Fenhexamid controls gray mold on a wide variety of crops and ornamentals. It is an important rotational fungicide as it is the only Group 17 mode of action registered on several agricultural commodities for managing *Botrytis cinerea*, which is susceptible to developing fungicide resistance.

Based on the current use pattern of fenhexamid, human health risks were shown to be acceptable for all uses with proposed risk mitigation measures. These risk mitigation measures include additional PPE, increased REIs, and reduction in number of applications for some crops.

When used according to the proposed label directions, environmental risks associated with the use of fenhexamid where shown to be acceptable.

---

5 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette,* Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613*. Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

6 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

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

List of Abbreviations

♂	males
♀	females
↑	increased
↓	decreased
%	percent
>	greater than
<	less than
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
AHETF	Agricultural Handler Exposure Task Force
ALP	alkaline phosphatase
ALT	alkaline aminotransferase
AR	Androgen receptor
ARA	applied radioactivity
ARfD	acute reference dose
ARTF	Agricultural Re-entry Exposure Task Force
AST	aspartate aminotransferase
BAF	bioaccumulation factor
BCF	bioconcentration factor
BCL-2	B-cell lymphoma 2
BG-1	bowman gray-1
bw	body weight
bwg	bodyweight gain
BZ	buffer zone
CAF	composite assessment factor
CALUX	Chemical Activated LUciferase gene eXpression
CEPA	Canadian Environmental Protection Act
cm	centimetre(s)
CO_2	Carbon dioxide
conc	concentration
COX	cyclooxygenase
d	day(s)
DFR	dislodgeable foliar residue
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
dw	dry weight
DW	drinking water
E2	estradiol
EAD	Environment Assessment Directorate of PMRA
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure

EEC	estimated environmental concentration
(h)ER	estrogen receptor hER alpha hER beta
EFS	European Food Safety Authority
EIIS	USEPA Ecological Incident Information System
ELS	early life stage
EPI	Estimation Program Interface
F_1	first generation
F_2	second generation
fc	food consumption
fe	food efficiency
FEX	fenhexamid
g	gram(s)
gen	generation
GD	gestation day
GGT	gamma glutamyl transferase
GI	gastrointestinal
GLDH	glutamate dehydrogenase
GUS	groundwater ubiquity score
ha	hectare(s)
hr(s)	hour(s)
HLC	Henry's law constant
IC_{20}	inhibitory concentration at 20%
IC_{50}	inhibitory concentration at 50%
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
K_d	soil-water partition coefficient
kg	kilogram(s)
K_{ow}	n–octanol-water partition coefficient
L	litre(s)
LC_{50}	lethal concentration required to kill 50% of the test group
LD	lactation day
LD_{50}	lethal dose required to kill 50% of the test group
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
LOC	level of concern
LR_{50}	lethal rate required to kill 50% of the test group
m^3	cubic meter
mg	milligram(s)
mL	millilitre(s)
M	molar
ManPHW	manually-pressurized hand wand
MechPHG	mechancially-pressurized hand gun
miR	micro ribonucleic acid
µM	micromolar
µg	microgram
mg	milligram(s)
MOE	margin of exposure

MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
nm	nanomolar
NERs	nonextractable residues
NIOSH	National Institute for Occupational Safety and Health
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
ppm	parts per million
P	parental generation
PCB	polychlorinated biphenyl
PCNA	proliferating cell nuclear antigen
PDC4	pyruvate decarboxylase 4 (protein)
PHED	Pesticide Handles Exposure Database
PMRA	Pest Management Regulatory Agency
PND	postnatal day
PPE	personal protective equipment
PTEN	phosphatase and tensin homolog (protein)
PWC	Pesticide in Water Calculator
QSAR	quantitative structure–activity relationship
rel	relative
RBC	red blood cells
REI	Restricted-Entry Interval
RQ	risk quotient
SFO	single first-order
$t_{1/2}$	half-life
$T_{1/2\ rep}$	representative half-life
TC	transfer coefficient
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
UDP	uridine diphosphate
USEPA	United States Environmental Protection Agency
VP	vapour pressure
WBC	white blood cells
WDG	water dispersible granular
wk(s)	week(s)
wt	weight
YES	yeast estrogen screen

Appendix I Registered Fenhexamid Products in Canada

Table 1 Products Subject to Proposed Label Amendments[1]

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Active ingredient (%)
25899	Technical	Arysta Lifescience North America, LLC.	Fenhexamid Technical	Solid	Fenhexamid (98.6)
25900	Commercial		Elevate 50 WDG Fungicide	Wettable Granules	Fenhexamid (50)
26132	Commercial		Decree 50 WDG Fungicide	Wettable Granules	Fenhexamid (50)

[1] as of 4 September 2019, excluding discontinued products or products with a submission for discontinuation

Appendix II Registered Commercial and Restricted Class Uses of Fenhexamid

Site	Pest(s)	Form-ulation	Application Method and Equipment	Maximum Single Application Rate (g a.i./ha)	Maximum Cumulative Application Rate per CROP CYCLE (g a.i./ha)	Maximum Cumulative Application Rate per YEAR (g a.i./ha)	Maximum Number of Applications per year[1, 2]	Minimum Interval Between Applications (Days)[1, 2]
Use-site category 5 – Greenhouse Food Crops								
Greenhouse tomato	Grey mould (*Botrytis cinerea*)	Wettable granule	[Ground equipment]	750	(1500)	(1500)	2 [2 per crop cycle; 1 crop cycle per year]	7
Greenhouse pepper	Grey mould (*Botrytis cinerea*)	Wettable granule	[Ground equipment]	750	(1500)	(1500)	2 [2 per crop cycle; 1 crop cycle per year]	7
Greenhouse cucumber	Grey mould (*Botrytis cinerea*)	Wettable granule	[Ground equipment]	750	[1500]	[4500]	6 [2 per crop cycle; 3 crop cycles per year]	7
Greenhouse lettuce	Grey mould (*Botrytis cinerea*)	Wettable granule	[Ground equipment]	750	[1500]	[15 000]	20 [2 per crop cycle; 10 crop cycles per year]	7
Field tomato transplants grown in greenhouse	Grey mould (*Botrytis cinerea*)	Wettable granule	[Ground equipment]	750	[1500]	[1500]	2 [2 per crop cycle; 1 crop cycle per year]	7
Greenhouse eggplant	Grey mould (*Botrytis cinerea*)	Wettable granule	(Ground equipment)	750	2250	Not stated	3 per crop cycle	7
Use-site category 6 – Greenhouse Non-Food Crops								
Greenhouse Ornamentals	Grey mould (*Botrytis cinerea*)	Wettable granule	[Ground equipment]	560	[3400]	[13 400]	24 [6 per crop cycle]	7
Use-site category 14 – Terrestrial Food Crops								
Bushberries (blueberry, currant, elderberry, gooseberry and huckleberry)	*Botrytis cinerea*	Wettable granule	Ground equipment only (such as boom type, air blast, hand gun or mist blower sprayers)	850	Not applicable	3400	4	7
Cherries, peaches, nectarines	*Monilinia* spp. (including blossom blight, twig or shoot blight and brown rot)	Wettable granule	Ground equipment: air blast or mist blowers only	850	Not applicable	3400	4	7
Ginseng	*Botrytis cinerea*	Wettable granule	Ground equipment only (such as boom type, air blast, hand gun or mist blower	850	Not applicable	3400	4	10

Site	Pest(s)	Form-ulation	Application Method and Equipment	Maximum Single Application Rate (g a.i./ha)	Maximum Cumulative Application Rate per CROP CYCLE (g a.i./ha)	Maximum Cumulative Application Rate per YEAR (g a.i./ha)	Maximum Number of Applications per year[1, 2]	Minimum Interval Between Applications (Days)[1, 2]
			sprayers)					
Grapes	Botrytis bunch rot (grey mould)	Wettable granule	Ground equipment only (such as boom type, air blast, hand gun or mist blower sprayers)	560	Not applicable	560	[1]	[Not applicable. Repeat application not necessary.]
	Powdery mildew (in tank-mix only), black rot (in tank-mix only)	Wettable granule	Ground equipment only (such as boom type, air blast, hand gun or mist blower sprayers)	560	Not applicable	1680	3	[14]
Raspberries (red and black), loganberry, blackberry	*Botrytis cinerea* (grey mould)	Wettable granule	Ground equipment only (such as boom type, air blast, hand gun or mist blower sprayers)	850	Not applicable	3400	4	7
Strawberries	*Botrytis cinerea* (grey mould)	Wettable granule	Ground equipment only (such as boom type, air blast, hand gun or mist blower sprayers)	850	Not applicable	3400	4	7
	Botrytis, leaf spot (in tank-mix only)	Wettable granule	Ground equipment only (such as boom type, air blast, hand gun or mist blower sprayers)	850	Not applicable	3400	4	7
Use-site category 27 – Outdoor Non-Food Crops								
Outdoor ornamentals (such as African Violet, Geranium, Petunia, Poinsettia and Rose)	*Botrytis cinerea* (grey mould)	Wettable granule	Ground equipment	560	3400	3400	6	7

1 As of 24 June 2019, excluding discontinued products or products with a submission for discontinuation.

2 All information is derived from registered product labels, except for information provided by registrants which is indicated by [ ], and data calculated by the PMRA which is indicated by ( ).

Appendix III Toxicity Profile and Endpoints for Health Risk Assessment

Table 1 Toxicological Reference Values for Use in Health Risk Assessment for Fenhexamid

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute Dietary	No endpoint of concern attributable to an acute exposure was identified; therefore, an ARfD was not established.		
Chronic Dietary (All populations)	One-year dog dietary toxicity study	NOAEL = 17 mg/kg bw/day Hematological changes in both sexes and adrenal effect in ♀	100
	ADI = 0.2 mg/kg bw/day		
Short- to intermediate-term dermal[2]	90-day dog dietary toxicity study	NOAEL = 34 mg/kg bw/day Hematological changes and liver effects, supported by the haematological findings noted in the one-year dog study after 90 days	100
Long term dermal[2]	One-year dog dietary toxicity study	NOAEL = 17 mg/kg bw/day Hematological changes in both sexes and adrenal effect in ♀	100
Short to intermediate-term inhalation	28-day rat inhalation toxicity study	NOAEL = 19 mg/kg bw/day Decreased body weight gain, decreased landing foot splay, increased lung weight, histopathological findings in the lungs and lung-associated lymph nodes in both sexes, decreased bodyweight in ♂	100
Cancer	A cancer risk assessment was not required as there was no evidence of oncogenic 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 assessments

[2]Since an oral NOAEL was selected, a dermal absorption factor of 20% was used in a route-to-route extrapolation

Table 2 Toxicity Profile of Technical Fenhexamid

Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted.

Study Type/ Animal/PMRA#	Study Results
Toxicokinetic Studies	
Metabolism Wistar Rat PMRA# 1179977	Vehicle: 0.5% aqueous gum tragacanth Dosing: Rats received either a single gavage low dose (1 mg/kg bw), a repeat gavage low dose (1 mg/kg bw/day for 14 days of unlabelled fenhexamid followed by a single labelled gavage dose of 1 mg/kg bw), or a single gavage high dose (100 mg/kg bw) of [^{14}C]-phenyl-fenhexamid

Study Type/ Animal/PMRA#	Study Results
	Absorption: ^{14}C-Fenhexamid was rapidly absorbed from the GI tract in both sexes regardless of dosing regimen. Maximum radioactivity concentration in plasma was very low for all dosing regimens. Peak plasma concentration occurred within 10 minutes following both single and repeated low dose administration, with a second less pronounced peak 2 – 3 hrs later. Following high-dose administration, a subproportional increase in plasma levels was observed, indicating possible saturation of absorption. Peak plasma levels were detected 40 – 90 minutes postdosing. The plasma maximum concentrations were independent of sex. Bile cannulation experiments showed that ≥ 97% of the administered dose (AD) was absorbed from the GI tract. These results are suggestive of a pronounced first pass effect and high degree of enterohepatic circulation in rats. **Distribution:** There was no evidence of tissue retention and residual radioactivity in organs/tissues for all dosing regimens was low after 48 or 72 hrs**.** Radioactivity residues were lower in ♀ than ♂ after single high dose administration. After 48 hrs, the total radioactivity in the body excluding the GI tract was <0.3% of AD. Highest levels of radioactivity were detected in the GI tract (3% of AD) and in the liver and kidneys. **Metabolism:** Unchanged fenhexamid was the main component detected in excreta in both sexes following oral administration and accounted for 62 – 75% of AD. The glucuronic acid conjugate of the fenhexamid was the only major metabolite identified and accounted for 4 – 23% of AD. Bile contained almost exclusively the glucuronide conjugate. Identification of residues ranged from 88 – 99%. Neither bile nor faeces contained any metabolite not detected in urine. The major proposed metabolic pathway is via conjugation of the aromatic hydroxyl group with glucuronic acid. Prior to excretion, hydrolysis in the intestine converts the conjugate back to the parent compound giving rise to enterohepatic circulation. **Excretion:** Rate of radiolabel excretion was relatively high with 70% of AD being eliminated within 24 hrs. The elimination half-life was approximately 10 hours. Fecal excretion was the predominant route of elimination regardless of sex or oral dosing regimen. After 48 hrs, 62 – 81% of the AD was found in faeces and 15 – 36% in urine. In the bile cannulation experiment, more than 90% of the administered radioactivity was eliminated in the bile. Excretion in expired air was negligible (0.02%). Slight sex-related differences in elimination were noted following low-dose administration with higher renal excretion observed in ♀ (~30% AD) as compared to ♂ (16 – 22% AD). In both sexes, renal excretion of radioactivity was significantly higher after a single low dose compared to single high dose.

Study Type/ Animal/PMRA#	Study Results
Plasma Kinetic Study (Dietary) Wistar rat JMPR, 2005 PMRA# 2859046	**Supplemental-non guideline** Dosing: 0, 58/78, 285/407, 576/897, 944/1493 or 1217/1897 mg/kg bw/day (♂/♀) for 8 weeks. Concentration of fenhexamid in urine and plasma determined after 3 or 4 weeks of treatment. There were no treatment-related mortalities, clinical signs of toxicity or bw changes ↑ fc (♀ at doses ≥ 1493 mg/kg bw/day and in ♂ at ≥ 1897 mg/kg bw/day) After 3 wks of dosing, plasma concentrations were below the detection limit in all treatment groups. Increased urinary excretion of conjugated fenhexamid was observed with ascending dose. Renal elimination of fenhexamid was calculated to be approximately <5.0% of the ingested compound. Measurable urinary excretion of conjugated fenhexamid in both sexes indicated that fenhexamid was bioavailable from the diet. Faecal excretion was not measured in this study. These results corroborate the results of the metabolism study in rats where rapid absorption and elimination were observed.
Acute Toxicity Studies	
Acute Oral Toxicity (Gavage) Wistar Rats PMRA# 1179932	**LD_{50} ≥ 5000 mg/kg bw (♂/♀)** No mortality or clinical signs **Low acute oral toxicity**
Acute Dermal Wistar Rat PMRA# 1179933	**LD_{50} ≥ 5000 mg/kg bw (♂/♀)** No mortality or clinical signs. Localized redness was observed at the application site in 3/5 ♀ **Low acute dermal toxicity**
Acute Dermal Toxicity NMRI Mouse PMRA# 2859046 JMPR, 2005	**LD_{50} ≥ 5000 mg/kg bw (♂/♀)** There were no mortalities or abnormalities detected at necropsy. At 5000 mg/kg bw, apathy and piloerection were recorded in all animals. **Low acute dermal toxicity**
Acute Inhalation Toxicity (Nose-only) Wistar Rat PMRA# 1179934	**LC_{50} ≥0.32 mg/L (aerosol ♂/♀)** **LC_{50} ≥ 5.06 mg/L (dust ♂/♀)** Due to poor solubility in the vehicle, the maximum achievable concentration of the aerosol was 0.32 mg/L Dust particles were only 20% respirable. There were no mortalities or clinical signs of toxicity. **Low acute inhalation toxicity**
Primary Eye Irritation New Zealand White Rabbit PMRA# 1179935	Ocular discharge detected in one/three animals at the one hr observation period. **Non-irritating to the eyes**

Study Type/ Animal/PMRA#	Study Results
Primary Skin Irritation New Zealand White Rabbit PMRA# 1179935	No skin reaction noted **Non-irritating to the skin**
Dermal Sensitization – Buehler's method Dunkin-Hartley Guinea Pig PMRA# 1179936	**Not a skin sensitizer**
Dermal Sensitization – Maximization Test Dunkin-Hartley Guinea Pig PMRA# 2764230	**Not a skin sensitizer**
Dermal Sensitization – Maximization Test Dunkin-Hartley Guinea Pig PMRA# 2764231	**Not a skin sensitizer**
Short-Term Toxicity Studies	
14-week Oral Toxicity (Dietary) (Range-finding) B6C3F1 Mouse PMRA# 1179943	**Supplemental-Range-finding** **3284/5151 mg/kg bw/day:** ↑ fc, ↓ fe, ↑ water consumption, ↓ kidney wt, ↑ liver wt (slight), ↑ basophilic cortical tubules in kidney (♂/♀); ↑ incidence of dense centrilobular hepatocytes (glycogen depletion) (♂)
90-day Oral Toxicity including Functional Observational Battery (Dietary) CD-1 Mouse PMRA# 2764233	**Supplemental: Non-guideline study due to incomplete gross and microscopic pathology** **≥ 323/574 mg/kg bw/day:** ↓ erythropoietin wk 13 (equivocal, not adverse) *(♀)* **3417/6145 mg/kg bw/day:** ↑ fc and water intake, ↑ creatinine, ↑ urea, ↑ incidence of pathological finding in the kidneys (basophilic tubules, tubular dilation and tubular cast) (♂/♀); ↓ kidney wt, ↑ incidence of kidneys with rough surface, deformation of the kidney, pale discolouration of the kidney (♂); ↑ incidence of siderosis in the spleen at interim sacrifice (♀)
28-day Oral Toxicity (Gavage) Wistar Rat PMRA# 1179939	Vehicle: 2% aqueous Cremophor EL **NOAEL ≥ 1000 mg/kg bw/day (♂/♀)** No treatment-related findings.

Study Type/ Animal/PMRA#	Study Results
90-day Oral Toxicity (Dietary) Wistar Rat PMRA# 1179940	**NOAEL = 415/1132 mg/kg bw/day (♂/♀)** **≥202/270 mg/kg bw/day:** ↑ fc (♂/♀); ↓ liver wt (♂) (non-adverse) **≥904 mg/kg bw/day:**↓ bw, ↓bwg, ↓ fe, ↑AST, ↑ALT, ↑ calcium (wk 4 only), ↓ bilirubin (♂) **1904/2824 mg/kg bw/day:** ↑ Kupffer cell proliferation (♂/♀); ↓ heart wt (♂); ↓ bwg first 2 wks of treatment, ↓ fe, ↓ liver wt, ↑ incidence of condensed hepatocytes and peripheral dark cells in the liver (♀) **Recovery: (Additional 10/sex/group in the control and high-dose group were allowed to recover for 4 weeks)** **1904/2824 mg/kg bw/day:** No clinical chemistry changes, alteration in organ weight or histopathological findings were noted after the recovery period. No effects on bw or bwg were observed in ♀ in the recovery group during. In ♂, bwg effects were limited to a transient decrease at week 1 which resulted in ↓ bw in wks 1 and 2.
90-day Oral Toxicity including Functional Observational Battery (Dietary) Wistar Rat PMRA# 2764232	**Supplemental: Non-guideline study due to incomplete gross and microscopic pathology** **≥38/47 mg/kg bw/day:** ↑ urinary pH [considered non-adverse] (♂/♀) **≥404/553 mg/kg bw/day:** ↑ urinary excretion (♂: dose-dependent ↑ in number of animals affected and number of days observed), ↑ water consumption **(**♂/♀**)**; ↑ fc (slight), ↓ reticulocytes (weeks 3 and 12) (♂) [all findings considered non-adverse] **5585/8101 mg/kg bw/day:** piloerection, ↓ motility and reactivity, ↓ bw, ↓ bwg, ↑ fc, ↑ calcium,↑ incidence of pathological finding in the kidneys (basophilic tubules, tubular dilation and tubular cast at interim and terminal sacrifice**) (**♂/♀**);** discoloured faeces, ↑ creatinine, ↑ urea, ↑ kidney wt (interim sacrifice), ↑ incidence of enlarged and discoloured kidneys (interim sacrifice) (♂)
28-day Oral Toxicity (Dietary) Beagle Dog PMRA# 2859046, JMPR 2005	**Supplemental-Range finding** **500 mg/kg bw/day:** ↓ methaemoglobin (slight, not toxicologically significant)
90-day Oral Toxicity (Dietary) Beagle Dog PMRA# 1179944	**NOAEL = 34/37 mg/kg bw/day (♂/♀)** **≥ 34/37 mg/kg bw/day:**↑ liver wt (♂/♀) (not adverse at this dose level) **≥ 239/261 mg/kg bw/day:** ↑ Heinz bodies wk 13 (♂/♀); ↑ ALP (♀) **1748/1866 mg/kg bw/day:** ↑ Heinz bodies wk 6 onwards, ↓ RBC, haemoglobin and haematocrit wk 13, ↑ spleen wt (♂/♀); ↑ liver wt (♂); ↑ ALP, ALT (♀)
1-year Oral Toxicity (Dietary) Beagle Dog	**NOAEL = 17/19 mg/kg bw/day (♂/♀)** **≥ 17/19 mg/kg bw/day:** ↑ Heinz bodies wk 52 (not adverse) (♀)

Study Type/ Animal/PMRA#	Study Results
PMRA# 1179945	**≥ 124/133 mg/kg bw/day:**↑ Heinz bodies wk 7 onwards, ↓ RBC, haemoglobin and haematocrit wk 7 onwards (♂/♀); ↑ glutathione-S-transferase activity in the liver, ↑ adrenal wt, ↑ incidence of intracytoplasmic vacuoles in the adrenal cortex (♀) **918/947 mg/kg bw/day:** ↑ incidence of thin appearance, ↓ bw and bwg (♂/♀); ↓ spleen wt (♂); ↓ iron wk 52, ↑ spleen wt, ↓ uterus and ovary wt, ↑ thymus wt (♀)
21-Day Dermal Toxicity New Zealand White Rabbit PMRA# 1179979	**NOAEL ≥ 1000 mg/kg bw/day** No evidence of systemic toxicity or skin irritation.
5-day Inhalation Toxicity (Nose-only) (Range-finding) Wistar Rat PMRA# 1179969	**Supplemental-Range finding** **≥ 0.1 mg/L (27 mg/kg bw/day):** ↑ incidence of grey lung colouration on day 7 (♂/♀) **1 mg/L (296 mg/kg bw/day):** ↑ lung wt day 7,↑ incidence of grey lung colouration on day 21 (♂/♀)
28-Day Inhalation Toxicity (Nose-only) Wistar Rat PMRA# 2764234	**NOAEC = 0.069 mg/L (19 mg/kg bw/day)** **≥ 0.069 mg/L (19 mg/kg bw/day):** ↑ grey discolouration of the lungs (slight at this dose level), ↑ bronchiolo-alveolar proliferation (Slight at this dose level) (♂/♀); ↓ landing foot splay, ↓ forepaw grip strength (equivocal.) (♂); ↓ WBC, ↑ juvenile neutrophils in bone marrow (slight) (♀) [all changes considered not adverse at this dose level] **0.487 mg/L (132 mg/kg bw/day):** ↓ bwg,↓ lymphocyte and ↑ segmented neutrophils (both slight and not adverse), ↑ lung wt, ↑ incidence of grey discolouration of lung-associated lymph nodes, pigment laden alveolar macrophages in the lungs and sinus histiocytosis in the lung-associated lymph nodes (♂/♀); ↓ bw, ↑ liver cytochrome P450 and O-demethylase (slight), ↑ juvenile neutrophils in bone marrow (♂); ↓ landing foot splay, ↑ urinary volume, ↑ band neutrophil in bone marrow (♀)
Chronic Toxicity/Oncogenicity Studies	
2-year Oncogenicity (Dietary) B6C3F1 Mouse PMRA# 1179970	**NOAEL = 247/1055 mg/kg bw/day (♂/♀)** **≥ 807 mg/kg bw/day:** ↓ kidney wt at interim and terminal sacrifice, ↓ vacuolation of proximal tubular epithelium cells (♂) **2355/3178 mg/kg bw/day:** ↑ water intake, ↑ liver wt (♂/♀); ↓ bw wk 43 onwards,↓ overall bwg, ↑ creatinine, ↑ bilirubin, ↑ albumin, ↑ incidence of chronic renal disease (♂); ↓ kidney wt at termination, ↑ incidence of basophilic cortical tubules (♀) **No evidence of carcinogenicity**
2-year Chronic Toxicity/carcinogenicity (Dietary) Wistar Rat PMRA# 1179971	**NOAEL = 28/40 mg/ kg bw/day (♂/♀)** **≥ 292/415 mg/kg bw/day:** ↓ GLDH, ↓ protein concentration and excretion in urine (♂/♀); ↑ incidence of cecal mucosa hyperplasia and inflammation and cecum necrosis/mineralization, ↑ splenic extramedullary haematopoiesis (♂); ↓ bw, ↓ bwg, ↑ fc, ↓ fe, ↑ water consumption (♀)

Study Type/ Animal/PMRA#	Study Results
1179972	**1280/2067 mg/kg bw/day**: ↑ reticulocytes at termination, ↑ incidence of enlarged spleen (slight), ↑ cellularity of the bone marrow in the femur and sternum (slight), ↑ incidence of thyroid follicular alteration (♂/♀); ↑ fc, ↓ fe, ↑ water consumption, ↑ALP at termination (slight), ↑ albumin (slight), ↑ thyroid follicular cell hyperplasia (♂); ↓ bw, ↑ spleen wt, ↑ uterine glandular hyperplasia (♀) **No evidence of carcinogenicity**
Developmental/Reproductive Toxicity Studies	
2-generation Reproductive Toxicity Study (Dietary) Sprague-Dawley Rat PMRA# 1179974	**<u>Parental Toxicity:</u>** **Parental NOAEL = 38/45 mg/kg bw/day (♂/♀)** **≥ 38/45 mg/kg bw/day:** ↑ALP in P and F_1 (not adverse at this dose level) (♀) **≥ 406/477 mg/kg bw/day:** ↓ bw during premating in P, ↓ fc in P wk 1 premating, ↑ ALP in P and F_1 (♂/♀); ↑ fc, ↑ creatinine in P, ↓ liver wt in P (♂); ↓ P bw during lactation, ↑ GGT in P, ↑ urea nitrogen in F_1(♀) **1814/2043 mg/kg bw/day:** ↑ mortality in F_1 postweaning (mortality considered to be the result of ↓ bw at weaning), ↓ kidney wt (slight, ♀ only in P); ↑ GGT in P, ↑ urea nitrogen in P and F_1 (♂); ↓ bw and bwg during gestation (P and F_1), ↑ fc (GD6-13, P only), ↓ bw during lactation in F_1 **<u>Reproductive Toxicity:</u>** **Reproductive NOAEL = 406/477 mg/kg bw/day (♂/♀)** **1814/2043 mg/kg bw/day:** ↓ litter size F_1 and F_2 **<u>Offspring Toxicity:</u>** **Offspring NOAEL = 45 mg/kg bw/day (♂/♀)** **≥ 477 mg/kg bw/day:** ↓ bw in F_1 and F_2 from PND 14 onwards, ↓ bwg (♂/♀) **2043 mg/kg bw/day:** ↓ bw in F_1 and F_2 from PND 4 onwards **No evidence of sensitivity of the young**
Developmental Toxicity Study (Gavage) Sprague-Dawley Rat PMRA# 1179976	Vehicle: aqueous 0.5% carboxy methylcellulose + 0.4% Tween 80 **Maternal** **LOAEL = 1044 mg/kg bw/day** **1044 mg/kg bw/day:**↓ bwg and fc during treatment **Developmental** **NOAEL = 1044 mg/kg bw/day** No developmental effects noted. **No evidence of sensitivity of the young** **No evidence of malformations**
Developmental Toxicity Study (Gavage) Sprague-Dawley Rat	Vehicle: aqueous 0.5% carboxymethylcellulose + 0.4% Tween 80 **Maternal** **NOAEL = 300 mg/kg bw/day**

Study Type/ Animal/PMRA#	Study Results
PMRA# 2859046, JMPR 2005	**≥1000 mg/kg bw/day:**↓ bwg during treatment, ↓ fc GD6-11 **Developmental** **NOAEL = 2000 mg/kg bw/day** No developmental effects observed. **No evidence of sensitivity of the young** **No evidence of malformations**
Developmental Toxicity Study Range-finding (Gavage) Himalayan Rabbit PMRA# 1179987	**Supplemental-Range-finding** **Maternal** **1000 mg/kg bw/day:** small scybala, and reduced and light coloured faeces, ↓ water consumption, ↓ fc and bwg
Developmental Toxicity Study (Gavage) Russian Rabbit PMRA# 1179998	Vehicle: aqueous 0.5% tylose **Maternal** **Maternal NOAEL = 100 mg/kg bw/day** **≥ 300 mg/kg bw/day**: ↑ clinical findings (discoloured urine, small scybala and ↓ faeces), ↓ placental wt **1000 mg/kg bw/day:** 2/15 dams had complete litter resorption, ↓ bwg and ↑ fc **Developmental** **Developmental NOAEL = 300 mg/kg bw/day** **1000 mg/kg bw/day:** 2/15 dams had complete litter resorption, ↓ bw of ♂ foetuses, ↑ delayed ossification (unossified 5th sternal segments, 15th caudal vertebrae, incomplete ossification of the digits of the medial phalanges bilaterally), **No sensitivity of the young** **No evidence of malformations**
Genotoxicity Studies	
Reverse Mutation Assay Salmonella typhimurium strains: TA98, TA100, TA1535, TA1537 E. coli WP2 uvrA PMRA# 1180003 2764235	Cytotoxicity at 700 µg/plate **Negative, with or without metabolic activation**

Study Type/ Animal/PMRA#	Study Results
Reverse Mutation Assay Salmonella typhimurium strains: TA98, TA100, TA1535, TA1537 PMRA# 1180002	Compound insolubility and excessive cytotoxicity at doses ≥ 2000 µg/plate Toxicity noted at ≥ 125 µg/plate **Negative, with or without metabolic activation**
Forward Mutation Assay Chinese Hamster Lung V79 Cells PMRA# 1180006	Cytotoxic at 150 µg/mL **Negative, with or without metabolic activation**
Chromosome Aberration Assay Chinese Hamster Ovary Cells PMRA# 1180004	**Negative, with or without metabolic activation.**
Unscheduled DNA Synthesis Primary Rat hepatocytes PMRA# 1180007	Cytotoxic at doses of 40 µg/mL **Negative**
DNA repair in bacterial system Bacillum subtilis H17 (Rec^+), M45 (Rec^-) PMRA# 2764236	**Supplemental, non-guideline study** **Negative**
In vivo Micronucleus Assay (Intraperitoneal) NMRI Mouse PMRA#1180005	One animal died during the study. Cytotoxic effects were noted in the bone marrow. **750 mg/kg bw/day**: Clinical signs of toxicity: (apathy, roughened fur, staggering gait, sternal recumbency, spasms and difficulty breathing) No ↑ in micronucleated polychromatic erythrocytes in any of the treated groups **Negative**
Neurotoxicity Studies	
Acute Neurotoxicity Study (gavage) Wistar Rat PMRA# 1179978	Vehicle: 2% aqueous Cremophor EL **NOAEL ≥ 2000 mg/kg bw** **2000 mg/kg bw:** ↓ body temperature (slight, not considered adverse) (♂) **No evidence of selective neurotoxicity**

Study Type/ Animal/PMRA#	Study Results
Published literature studies	
In vitro anti-androgenic assay MDA-kb2 human breast cancer cells transfected with androgen receptor gene PMRA# 2816971	QSAR predicted AR antagonist activity for fenhexamid. Assay in MDA-Kb2 transfected with the AR gene confirmed anti-androgenic activity; IC_{20} = 2.02 µM Fenhexamid was negative as an AR agonist
In vitro oestrogen receptor assay Yeast and MCF-7 human breast cancer cells PMRA# 2921189	Fenhexamid was a hERα agonist in the yeast oestrogen assay with a potency of 9.0 µM. EC_{50} values could not be obtained for the yeast androgen assay because the pesticide did not exhibit high enough agonistic activity but fenhexamid had agonistic activities at the highest concentration (100 µM) In MCF-7 cells, fenhexamid showed ERα agonist activities at 10 µM. At 100 µM, strong inhibition of cell growth was seen. In this cell line, exposure to fenhexamid for 4 or 24 hrs induced the expression of cyclin D2, progesterone receptor but not Nuclear respiratory factor 1. Fenhexamid suppressed expression of the retinoic acid receptor β2 and enhanced the oestradiol dependent downregulation of this gene. It also ↑ ERβ expression at low dose levels but there was no evidence of a dose-response. In summary, fenhexamid showed agonistic activities in MCF-7 cells via endogenous ER.
Cancer cell proliferation assays i) BG-1 human ovarian cancer cells ii) 7 ♀ BALB/c nude Mice with tumours formed by BG-1 cells. PMRA# 2816976	i) In vitro assay Fenhexamid, ↑ cell proliferation at a concentration of 10^{-5} M in BG-1 cells. Fenhexamid showed apparent oestrogen mimetic effect due to ability to induce the growth of oestrogen-responsive BG-1 cells. Co-incubation with ICI 182 780 (an ER antagonist) ↓ cell proliferation to negative control values (MTT cell proliferation assay). Fenhexamid ↑ cyclin D1 and cyclin E expression in BG-1 cells. No change in the expression of these proteins was observed when cells were co-incubated with fenhexamid and ICI 182 780 (protein expression in Western blot assay). Fenhexamid stimulated BG-1 cell migration in a wound-healing assay. Migration was inhibited with co-treatment with ICI 182 780, suggesting that migration was mediated by an ER-dependent pathway. Fenhexamid ↑ cathepsin D expression (protein known to promote transport and metastasis of tumour cells); however, expression slightly ↓ when co-treated with ICI 182 780. ii) In vivo assay Animals were ovariectomized once the tumour volume reached 40 mm^3. Animals then received 20 mg/kg bw/day of fenhexamid by intraperitoneal injection every 3 days for a period of 80 days. Fenhexamid did not induce tumour growth above controls; however mice died within 60 days. In tumour sections, haematoxylin and eosin staining showed that fenhexamid induced proliferative cellular formation but immunohistochemical staining showed no increase in PCNA cathepsin D, cyclin D1 or cyclin E expression. In summary, in vitro assays suggested that fenhexamid may increase cancer cell proliferation and metastasis; however, similar effects on cell proliferation and

Study Type/ Animal/PMRA#	Study Results
	metastasis were not observed in the in vivo assay.
High throughput screening analysis of reproductive toxicants PMRA# 2921188	Fenhexamid was identified as a strong oestrogen receptor activator in the ToxCast Receptor Profiling.
In vitro effect on oncomiR expression Human breast cancer cells MCF-7 and T47D and normal MCF-10A breast epithelial cells PMRA# 2921194	The effect of fenhexamid on the oncomiR miR-21 in normal and cancerous breast epithelial cell lines was examined. Fenhexamid ↑ the expression of miR-21 in MCF-7 and T47D cells but not in MCF-10A cells. This finding was suggestive that the induction of miR21 was not cell line specific but may be related to ERα expression. The increase in miR-21 in MCF-7 was blocked by fulvestrant and bicalutamide suggesting that fenhexamid acted via ERα and AR to induce miR-21 expression in these cells. As a result of the ↑ miR-21, known target genes in breast cancer cells, PDC4 and PTEN, were ↓ and another target, BCL-2, showed ↓ protein levels. Fenhexamid also affected the expression of other oncomiR. The expression of tumour suppressors miR-125b and miR181was decreased, while expression of tumour suppressor miR-200a was ↑. Consistent with ↑ miR200a, cell motility was inhibited by fenhexamid in a wound healing assay.
Effects on prostaglandin D2 synthesis SC5 juvenile mouse Sertoli cells PMRA# 2816979	Prostaglandin D2 is involved in generating a feedback loop to ensure male differentiation of the surrounding gonadal somatic cells. i) Fenhexamid inhibited prostaglandin D2 synthesis in Sertoli cells. IC_{50} = 7370 nM ii) Addition of arachidonic acid had no effects on prostaglandin D2 suppression by fenhexamid, suggesting mode of action is inhibition of cyclooxygenase (COX) isoforms; molecular modelling confirmed fenhexamid could fit into the ligand-binding packet of COX-2.
Effect on oestrogen receptor activity Yeast and Human osteosarcoma U2-OS cells PMRA# 2921192	Fenhexamid showed oestrogenic activity with concentration dependant curves in the Yeast-based oestrogen screen assay (YES). YES EC_{10} = 0.2 µM Dose dependant anti-oestrogenic effects were noted in this assay when fenhexamid was tested in combination with 17β-oestradiol. In this assay, fenhexamid led to an inhibition of the 17β-oestradiol effects by 79%. Estrogenic activity was also shown in the ERα chemically activated luciferase gene expression (CALUX) assay in human U2-OS cells ERα CALUX EC_{10}= 2.63 µM. In this assay, when fenhexamid was tested in combination with 17β-oestradiol, there was no evidence of any anti-estrogenic effects. Fenhexamid showed a dose-dependent estrogenic activity at the hERβ in the hERβ CALUX assay. ERβ CALUX EC_{10}= 5.01 µM

Appendix IV Dietary Exposure and Risk Assessments for Fenhexamid

Table 1 Summary of Chronic Dietary Exposure and Risk Assessment

Population Subgroup	Food Only[1]		Food and Water[1]	
	Exposure (mg/kg bw/day)	%ADI	Exposure (mg/kg bw/day)	%ADI
General Population	0.011871	6	0.013831	7
All Infants (< 1 year old)	0.017948	9	0.025269	13
Children 1–2 years old	0.029902	15	0.032598	16
Children 3–5 years old	0.023707	12	0.025901	13
Children 6–12 years old	0.013284	7	0.014915	8
Youth 13–19 years old	0.008380	4	0.009762	5
Adults 20–49 years old	0.010180	5	0.012127	6
Adults 50+ years old	0.011346	6	0.013239	7
Females 13–49 years old	0.010786	5	0.012700	6

[1] Acceptable Daily Intake (ADI) of 0.2 mg/kg bw/day applies to the general population

Appendix V Food Residue Chemistry Summary

Fenhexamid is a systemic protectant fungicide and is registered for use on food crops (greenhouse and terrestrial) and ornamentals. Fenhexamid is applied by ground equipment only (boom, hand gun, air blast, and mist blowers). Since fenhexamid is not registered for direct animal use and feed crops in Canada, animal metabolism and residue chemistry data are not required and no residue definition in animal commodities are established.

The dietary exposure assessment was updated to incorporate new toxicological reference values (ADI), the use of the latest available version of DEEM-FCID/NHANES and new drinking water exposure estimates.

The nature of the residues in plants and animals is adequately understood based on acceptable metabolism studies conducted on apples, grapes, greenhouse tomatoes, greenhouse lettuces and lactating goat. Metabolism studies for the four different crop groups: pome fruits, small fruit and berries, leafy vegetables and fruiting vegetables had similar metabolic pathway; additional plant metabolism studies are not required. A lactating goat study was submitted as part of a joint review with the USEPA to support the use on almonds and almond hulls, for livestock. Although not required by the PMRA, the study was previously reviewed. The current residue definition (RD) for enforcement purposes is: N-(2,3-dichloro-4-hydroxyphenyl)-1-methylcyclohexanecarboxamide. No changes to the residue definition for risk assessment or enforcement are proposed for this re-evaluation. Similarly, there are no proposed changes to the established MRLs.

Analytical method Bayer AG Method 00362 was previously reviewed and deemed acceptable for data gathering and enforcement purposes. Residues are extracted with acetone and liquid-liquid partition on a ChemElut-column with cyclohexane-ethyl acetate as eluant. Fenhexamid is determined by reverse phase liquid chromatography (HPLC) coupled with an electrochemical detector (ECD). The method tests for the parent compound only and has been validated by an independent laboratory. The method LOQ ranged from 0.02 ppm – 0.05 ppm, depending on the matrix.

Acceptable freezer storage stability studies have been completed on eight diverse crops groups: small fruit and berries (CG13), stone fruit (CG12-09), pome fruit (CG11-09), root and tuber vegetables (CG1), fruiting vegetables (CG8-09), leafy vegetables (CG4-13), and bulb vegetable (CG3-07). The data on file demonstrates that when spiked at levels ranging from 0.02-0.5 ppm, fenhexamid resides are stable in frozen storage (−18° to -21°C). Storage duration ranged from 4 to 17.5 months in grape juice, raisins, raisin waste, tomatoes, grapes, strawberries, peaches, plums cherries, ginseng, greenhouse pepper, greenhouse cucumber, greenhouse tomato, greenhouse lettuce, blueberries and onions, and 2 years in apple.

Supervised field trials were previously reviewed for a number of terrestrial and greenhouse commodities. The zone requirements met the PMRA's current "Residue Chemistry Guidelines" (Regulatory Directives DIR98-02 and DIR2010-05) in caneberry/raspberry, ginseng, grapes, greenhouse vegetables and plums. However, the requirements were not met for blueberries, onions, peaches, sweet cherries, tart cherries and strawberries. Given that the trials were conducted in different zones, representing diverse soil and climate conditions, and that the trials

were conducted at ≥GAP (ranged from 0.97-2 × GAP), it was determined that sufficient information was available to support these crop uses.

Adequate data and reviews were available for confined crop rotation. The confined rotational study demonstrated that fenhexamid residues may accumulate in Swiss chard at >0.01 ppm (maximum 0.03 ppm found). A waiver was submitted for a field crop rotation study requirement. Given that applications in confined rotation studies are applied directly to soil (registered as a foliar use), trial was conducted at an exaggerated rate, the LOQ for registered rotated crop is 0.05 ppm and a 30-day plant back interval exist in the current end-use product labels, the wavier was accepted.

Processing studies were previously reviewed and deemed acceptable. Experimental processing factors from these studies were applied in the risk assessment for grape juice, grape wine, raisin, tomato paste, and tomato juice.

Overall, sufficient information was available to adequately assess the dietary exposure and risk from fenhexamid.

Appendix VI Agricultural Mixer/Loader/Applicator Exposure and Risk Assessment

Table 1 Short-to Intermediate-Term Mixer/Loader/Applicator Exposure and Risk Assessment for Fenhexamid

Application Method	Use[a]	Rate[b]	ATPD[c]	Exposure (ug/kg bw/day)[d]		MOE (Target = 100)	
				Dermal	Inhalation	Dermal[e]	Inhalation[f]
Single Layer, CR Gloves (M/L/A)							
Air blast	Outdoor crops-max rate	0.85 kg a.i./ha	20 ha	164	6.56	208	2900
Groundboom	Outdoor crops-max rate	0.85 kg a.i./ha	26 ha	6.05	6.49	5620	2930
Backpack	Greenhouse crops-max rate	1.5 g a.i./L	150 L	3.11	0.24	10 900	80 500
	Outdoor crops-max rate	1.7 g a.i./L	150 L	3.53	0.27	9640	71 000
MechPHG	Greenhouse crops-max rate	1.5 g a.i./L	3800 L	80.8	12.3	421	1540
	Outdoor crops-max rate	1.7 g a.i./L	3800 L	91.6	14.0	371	1360
ManPHW	Greenhouse crops-max rate	1.5 g a.i./L	150 L	0.58	0.19	58 800	101 000
	Outdoor crops-max rate	1.7 g a.i./L	150 L	0.66	0.21	51 900	89 000
Single layer, CR gloves (M/L), CR coveralls with hood over single layer, CR gloves, respirator (A)							
HH AB/MB	Greenhouse crops-max rate	0.75 kg a.i./ha	2 ha	122	46.1	278	412
	Outdoor crops-max rate	0.85 kg a.i./ha		138	52.3	245	364

ATPD = Area Treated Per Day, MOE = Margin of Exposure, M/L = Mixer/Loader A =Applicator, CR = Chemical Resistant; Single layer = long-sleeved shirt, long pants; Max = maximum; ManPHW = manually pressurized hand wand; MechPHG = mechanically-pressurized hand gun; HH AB/MB = handheld air blast/mistblower

[a] The highest rate for greenhouse or outdoor crops was used in the risk assessment, as applicable for each application equipment.

[b] Rate on the label is expressed in kg a.i./ha. The minimum spray volume on the label of 500 L/ha was used to calculate the rate in g a.i./L.

[c] Default ATPD values were used.

[d] Exposure was calculated: unit exposure × application rate × ATPD × dermal absorption of 20% (for dermal exposure route)/body weight (80 kg).

[e] Calculated using a NOAEL of 34 mg/kg bw/day from a 90-day dog oral dose toxicity study and target MOE of 100.

[f] Calculated using an inhalation NOAEC of 0.069 mg/L (≈19 mg/kg bw/day) from a 28 day inhalation study and target MOE of 100.

Appendix VII Occupational Postapplication Exposure and Risk Assessment

Table 1 Postapplication Occupational Exposure and Risk Assessment for Fenhexamid

Use(s)	Rate (kg a.i/ha)	App #	Int (days)	Activity	TC[a] (cm^2/hr)	DFR_0 [b]	Day 0 MOE[c]	REI[d] (days)
Greenhouse ornamentals	0.56	6	7	Cut flower: Disbudding, hand harvesting, hand pruning (high crops)	4000	5.81	**37**	44
				Cut flower: Container moving, pinching, plant support/staking, hand pruning (low crops), scouting, transplanting, weeding Non-cut flower: all activities	230		**636**	12 hours
				Irrigation (non-handset), mechanical weeding	No TC[e]	12 hours		
		1	N/A	Cut flower: Disbudding, hand harvesting, hand pruning (high crops)	4000	1.40	**636**	12 hours
Greenhouse cucumber, tomato, pepper	0.75	2	7	All activities	1400	3.75	**162**	12 hours
Greenhouse eggplant	0.75	3	7	All activities	1400	5.63	**108**	
Greenhouse lettuce	0.75	2	7	All activities	230	3.75	**986**	
Greenhouse tomato for transplant	0.75	2	7	All activities	230	3.75	**1970**	
Cherry, peach, nectarine	0.85	4	7	Thinning fruit by hand	3000	6.71	**85**	3 days
				Hand harvesting	1400		**181**	12 hours
				Scouting, hand pruning, training	580		**437**	
				Transplanting	230		**1100**	
				Orchard maintenance, hand weeding, bird control, propping	100		**2540**	
				Irrigation, fertilizing, mechanical weeding, mechanical harvesting, spreading bins, thinning fruit with no contact with treated foliage, frost	No TC[e]	12 hours		

Use(s)	Rate (kg a.i/ha)	App #	Int (days)	Activity	TC[a] (cm^2/hr)	DFR_0 [b]	Day 0 MOE[c]	REI[d] (days)
				control				
Strawberry	0.85	4	7	Hand harvesting	1100	6.71	**230**	12 hours
				Transplanting	230		**1100**	
				Scouting	210		**1210**	
				Hand weeding, canopy management,	70		**3620**	
				Irrigation (non-hand set), mechanical weeding	No TC[e]	12 hours		
Raspberry, blackberry, loganberry, high bush blueberry, currant, gooseberry, elderberry, huckleberry	0.85	4	7	Irrigation (hand set)	1750	5.36	**181**	12 hours
				Hand harvesting, tying/training (full foliage)	1400		**226**	
				Scouting, hand pruning, hand weeding, tying/training (minimum foliage), bird control, frost control (high bush blueberry, huckleberry only)	640		**495**	
				Transplanting	230		**1380**	
				Irrigation (non-handset), mechanical harvesting, mechanical weeding, burn down, frost control	No TC[e]	12 hours		
Low bush blueberry	0.85	4	7	Irrigation (hand set)	1750	6.71	**145**	12 hours
				Hand harvesting, scouting	1100		**230**	
				Transplanting	230		**1100**	
				Hand weeding	70		**3620**	
				Mechanical harvesting, mechanical weeding, irrigation (non-hand set)	No TC[e]	12 hours		
Ginseng	0.85	4	10	Irrigation (hand set)	1750	6.12	**159**	12 hours
				Hand harvesting, deflowering and hand picking seeds (berries)	1100		**252**	
				Scouting	210		**1320**	
				Hand weeding	70		**3970**	
				Mechanical harvesting, mechanical weeding, irrigation (non-handset)	No TC[e]	12 hours		
Grape	0.56	3	14	Girdling, Turning	19300	2.48	**35**	40
				Hand harvesting, leaf pulling by	8500		**81**	5

Use(s)	Rate (kg a.i/ha)	App #	Int (days)	Activity	TC[a] (cm^2/hr)	DFR_0 [b]	Day 0 MOE[c]	REI[d] (days)
				hand, tying/training (full foliage)				
				Irrigation (hand set)	1750		**391**	12 hours
				Scouting, hand pruning, hand weeding, bird control, propagating, trellis repair	640		**1070**	
				Transplanting	230		**2980**	
				Mechanical harvest, mechanical weeding, mechanical leaf pulling, mechanical pruning, burn down, ditching, irrigation (non-handset)	No TC[e]	12 hours		
Outdoor ornamentals (cut flowers)	0.56	6	7	Hand harvesting, disbudding, hand pruning (high crops)	4000	5.73	**74**	9
				Irrigation (hand set)	1750		**170**	12 hours
				Hand weeding, hand pruning (low crops), scouting, container moving, pinching, plant support/staking, transplanting	230		**1290**	
				Irrigation (non-handset), mechanical weeding	No TC[e]	12 hours		
		4	7	Hand harvesting, disbudding, hand pruning (high crops)	4000	4.42	**96[f]**	12 hours
Outdoor ornamentals (non-cut flowers)	0.56	6	7	Irrigation (hand set)	1750	5.73	**170**	12 hours
				All activities (except hand set irrigation)	230		**1290**	

Shaded cells indicate where the MOE is below or not within range of the target MOE on Day 0 and risks are not shown to be acceptable.

App # = Number of applications per year or crop cycle; Int = Application Interval; TC = Transfer Coefficient; DFR = Dislodgeable Foliar Residue; Peak = Peak DFR expressed as a percent of the application rate; Disp = Percent dissipation per day; DFR_0 = DFR on the day of the final application (ug/cm^2); Day 0 = day of application, after sprays have dried; Exp = Exposure (ug/kg bw/day); MOE = Margin of Exposure; REI = Restricted Entry Interval

[a] Transfer coefficients and activities from the PMRA Ag TC table (PMRA, 2012a) were used.

[b] For greenhouse crops, the default DFR values (peak of 25% of the application rate, 2.3% dissipation per day for ornamentals and 0% per day for vegetables) were used to calculate the DFR on Day 0 after the last application. For all outdoor crops, the daily dissipation rate of 2.4% per day was used. For grapes and trellis crops, the peak DFR after a single application from the grape DFR study was used (20%). For all other outdoor crops, the default peak DFR of 25% of the application rate was used.

[c] MOE = exposure on Day 0 [DFR_0 × Transfer Coefficient × 8 hr × 20% dermal absorption / 80 kg] /NOAEL × 1000 ug/mg. Based on a NOAEL of 34 mg/kg bw/day from an oral dog toxicity study and target MOE of 100 for intermediate-term exposure all crops except for greenhouse lettuce, cucumber, peppers, tomatoes (excluding those for field transplant), eggplant and ornamentals. For these crops, the MOE is calculated based on a NOAEL of 17 mg/kg bw/day from an oral dog toxicity study and target MOE of 100 for long-term exposure.

[d] Amount of time required for residues to decline to a level where the MOE reaches or is in range of the target MOE and risks are shown to be acceptable. The minimum REI of 12 hours was applied when the MOE reached the target MOE on day 0.
[e] Not considered to be a hand labour activity. Postapplication worker risks are acceptable provided the minimum 12 hours REI is followed.
[f] MOE is considered to be within range of the target MOE, given the conservatisms in the risk assessment, such as the DA value and the dissipation rate from the grape DFR study.

Appendix VIII Environmental Assessment

Table 1 Summary of fate and behaviour in the terrestrial environment.

Property	Value (Fenhexamid alone)	Value (Fenhexamid combined with non-extractable residues)	Comments	PMRA#
Abiotic transformation				
Phototransformation on soil DT_{50} (days)	Stable	Stable	Stable	PMRA# 1180045
Phototransformation in air DT_{50} (days)	No study	No study	EPISuite calculations indicate a $t_{1/2}$ in air of 0.61 days, however, sorption to airborne particulate is 97% which is unavailable for photo-oxidation, making the $t_{1/2}$ in air inaccurate.	-
Biotransformation				
Biotransformation in aerobic soil DT_{50} (days)	0.09 – 1.4	376 – 1248	FEX: non-persistent FEX + NERs = persistent	PMRA# 1180049, PMRA# 2748880
Biotransformation in anaerobic soil DT_{50} (days)	76 – 118	645	FEX: non-persistent FEX + NERs = persistent	PMRA# 2983491
Mobility				
Adsorption / desorption in soil K_{oc} (mL/g)	383 – 3106	No information	FEX: Potential for leaching	PMRA# 1180011
Leaching potential	-	-	GUS and Cohen scores indicate FEX is likley not a leacher.	-
Volatilization	No studies	-	VP and HLC indicate FEX is non-volatile.	-
Field studies				
Field dissipation DT_{50} (days)	<1 – 3.2	No information	non-persistent, however, no information on NERs and transformation products.	PMRA# 1179641, PMRA# 2982480
Carry-over potential	No	No information	FEX: No carry over potential FEX+NERs: No field information	-
Field lysimeter	Detected in 30-cm deep layer	No information	Little potential to reach groundwater.	PMRA# 1179997

Table 2 Summary of fate and behaviour in the aquatic environment.

Study type	Value (Fenhexamid alone)	Value (Fenhexamid combined with NERs)	Comments	PMRA#
Abiotic transformation				
Hydrolysis DT_{50} (days)	Stable	Stable	Stable	PMRA# 1180045
Phototransformation in water $t_{1/2rep}$ (days)	0.03	No information	Important route of transformation	PMRA# 1180047
Biotransformation				
Biotransformation in aerobic water systems DT_{50} (days)	7.35 – 15.9	110 – 1325	FEX: Non- to slightly persistent FEX + NERs: Persistent	PMRA# 1180010, PMRA# 2748881, PMRA# 1180000, PMRA# 2748882
Biotransformation in anaerobic water systems DT_{50} (days)	60.7 – 115	58.4 – 1026	FEX: Moderately persistent to persistent	
Partitioning				
Adsorption / desorption in sediment Koc (mL/g)	-	-	Formation of non-extractable residues reached a maximum of 75% in aerobic and anaerobic aquatic studies.	
Field studies				
Field dissipation	No studies available			
Bioaccumulation				
Fish Bioconcentration	BCF in whole fish = 132 – 185		Low potential for accumulation in aquatic biota	PMRA# 1180026

Table 3 Selected endpoints used in the terrestrial and aquatic risk assessments and uncertainty factors applied to the toxicity endpoints.

Organism	Exposure	Endpoint	Value	Uncertainty factor to be applied[1]
Earthworm	Acute	14-d LC_{50}	≥1000 mg a.i./kg dw	2
	Chronic	56-d NOEL	5000 g a.i./ha or 19.8 mg a.i./kg	1
Bee	Oral Contact Adult feeding Larval feeding	48-h LD_{50} 48-h LD_{50} 10-d NOAEL 21-d NOAEL	≥102.1 µg a.i./bee ≥200 µg a.i./bee ≥3.52 µg a.i./bee/day 79 µg a.i./larva/day	1
Beneficial Insects	Acute (*T. pyri*) Chronic *(Aleochara bilineata)*	14-d LR_{50} 28-d LR_{50}	≥1.98 kg a.i./ha ≥1.98 kg a.i./ha	1
	T. pyri and *A. rhopalosiphi* (glass plate)	Acute LR_{50}	≥4.97 kg a.i./ha	1
Birds - Bobwhite quail	Acute	LD_{50}	≥2000 mg a.i./kg bw	10
	Dietary	5-d-LD_{50}	≥5000 mg a.i./kg bw	10
	Reproduction	23-week	154 mg a.i./kg bw/day	1

		NOAEL		
Mammals - Rat	Acute	LD_{50}	≥2000 mg a.i./kg bw	10
	Chronic	90-d NOAEL	415 mg a.i./kg bw/day	10
	Reproduction	2-generation	38 mg a.i./kg bw/day	1
Terrestrial vascular plants	Seedling emergence	21-d EC_{25}	3800 g a.i./ha	1
	Vegetative vigour	17-d EC_{25}	4500 g a.i./ha	1
Freshwater invertebrates	Acute (*D. magna*)	48-h LC_{50}	≥18.8 mg a.i./L	2
	Chronic (*D. magna*)	21-d NOEC	1.0 mg a.i./L	1
	Pore water (*C. dilutus*)	10-d LC_{50}	≥7.6 mg a.i./L	2
	Acute sediment (*C. riparius*)	10-d LC_{50}	≥90 mg a.i./kg	2
	Chronic Sediment (*C. riparius*)	28-d NOEC	52.8 mg a.i./kg	1
Freshwater fish	Acute (rainbow trout)	96-h LC_{50}	1.23 mg a.i./L	10
	Chronic/ELS (rainbow trout)	96-d NOEC	0.101 mg a.i./L	1
Amphibians[2]	Acute (trout surrogate)	96-h LC_{50}	1.23 mg a.i./L	10
	Chronic (trout surrogate)	96-d NOEC	0.101 mg a.i./L	1
Aquatic vascular plants	Acute	14-d EC_{50}	≥1.0 mg a.i./L	2
Algae	Acute *(Selanstrum capricornutum)*	72-h EC_{50}	1.33 mg a.i./L	2
Saltwater invertebrates	Acute (*M. bahia*)	96-h LC_{50}	4.6 mg a.i./L	2
	Chronic (*A. bahia*)	28-d NOAEC	0.91 mg a.i./L	1
	Pore water (*L. plumulosus*)	10-d LC_{50}	≥5.3 mg a.i./L	2
	Sediment (*L. plumulosus*)	10-d LC_{50}	≥77 mg a.i./kg	2
Saltwater fish	Acute (Sheepshead minnow)	96-h LC_{50}	11 mg a.i./L	10
	Chronic	-	No data	1
Saltwater algae	Acute (*Skeletonema costatum*)	96-h LC_{50}	≥1.95 mg a.i./L	2

[1] as per the 2019 PMRA Guidance Manual
[2] no information was found in an extensive literature search on toxicity to amphibians.

Table 4 Summary of screening level risk to terrestrial organisms.

Organism	Exposure	Endpoint	Endpoint for Risk Assessment Value	Maximum EEC (EDE for birds and mammals)	RQ	LOC Exceeded
Earthworm	Acute	14-d LC_{50}	≥500mg a.i./kg dw	1.5 mg a.i./kg	<0.003	NO
	Chronic	56-d NOEL	19.8 mg a.i./kg	1.5 mg a.i./kg	0.07	NO
Bee	Oral	48-h LD_{50}	≥102.1 µg a.i./bee	2.04 µg a.i./bee	<0.01	NO
	Contact	48-h LD_{50}	≥200 µg a.i./bee	24.65 µg a.i./bee	<0.24	NO
	Adult feeding	10-d NOAEL	≥3.52 µg a.i./bee/day	24.65 µg a.i./bee	**<7**	**MAYBE**
	Larval feeding	21-d NOAEL	79 µg a.i./larva/day	10.2 µg a.i./larva	0.13	NO
Beneficial Insects	Acute (*T. pyri*)	14-d LR_{50}	≥1.98 kg a.i./ha	1.7 kg a.i./ha[1]	<0.85	NO
	Chronic *(Aleochara bilineata)*	28-d LR_{50}	≥1.98 kg a.i./ha	3.4 kg a.i./ha[2]	**<1.72**	**MAYBE**
	T. pyri *A. rhopalosiphi*	Glass plate LR_{50}	≥4.97 kg a.i./ha	3.4 kg a.i./ha[2]	<0.68	NO
Birds - Bobwhite quail	Acute	LD_{50}	≥2000 mg a.i./kg bw	154.15[3]	<0.77	NO
	Dietary	5-d LD_{50}	≥5000 mg a.i./kg bw	154.15[3]	<0.31	NO
	Reproduction	23-week NOAEL	154 mg a.i./kg bw/day	154.15[3]	**1.0[3]**	**YES**

Organism	Exposure	Endpoint	Endpoint for Risk Assessment Value	Maximum EEC (EDE for birds and mammals)	RQ	LOC Exceeded
Mammals - Rat	Acute	LD_{50}	≥2000 mg a.i./kg bw	172[4]	<0.86	NO
	Reproduction	2-gen. NOAEL	38 mg a.i./kg bw/day	172[4]	**4.53[4]**	**YES**
Terrestrial vascular plants	Seedling emergence	21-d EC_{25}	3800 g a.i./ha	2550 g a.i./ha[5]	0.67	NO
	Vegetative vigour	17-d EC_{25}	4500 g a.i./ha	2550 g a.i./ha[5]	0.57	NO

[1] 2 applications at 850 g a.i./ha at 7-day intervals (14 days) = 1700 g a.i./ha; dissipation not taken into consideration between applications.
[2] 4 applications at 850 g a.i./ha at 7-day intervals (28 days) = 3400 g a.i./ha; dissipation not taken into consideration between applications.
[3] Maximum EDE calculated was for small birds.
[4] Maximum EDE calculated was for medium-sized mammals.
[5] 3 × 850 g a.i./ha at 7-day intervals (21 days) = 2550 g a.i./ha; dissipation not taken into consideration between applications.

Table 5 Summary of screening level risk to aquatic organisms.

Organism	Exposure	Endpoint	Endpoint for Risk Assessment (mg a.i./L)	EEC (mg a.i./L)	RQ	LOC Exceeded
Freshwater invertebrates	Acute (*D. magna*)	48-h LC_{50}	≥9.4	0.41	<0.04	NO
	Chronic (*D. magna*)	21-d NOEC	1.0	0.41	0.41	NO
Freshwater fish	Acute (rainbow trout)	96-h LC_{50}	0.123	0.41	**3.34**	**YES**
	Chronic ELS (rainbow trout)	96-d NOEC	0.101	0.41	**4.07**	**YES**
Amphibians[2]	Acute (trout surrogate)	96-h LC_{50}	0.123	2.19	**17.8**	**YES**
	Chronic (trout surrogate)	96-d NOEC	0.101	2.19	**21.7**	**YES**
Aquatic vascular plants	Acute	14-d EC_{50}	≥0.5	0.41	<0.82	NO
Algae	Acute *(Selenastrum capricornutum)*	72-h EC_{50}	0.67	0.41	0.61	NO
Saltwater invertebrates	Acute (*M. bahia*)	96-h LC_{50}	2.3	0.41	0.18	NO
	Chronic (*A. bahia*)	28-d NOAEC	0.91	0.41	0.45	NO
Saltwater fish	Acute (Sheepshead minnow)	96-h LC_{50}	1.1	0.41	0.37	NO
Saltwater algae	Acute (*Skeletonema costatum*)	96-h LC_{50}	≥0.98	0.41	<0.42	NO

Table 6 Risk to aquatic organisms due to maximum drift from early season air blast applications (risk from ground boom applications not shown but are reflected in BZ calculations).

Organism	Exposure	Endpoint	Endpoint for Risk Assessment (mg a.i./L)	Drift Airblast EEC (mg a.i./L)	RQ	LOC Exceeded
Freshwater fish	Acute (rainbow trout)	96-h LC_{50}	0.123	0.30	**2.44**	YES
	Chronic / ELS (rainbow trout)	96-d NOEC	0.101	0.30	**2.97**	YES
Amphibians	Acute (trout surrogate)	96-h LC_{50}	0.123	1.62	**13.2**	YES
	Chronic (trout surrogate)	96-d NOEC	0.101	1.62	**16.0**	YES

Table 7 Risk to aquatic organisms due to runoff.

Organism	Exposure	Endpoint	Endpoint for Risk Assessment (mg a.i./L)	Runoff EEC (mg a.i./L)	RQ	LOC Exceeded
Freshwater fish	Acute (rainbow trout)	96-h LC_{50}	0.123	0.21	**1.7**	YES
	Chronic ELS (rainbow trout)	96-d NOEC	0.101	0.19	**1.9**	YES
Amphibians	Acute (trout surrogate)	96-h LC_{50}	0.123	0.97	**7.9**	YES
	Chronic (trout surrogate)	96-d NOEC	0.101	0.84	**8.3**	YES

Table 8 Summary of risk to sediment-dwelling biota. EEC for pore water calculated via Ecoscenario modelling.

Organism	Exposure	Endpoint	Endpoint for Risk Assessment (mg a.i./L)	21-day EEC (mg a.i./L)	RQ	LOC Exceeded
Freshwater invertebrates	Pore water (*C. dilutus*)	10-d LC_{50}	≥3.8	0.19	<0.05	NO
Saltwater invertebrates	Pore water (*L. plumulosus*)	10-d LC_{50}	≥2.65	0.19	<0.07	NO

Table 9 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria.

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Fenhexamid Endpoints	Transformation Products and NERs Endpoints
CEPA toxic or CEPA-toxic equivalent[1]	Yes		yes	yes
Predominantly anthropogenic[2]	Yes		yes	yes
Persistence[3]:	Soil	Half-life ≥ 182 days	no	yes
	Water	Half-life ≥ 182 days	no	yes
	Sediment	Half-life ≥ 365 days	no	yes
	Air	Half-life ≥ 2 days or evidence of long range transport	no	no information
Bioaccumulation[4]	Log K_{OW} ≥ 5		no: 2.23 – 3.62	No information
	BCF ≥ 5000		no: 185	No information
	BAF ≥ 5000		Not available	No information
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet all TSMP Track 1 criteria.	No, does not meet all 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.
[4]Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, log K_{ow}).

Appendix IX Proposed Label Amendments for Products Containing Fenhexamid

Information on labels of currently registered products should not be removed unless it contradicts the label statements provided below.

Label Amendments for Technical Class Products

a) On the primary display panel, replace "GUARANTEE" with "ACTIVE INGREDIENT"
b) The following statements are to be added to the "Environmental Hazards/Precautions" section of the fenhexamid technical labels:

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

c) The following statements are required under the "Disposal" Section of the label for technical grade fenhexamid:

- Canadian manufacturers should dispose of unwanted active ingredients and containers in accordance with municipal or provincial regulations. For additional details and cleanup of spills, contact the manufacturer or the provincial regulatory agency.

Label Amendments for Elevate 50WDG Fungicide – Reg. No. 25900

1. Label Amendments Relating to the Health Risk Assessment

a) On the primary display panel:
- Replace:
  "Not for Residential Use"
  With:
  "DO NOT use in residential areas. Residential areas are defined as sites where bystanders including children may be potentially exposed during or after spraying. This includes around homes, school, parks, playgrounds, playing fields, public buildings or any other areas where the general public including children could be exposed."

b) Move the ''**PRECAUTIONS** section up to before **'DIRECTIONS FOR USE'**. '**FIRST AID'** and **'TOXICOLOGICAL INFORMATION'** should be moved from within the '**PRECAUTIONS'** section to a separate section before '**PRECAUTIONS'.** The order of these sections should be the same as on the label for product with registration number 26132.

c) Under **'PRECAUTIONS'**, the product label must be amended as follows:
- Replace:
  "DO NOT reenter treated area within 4 hours"
  With:

"**DO NOT** enter or allow worker entry into treated areas during the restricted entry intervals (REIs) specified in the following table:"

Crop	Activity	REI
Bushberries (blueberry, currant, elderberry, gooseberry, and huckleberry), ginseng, raspberries (red and black), loganberries and blackberries, strawberries	All activities	12 hours
Cherries and peaches/nectarines	Thinning fruit by hand	3 days
	All other activities	12 hours
Grapes	Girdling, turning	40 days
	Harvesting (hand, mechanical)	7 days
	Leaf pulling by hand, tying/training (full foliage)	5 days
	All other activities	12 hours

REI = Restricted entry interval

- Replace:
  "Avoid spray drift"
  With:
  "Avoid spray drift. Apply only to agricultural crops when the potential for drift to areas of human habitation and human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings."

- Replace:
  "Wear long sleeved shirt and long pants during all activities. In addition, wear chemical resistant gloves during mixing, loading, cleanup and repair activities."
  With:
  "For application using handheld air blast/mistblower, wear chemical-resistant coveralls with a chemical-resistant hood over long-sleeved shirt, long pants, chemical-resistant gloves, socks, chemical-resistant footwear 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 all other application equipment, and during mixing, loading, clean-up, and repair wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. Gloves are not required during application within a closed cab."

- Remove:
  "For application to cherries, peaches and nectarines, wear a hat during activities. Also, use either a respirator with a NIOSH/MSHA/BHSE approved organic-vapour-removing cartridge and a prefilter approved for pesticides OR a NIOSH/MSHA/BHSE canister approved for pesticides."

2. Label Amendments Relating to the Environmental Risk Assessment

a) The following statements are to be added to the "Environmental Precautions" section:

- Toxic to aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE.
- Toxic to small wild mammals.

b) The following statements are required under the "Directions for Use" Section on all product labels:

- To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.
- Avoid application of this product when heavy rain is forecast.
- Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative filter strip between the treated area and the edge of the water body.
- DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
- As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests.
- Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Boom height must be 60 cm or less above the crop or ground.
- Air blast application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.
- **DO NOT** apply by aerial application equipment.

- **Buffer zones:**

    - Spot treatments using hand-held equipment **DO NOT** require a buffer zone.
    - The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

Method of application	Crop		Buffer Zones (metres) Required for the Protection of:	
			Freshwater Habitat of Depths:	
			Less than 1 m	Greater than 1 m
Field sprayer	Blueberry, currant, elderberry, gooseberry, huckleberry, raspberry, loganberry, blackberry, strawberry, ginseng		1	1
	Grapes		1	0
Air blast	Blueberry, currant, elderberry, gooseberry, huckleberry, cherry, peach, nectarine, raspberry, loganberry, blackberry, strawberry, ginseng	Early growth stage	20	1
		Late growth stage	10	1
	Grapes (for control of *Botrytis cinera*)	Early growth stage	10	0
		Late growth stage	5	0
	Grapes (for control of powdery mildew)	Early growth stage	3	0
		Late growth stage	2	0

- For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.
- The buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator on the Pest Management Regulatory Agency web site.

c) The following statement is required under the STORAGE heading

- To prevent contamination, store this product away from food and feed

d) The following statements are required under the DISPOSAL heading, inclusion of these statements is dependant on the end-use product.

- The following statements should be used for commercial and restricted class products other than agriculture and non-crop land, where non-recyclable, non-returnable or non-refillable containers are used:

1. ***Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.***

2. ***Follow provincial instruction for any required additional cleaning of the container prior to its disposal.***

3. ***Make the empty container unsuitable for further use.***

4. ***Dispose of the container in accordance with provincial requirements.***

5. ***For information on disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.***

- For recyclable containers

The following statement would apply to plastic or metal containers that contain agricultural and non-crop land uses (for example, forestry) pesticide products, and that are designed to contain 23 L or less of product.

Disposal of Container*:*

DO NOT reuse this container for any purpose. This is a recyclable container, and is to be disposed of at a container collection site. Contact your local distributor/dealer or municipality for the location of the nearest collection site. Before taking the container to the collection site:

1. Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.

2. Make the empty, rinsed container unsuitable for further use.

If there is no container collection site in your area, dispose of the container in accordance with provincial requirements.

- For returnable containers

Disposal of Container:

DO NOT reuse this container for any purpose. For disposal, this empty container may be returned to the point of purchase (distributor/dealer).

- For containers that can be refilled for the user by the distributor/dealer

  Disposal of Container:

  For disposal, this container may be returned to the point of purchase (distributor/dealer). It must be refilled by the distributor/dealer with the same product. Do not reuse this container for any other purpose.

- Disposal of unused, unwanted product

  A revised standard label statement providing directions for the disposal of unused, unwanted product will be added to labels of agricultural and non-crop land control products:

  For information on disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

3. Label Amendments Relating to the Value Risk Assessment

a) On the primary display panel:
Replace
"GUARANTEE"
With
"ACTIVE INGREDIENT"

b) Page 2 of 8, under the "Resistance Management" Recommendations: As per Regulatory Directive DIR2013-04, Pesticide Resistance Management Labelling Based on Target Site/Mode of Action, verify the resistance management statement is updated to reflect current wording as follows:

"To delay fungicide resistance:

- Where possible, rotate the use of ELEVATE 50 WDG or other Group 17 fungicides with different groups that control the same pathogens. Avoid application of more than 2 consecutive sprays of ELEVATE 50 WDG or other Group 17 fungicides in the same season.
- Use tank mixtures with fungicides from a different group when such use is permitted.
- Fungicide use should be based on an integrated disease management program that includes scouting, historical information related to pesticide use and crop rotation and considers host plant resistance, impact of environmental conditions on disease development, disease thresholds, as well as cultural, biological and other chemical control practices.
- Where possible, make use of predictive disease models to effectively time fungicide applications.

- Monitor treated fungal populations for resistance development.
- If disease continues to progress after treatment with this product, do not increase the use rate. Discontinue use of this product and switch to another fungicide with a different target site of action, if available.
- Contact your local extension specialist or certified crop advisors for any additional pesticide resistance-management as per Dir 99-06 and/or IPM recommendations for specific crops and pathogens.
- For further information and to report suspected resistance, contact ARYSTA LIFESCIENCE NORTH AMERICA LLC at 1-866-761-9397."

c) Page 3 of 8, under the "APPLICATION" section, last sentence:
Replace
"Do not use overhead …"
With
"**DO NOT** use overhead…"

d) Page 3 of 8, under the "BUSHBERRIES …" section, 1st sentence:
Replace
"… minimum interval …"
With
"… minimum re-application interval …"

e) Page 3 of 8, under the "BUSHBERRIES …" section, immediately following "Ground applications only", insert the following sentence:
"A spray volume of 500-1500 L/ha is recommended."

f) Page 4 of 8, under the "CHERRIES AND PEACHES/NECTARINES" section, 1st paragraph, immediately following "…four applications per season for control of all diseases.", insert the following sentence:
"A spray volume of 500-1500 L/ha is recommended."

g) Page 4 of 8, under the "CHERRIES AND PEACHES/NECTARINES" section, 1st paragraph:
Replace
"Minimum interval of seven days."
With
"Minimum re-application interval of seven days must be observed."

h) Page 4 of 8, under the "CHERRIES AND PEACHES/NECTARINES" section, 3rd paragraph:
Replace:
Both instances of "3000 litres of water"
With
"1500 litres of water"

i) Page 4 of 8, under the "GINSENG" section, 1st paragraph: immediately following "…at 10-14 days intervals.", insert the following sentence:
"A spray volume of 500-1500 L/ha is recommended."

j) Page 5 of 8, under the "GRAPES" section, 1st paragraph, replace the entire paragraph with the following text:

"**GRAPES**

A maximum of 3 applications per year are permitted on grapes.

For the control of *Botrytis* bunch rot (gray mold) on grapes, apply 1.12 kg product per hectare (0.56 kg ai/ha) tank mixed with Agral 90 at 0.02% v/v. A spray volume of 500-1500 L/ha is recommended. Apply preventatively prior to disease establishment, when conditions favour disease development. Applications can be made at early bloom, bunch preclosure, veraison (beginning of fruit ripening) to two weeks after veraison, or up to 7 days before harvest (PHI = 7 days). Make only one application per year when targeting *Botrytis*.

For control of powdery mildew, and blackrot, ELEVATE 50 WDG may be tankmixed with NOVA® FUNGICIDE when conditions favour disease development. Consult the NOVA FUNGICIDE label for the appropriate application rates. DO NOT make more than 3 applications per season when targeting powdery mildew or blackrot. DO NOT apply more than 3.4 kg of product per hectare per year (1.7 kg ai/ha/yr)."

k) Page 5 of 8, under the "RASPBERRIES …" section, replace the entire paragraph with the following text:

"RASPBERRIES (red and black), LOGANBERRIES AND BLACKBERRIES
For the control of *Botrytis cinerea* (Gray Mold) on red and black raspberries, loganberries and blackberries, apply 1.7 kg product per hectare (0.85 kg ai/ha) as a foliar spray. A spray volume of 500-1500 L/ha is recommended. Begin application at 10% bloom and continue up to 1 day prior to harvest (PHI = 1 day). Minimum re-application interval of 7 days must be observed. DO NOT make more than 4 applications per year. Ground applications only. DO NOT apply more than 6.8 kg product per hectare per year (3.4 kg ai/ha/yr)."

l) Page 5 of 8, under the "STRAWBERRIES …" section, 7th line:
Replace
"DO NOT make more than 4 applications per season"
With
DO NOT make more than 4 application of ELEVATE 50 WDG per season."

Label Amendments for Decree 50WDG Fungicide – Reg. No. 26132

1. Label Amendments Relating to the Health Risk Assessment

a) On the primary display panel:

- Replace:
  "Not for Residential Use"
  With:
  "DO NOT use in residential areas. Residential areas are defined as sites where bystanders including children may be potentially exposed during or after spraying. This includes around homes, school, parks, playgrounds, playing fields, public buildings or any other areas where the general public including children could be exposed."

b) Under **'PRECAUTIONS'**, the product label must be amended as follows:

- Replace:
  "DO NOT reenter treated area within 4 hours"
  With:
  "**DO NOT** enter or allow worker entry into treated areas during the restricted entry interval (REI) of 12 hours."

- Replace:
  "Avoid spray drift"
  With:
  "Avoid spray drift. Apply only to agricultural crops when the potential for drift to areas of human habitation and human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings."

- Replace:
  "Wear long sleeved shirt and long pants during all activities. In addition, wear chemical resistant gloves during mixing, loading, cleanup and repair activities."
  With:
  "For application using handheld air blast/mistblower, wear chemical-resistant coveralls with a chemical-resistant hood over long-sleeved shirt, long pants, chemical-resistant gloves, socks, chemical-resistant footwear 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 all other application equipment, and during mixing, loading, clean-up, and repair wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. Gloves are not required during application within a closed cab."

c) Under **'Directions for Use'**, the product label must be amended as follows:
   - Remove:
     "Do not apply this product using fogging equipment (handheld or automated), or using handheld mist blowers/air blast equipment."

d) Under **'Directions for Use'** 'Ornamentals – outdoor-grown and greenhouse-grown', last paragraph, replace the entire paragraph with the following text:
   - For outdoor-grown ornamentals (non-cut flowers), DO NOT apply more than 6.8 kilograms product per hectare per year (3.4 kg ai/ha/year). DO NOT apply more than 6 times per year.

     For outdoor ornamentals grown for cut flowers, DO NOT apply more than 4.48 kg product per hectare per year (2.24 kg ai/ha/year). DO NOT apply more than 4 times per year.

     For greenhouse grown ornamentals (non-cut flowers), DO NOT apply more than 6.8 kilograms product per hectare per crop (3.4 kg ai/ha/crop cycle). DO NOT apply more than 6 times per crop cycle.

     For greenhouse grown ornamentals (cut-flowers), DO NOT apply more than 1.12 kg product per hectare per crop (560 g ai/ha/crop cycle). DO NOT make more than 1 application per crop cycle."

2. Label Amendments Relating to the Environmental Risk Assessment

a) The following statements are to be added to the "Environmental Precautions" section:

   - Toxic to aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE.

   - Toxic to small wild mammals.

b) The following statements are required under the "Directions for Use" Section on all product labels:
   - To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.

   - Avoid application of this product when heavy rain is forecast.

   - Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative filter strip between the treated area and the edge of the water body.

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

- As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests.

- Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Boom height must be 60 cm or less above the crop or ground.

- Air blast application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

- **DO NOT** apply by aerial application equipment.

- **Buffer zones:**

    - Spot treatments using hand-held equipment **DO NOT** require a buffer zone.
    - The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

Method of application	Crop		Buffer Zones (metres) Required for the Protection of:	
			Freshwater Habitat of Depths:	
			Less than 1 m	Greater than 1 m
Field sprayer	Outdoor ornamental		2	1
	Blueberry, currant, elderberry, gooseberry, huckleberry, raspberry, loganberry, blackberry, strawberry, ginseng		1	1
	Grapes		1	0
Air blast	Outdoor ornamental, blueberry, currant, elderberry, gooseberry, huckleberry, cherry, peach, nectarine, raspberry, loganberry, blackberry, strawberry, ginseng	Early growth stage	20	1
		Late growth stage	10	1
	Grapes (for control of *Botrytis cinera*)	Early growth stage	10	0
		Late growth stage	5	0
	Grapes (for control of powdery mildew)	Early growth stage	3	0
		Late growth stage	2	0

- For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.
- The buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator on the Pest Management Regulatory Agency web site.

c) The following statement is required for greenhouse uses

- DO NOT allow effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other waters

d) The following statement is required under the STORAGE heading

- To prevent contamination, store this product away from food and feed

e) The following statements are required under the DISPOSAL heading, inclusion of these statements is dependant on the end-use product.

- The following statements should be used for commercial and restricted class products other than agriculture and non-crop land, where non-recyclable, non-returnable or non-refillable containers are used:

1. Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.

2. Follow provincial instruction for any required additional cleaning of the container prior to its disposal.

3. Make the empty container unsuitable for further use.

4. Dispose of the container in accordance with provincial requirements.

5. For information on disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

- <u>For recyclable containers</u>

The following statement would apply to plastic or metal containers that contain agricultural and non-crop land uses (for example, forestry) pesticide products, and that are designed to contain 23 L or less of product.

Disposal of Container*:*

DO NOT reuse this container for any purpose. This is a recyclable container, and is to be disposed of at a container collection site. Contact your local distributor/dealer or municipality for the location of the nearest collection site. Before taking the container to the collection site:

1. Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.

2. Make the empty, rinsed container unsuitable for further use.

If there is no container collection site in your area, dispose of the container in accordance with provincial requirements.

- For returnable containers

  Disposal of Container:

  DO NOT reuse this container for any purpose. For disposal, this empty container may be returned to the point of purchase (distributor/dealer).

- For containers that can be refilled for the user by the distributor/dealer

  Disposal of Container:

  For disposal, this container may be returned to the point of purchase (distributor/dealer). It must be refilled by the distributor/dealer with the same product. Do not reuse this container for any other purpose.

- Disposal of unused, unwanted product

  A revised standard label statement providing directions for the disposal of unused, unwanted product will be added to labels of agricultural and non-crop land control products:

  For information on disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

3. Label Amendments Relating to the Value Risk Assessment

a) On page 4, under the "Resistance Management" Recommendations, 1st bullet:
Replace
"Avoid application of more than 2 consecutive sprays of DECREE 50 WDG Fungicide or other fungicides in the same group in a season."
With
"Avoid application of more than 2 consecutive sprays of DECREE 50 WDG Fungicide or other Group 17 fungicides in a season."

b) On page 5, under the "APPLICATION" section, last paragraph, replace the entire paragraph with the following:

"Avoid making more than two (2) consecutive applications of this product. After the second application, alternate with a non-Group 17 Fungicide for two consecutive applications before reapplying the active ingredient in this product. Consult your local Horticultural Advisor for the most appropriate alternative products.

c) Page 5, under the "FIELD TOMATO TRANSPLANTS …" section, replace the entire paragraph with the following text:

"FIELD TOMATO TRANSPLANTS GROWN IN GREENHOUSE
Begin applications when greenhouse conditions favour disease development. For the control of *Botrytis cinerea* (Gray mold) on field tomato transplants grown in greenhouse, apply 1.5 kg product per hectare (0.75 kg ai/ha) as a foliar spray. Make a second application 7 - 10 days later if conditions continue to favour disease development. Do not make more than 2 applications per crop cycle. Do not exceed a total 3.0 kg/ha per crop cycle. Applications can be made up to transplanting, but not less than sixty days prior to harvest (PHI = 60 days)."

d) Page 5, under the "GREENHOUSE CUCUMBER" section, replace the entire paragraph with the following text:

"GREENHOUSE CUCUMBER
For the control of *Botrytis cinerea* (Gray mold) on greenhouse cucumber, apply 1.5 kg product per hectare (0.75 kg ai/ha) as a foliar spray. Apply in a spray volume of approximately 500 L (small plants) to 1500L (large/mature plants) per hectare. Begin application when greenhouse conditions favour disease development. Repeat after 7 days if conditions continue to favour disease. Do not make more than 2 applications per crop cycle (Maximum of 3.0 kg of DECREE per ha/crop cycle). Applications can be made up to 1 day prior to harvest (PHI = 1 day). The application rate should be based on 1.5 kg product per hectare applied in the appropriate volume of carrier to achieve thorough coverage of all plant surfaces. For example, if you apply 1000 litres of water per hectare, thoroughly mix 1.5 kg of product in 1000 litres of water and apply for coverage of all above-ground plant surfaces. Use care in mixing and application to avoid exceeding rates of 1.5 kg product per hectare regardless of the selected spray volume."

e) Pages 5-6, under the "GREENHOUSE LETTUCE" section, replace the entire paragraph with the following text:

"**GREENHOUSE LETTUCE**
For the control of *Botrytis cinerea* (Gray mold) on greenhouse lettuce, apply 1.5 kg product per hectare (0.75 kg ai/ha) as a foliar spray in a recommended spray volume of 500 to 1500 L/ha. Begin application when greenhouse conditions favour disease development.
Repeat after 7 days if conditions continue to favour disease. Do not make more than 2 applications per crop cycle (Maximum of 3.0 kg of DECREE per ha/crop cycle). Applications can be made up to three days prior to harvest (PHI = 3 days)."

f) Page 6, under the "GREENHOUSE TOMATOES" section, replace the entire paragraph with the following text:

"**GREENHOUSE TOMATOES**
Begin applications when greenhouse conditions favour disease development. For the control of *Botrytis cinerea* (Gray Mold) on greenhouse tomatoes, apply 1.5 kg product per hectare (0.75 kg ai/ha) as a foliar spray in a recommended spray volume of 500-1500 L/ha. Make a second application 7-10 days later if conditions continue to favour disease. Do not make more than 2 applications per crop cycle. (Maximum of 3.0 kg of DECREE per ha/crop cycle). Applications can be made up to one day prior to harvest (PHI= 1 day). **TREATED GREENHOUSE TOMATOES CANNOT BE USED FOR PROCESSING**."

g) Page 6, under the "GREENHOUSE PEPPERS" section, replace the entire paragraph with the following text:

"**GREENHOUSE PEPPERS**
Begin applications when greenhouse conditions favour disease development. For the control of *Botrytis cinerea* (Gray Mold) on greenhouse peppers, apply 1.5 kg product per hectare (0.75 kg ai/ha) as a foliar spray in a recommended spray volume of 500-1500 L/ha. Make a second application 7-10 days later if conditions continue to favour disease. Do not make more than 2 applications per crop cycle. (Maximum of 3.0 kg of DECREE per ha/crop cycle). Applications can be made up to one day prior to harvest (PHI= 1 day)."

h) Page 6, under the "GREENHOUSE EGGPLANT" section, add the following text:

"**GREENHOUSE EGGPLANT**
Begin applications when greenhouse conditions favour disease development."

i) Page 7, under the “ORNAMENTALS - OUTDOOR-GROWN AND GREENHOUSE-GROWN” section, second paragraph, replace the entire paragraph with the following text:

“For control of *Botrytis cinerea* (Gray mold) on ornamentals, apply 1.12 kg product per hectare (0.56 kg ai/hectare). Begin applications when conditions favour disease development but prior to the establishment of disease. Excluding greenhouse grown ornamentals for cut flowers, applications should be made on a 7 to 14-day interval when new terminal growth is present using equipment capable of achieving thorough coverage. When conditions favour severe disease development, apply on a 7-day interval.”

References

Studies Considered in the Chemistry Assessment

A. Studies/Information Submitted by Registrant

PMRA Document Number	Reference
2907092	2017, Supporting data to justify the specification limits for Fenhexamid technical grade active substance for Australia, DACO: 2.11.4,2.12 CBI
2947086	2017, Supporting data to justify the specification limits for Fenhexamid technical grade active substance for Australia, DACO: 2.13.4 CBI
2947087	2011, Analytical procedure for the [CBI Removed] in Fenhexamid (KBR 2738) technical active substance, DACO: 2.13.1 CBI
2947088	2011, Validation of AM012011MP1 Analytical procedure for the [CBI Removed] in Fenhexamid (KBR2738) technical active substance, DACO: 2.13.1 CBI
2947089	2011, Analytical Method - Fenhexamid (KBR 2738) Determination of technical grade active substance HPLC -ESTD, DACO: 2.13.1
2947090	2011, Analytical Method - Fenhexamid (KBR 2738) Impurities in technical grade active substance HPLC – external standard, DACO: 2.13.1 CBI
2947091	2011, Validation of AM016811MP1 Fenhexamid (KBR 2738) Determination of technical grade active substance HPLC-ESTD, DACO: 2.13.1 CBI
2947092	2011, Validation of AM016511MP1 Fenhexamid(KBR 2738) Impurities in technical grade active substance HPLC-ESTD, DACO: 2.13.1 CBI
2989437	2019, Fenhexamid Technical - Reg. No. 25899 Reference Number 2015-4418 Explanation of SPS updates: Fenhexamid: SPS Update Requested for Re-evaluation 2015-4418, DACO: 2.12 CBI
2706346	2011, Material accountability of technical Fenhexamid (KBR 2738) (AE C629364), DACO: 2.13.3 CBI
2746705	2011, Fenhexamid Technical Grade Active Substance Description of the Manufacturing Process of the technical A.S., DACO: 2.11.3
2746706	2017, Supporting data to justify the specification limits for Fenhexamid technical grade active substance for Australia, DACO: 2.11.4 CBI
2746707	2017, Response to PMRA Request for Impurities of concern in Fenhexamid TGAS, DACO: 2.13.4 CBI
2964146	1999, DACO: 2.13.4 CBI

1816170	2000, FEX-BBA-5 Material Accountability of Fenhexamid D (KBR 2738 D) (Amended) and Confidential Appendix., DACO: 2.13.3,2.13.4

Studies Considered in the Human Health Assessments

A. Studies/Information Submitted by Registrant

PMRA Document Number	Reference
2748897	2013, Fenhexamid: summary of Hazard and Science Policy Council (HASPOC) meeting of December 5, 2013: Recommendations on the Need for an Immunotoxicity Study for Fenhexamid, DACO: 4.5.15
2875281	2018, Derek Nexus Report Compound - 1-methylcyclhexane-1-carboxylic acid 2015-4418, DACO: 4.8
2875282	2018, Derek Nexus Report Compound - Fenhexamid 2015-4418, DACO: 4.8
2875283	2018, Derek Nexus Report Compound - M9/WAK6920 2015-4418, DACO: 4.8
2875284	2018, Derek Nexus Report Compound - M10/WAK7004 2015-4418, DACO: 4.8
1179932	1991, KBR2738: Study For Acute Oral Toxicity In Rats, DACO: 4.2.1
1179933	1991, Study For Acute Dermal Toxicity In Rats, DACO: 4.2.2
1179934	1991, KBR2738: Studies Of The Acute Inhalation Toxicity In Rats, DACO: 4.2.3
1179935	1996, KBR2738: Study For Skin And Eye Irritation/Corrosion In Rabbits (Including Amendment), DACO: 4.2.4, 4.2.5
1179936	1996, KBR2738: Studies On Skin Sensitization Effect In Guinea Pigs (Buehler Test)(Including Amendment), DACO: 4.2.6
1179939	1997, Subacute Oral Toxicity Study On Wistar Rats (Administered Per Gavage Over 28 Days)(Including Amendment), DACO: 4.3.3
1179940	1997, Investigations Of Subchronic Toxicity In Wistar Rats (Feeding Study Over 13 Weeks With A Subsequent Recovery Period Over 4 Weeks) (Including Amendment). DACO: 4.3.1
1179943	1997, KBR2738: Range-Finding Subchronic Toxicological Investigation For A 2-Year Feeding Study With B6C3F1 Mice (Administered In Feed Over Approximately 14 Weeks). DACO: 4.3.1
1179944	1997, KBR2738: Subchronic Toxicity Study In Beagle Dogs (13-Week Feeding Study)(Including Amendments 1 And 2), DACO: 4.3.1
1179945	1996, Chronic Toxicity Study In Beagle Dogs (52 Week Feeding Study)(Including Amendment), DACO: 4.3.2
1179969	1991, KBR2738: Preliminary Investigations For a Subacute Inhalation Toxicity Study in the Rat (5 X 6 Hour Exposures) (Including Amendment). DACO: 4.3.6
1179970	1997, Oncogenicity Study in B6C3F1 Mice (Administration In The Diet Over 2 Years), DACO: 4.4.3
1179971	1997, Study On Chronic Toxicity and Carcinogenicity in Wistar Rats (Administration In The Diet Over 2 Years), DACO: 4.4.4
1179972	1996, (Cont'd From Roll#1,824) Study On Chronic Toxicity And Carcinogenicity in Wistar Rats (Administration In The Diet Over 2 Years), DACO: 4.4.4

1179974	1997, A Two Generation Dietary Reproduction Study In Rats Using Technical Grade KBR2738 (Including Amendment), DACO: 4.5.1
1179976	1998, A Developmental Toxicity Study With KBR2738 Technical In The Sprague-Dawley Rat. DACO: 4.5.2
1179977	1997, [Phenyl-Ul-14c]KBR2738: Investigation of the Biokinetic Behavior And The Metabolism in the Rat. DACO: 4.5.9
1179978	1996, Acute Oral Neurotox Screening Study in Wistar Rats. DACO: 4.5.11
1179987	1997, KBR2738: Developmental Toxicity Dose Range Finding In Rabbits, DACO: 4.5.3
1179998	1996, KBR2738: Developmental Toxicity Study in Rabbits After Oral Administration (Including Amendment). DACO: 4.5.3
1180002	1997, KBR2738: Salmonella/Microsome Test. B.Herbold. DACO: 4.5.4
1180003	1995, KBR2738: Reverse Mutation Assay (Salmonella Typhimurium And Escherichia Coli). DACO: 4.5.4
1180004	1997, KBR2738: In Vitro Mammalian Chromosomal Aberration Test with Chinese Hamster Ovary (CHO) Cells, DACO: 4.5.6
1180005	1993, KBR2738: Micronucleus Test on the Mouse, DACO: 4.5.7
1180006	1997, KBR2738: Mutagenicity Study For The Detection Of Induced Forward Mutations In The V79-HGPRT Assay In Vitro, DACO: 4.5.8
1180007	1997, KBR2738: Mutagenicity Test On Unscheduled DNA Synthesis In Rat Liver Primary Cell Structures In Vitro. DACO: 4.5.8
2764230	1996, KBR 2738 - Studies for the skin sensitization effect in guinea pigs (Guinea pig maximization tests according Magnusson and Kligman), DACO: 4.2.6
2764231	2000, Examination of Fenhexamid (KBR 2738) in the skin sensitisation test in guinea pigs according to Magnusson and Kligman (maximisation test), DACO: 4.2.6
2764232	1999, KBR 2738 - Study for subchronic oral toxicity in rats (feeding study over 13 weeks), DACO: 4.3.1
2764233	1999, KBR 2738 - Study for subchronic oral toxicity in mice (feeding study over 13 weeks), DACO: 4.3.1
2764234	1996, KBR 2738 (Fenhexamid) - Study on subacute inhalation toxicity in rats exposure: 5x6 hrs/week for 4 weeks) according to OECD protocol 412, DACO: 4.3.7
2764235	1995, KBR 2738 - Reverse mutation assay (salmonella typhimurium and escherichia coli), DACO: 4.5.4
2764236	1997, KBR 2738 - DNA repair test in bacterial system, DACO: 4.5.8

B. Additional Information Considered

i) Published Information

PMRA Document Number	Reference
2822780	1999, FENHEXAMID. New Reduced-Risk Fungicide. Data Evaluation Records (DERs) for All Toxicology Studies Submitted in Support of Registration of Technical Grade Product (Fenhexamid Technical, EPA ID #66330--GA, Containing 95.4% a.i.), and Formulated Product (Elevate 50 WDG Fungicide, EPA ID #66330-GL, Containing 50% a.i.) and PP# 7F04890 (Fenhexamid in/on Grapes and Strawberries)., DACO: 12.5.4
2859046	EFSA (European Food Safety Authority), 2013, Draft Assessment Report for Fenhexamid (http://dar.efsa.europa.eu/dar-web/download?h=2A6B390B6A715F98AC494138C78D9AE9&d=4228&da=24/01/2018%2020:15:24), Fenhexamid Volume 3, Annex B.8: Environmental Fate and Behaviour, DACO: 12.5.8
2866919	EFSA (European Food Safety Authority), 2014, EFSA Journal 2014;12(7):3744, Conclusion on the peer review of the pesticide risk assessment of the active substance fenhexamid, DACO: 12.5.8,12.5.9
2921187	Kugathas, Subramaniam et al, 2016, Effects of Common Pesticides on Prostaglandin D2 (PGD2) Inhibition in SC5 Mouse Sertoli Cells, Evidence of Binding at the COX-2 Active Site, and Implications for Endocrine Disruption - Environmental Health Perspectives, Volume 124, Number 4, Pages 452 to 459, DACO: 4.8
2921188	Martin, Matthew T. et al, 2017, Predictive Model of Rat Reproductive Toxicity from ToxCast High Throughput Screening - Biology of Reproduction, Volume 85, Number 2, Pages 327 to 339, DACO: 4.8
2921189	Medjakovic, Svjetlana et al, 2014, Effect of Nonpersistent Pesticides on Estrogen Receptor, Androgen Receptor, and Aryl Hydrocarbon Receptor - Environmental Toxicology, DOI 10.1002/tox, DACO: 4.8
2921191	Regueiro, Jorge et al, 2015, Toxicity evaluation of new agricultural fungicides in primary cultured cortical neurons - Environmental Research, Volume 140 Pages 37 to 44, DACO: 4.8
2921192	Seeger, B. et al, 2016, Mixture Effects of Estrogenic Pesticides at the Human Estrogen Receptor and - PLoS ONE Volume 11, Number 1, Pages 1 to 15, DACO: 4.8
2921194	Teng, Yun et al, 2012, Endocrine Disruptors Fludioxonil and Fenhexamid Stimulate miR-21 Expression in Breast Cancer Cells - Toxicological Sciences, Volume 131, Volume 1, Pages 71 to 83, DACO: 4.8

Studies Considered in the Dietary Assessment

A. Studies/Information Submitted by Applicant/Registrant

PMRA Document Number	Reference
1192146	1998, MRL Data 1999-0059, [Phenyl-UL-14C]KBR 2738 Absorption, Distribution, Excretion and Metabolism in the Lactating Goat, DACO: 6.2
1179986	1996, Metabolism of KBR2738 in Apples, DACO: 6.3
1179988	1996, Metabolism of KBR2738 in Grapes, DACO: 6.3
1179989	1996, Metabolism of KBR2738 in Tomatoes (Including Amendment), DACO: 6.3
1092813	1999, Metabolism of KBR 2738 in Lettuce, DACO: 6.4
1179990	1997, Supplementary Report on the Investigation of 2,3-dichloro-4-hydroxyaniline (DCHA) as a Possible Metabolite of KBR2738 in Plants, DACO: 6.3
1179991	1997, Rationale for the TM-402 (KBR2738) Radiolabelling Position Used in the Crop Metabolism Studies, DACO: 6.3
1179992	1996, Aqueous Hydrolysis of KBR2738 Under Conditions of Processing Studies, DACO: 6.3
1180019	1995, Method for the Determination of KBR2738 Residues in Plant Material by HPLC, DACO: 8.2.2.4
1106835	1996, Supplement 001 of the Method 00362 for the Determination of Residues of KBR2738 in/on Strawberry, Raspberry, Black Currant, Cherry, Kiwi, Nectarine, Plum and Tomato, DACO: 7.2.1,7.8
1061385	Analytical Methodology Method for the Determination of KBR 2738 Residues in Plant Material by HPLC. Included as Appendix 4 of Fenhexamid: Magnitude of the Residue on Ginseng. IR-4 PR #07846. GLP. Unpublished., DACO: 7.2.1
2807117	1995, Reference Method for Analysis of Fenhexamid - Method for Determination of KBR 2738 Residues in Plant Material by HPLC, DACO: 7.2.1
1179620	1997, Independent Laboratory Confirmation of the Residue Enforcement Method of TM-402 in Raw Agricultural Commodities, DACO: 7.2.1
1179623	1996, Determination of Storage Stability of KBR 2738 Residues in Fortified Analytical Samples of Grapes, Processed Commodities of Grape, Peach, Tomato and Strawberry, DACO: 7.3
1179624	1997, Storage Stability of TM-402 in Strawberries and Grapes - Extended Interval, DACO: 7.3
1179625	1996, Method Validation and Storage Stability for TM-402 in Strawberries and Grapes, DACO: 7.3
1192121	1997, MRL Data 1999-0059, Storage Stability for TM-402 in Peaches, Plums, and Cherries - Extended Interval, DACO: 7.3
1192161	1996, Method Validation and Storage Stability for TM-402 in Peaches, Plums, and Cherries, DACO: 7.2.1,7.2.2,7.3
1192158	1998, Method Validation and Storage Stability for TM-402 in Almond Meat and Hulls, DACO: 7.2.1,7.2.2,7.2.5
1192125	1998, Magnitude of the residue of TM-402 Fungicide (50 WDG) on Almonds (including amendment), DACO: 7.4.1
1106840	2001, Fenhexamid: Magnitude of the Residue on blueberry, DACO: 7.8
1062964	2001, Magnitude of the Residue on Caneberry (Raspberry), DACO: 7.4

1061386	Freezer Storage Stability Supervised Residue Trial Study Residue Decline Study Fenhexamid: Magnitude of the Residue on Ginseng. IR-4 PR # 07846. GLP. Unpublished., DACO: 3.5.10,7.3,7.4.1,7.4.2
1179635	1997, Magnitude of TM-402 Residue in Grapes (amended), DACO: 7.4.1
1179626	1998, Elevate 50 WDG Fungicide: Magnitude of the Residues in Grapes from the 1996 and 1997 field trials conducted in Ontario, Canada, DACO: 7.4.1
1090181	1996, Determination of Residues of KBR 2738 50 WG on Tomato in France and Italy, DACO: 7.8
1090182	1996, Determination of Residues of KBR 2738 50 WG on Tomato in the Federal Republic of Germany, Italy, Belgium and Greece, DACO: 7.8
1092814	2002, Determination of Residues of KBR 2738 after Spray Application of Teldor 50 WG on Lettuce in the Greenhouse in Germany and Italy, DACO: 7.8
1092815	2002, Determination of Residues of Teldor (50 WG) in/on Lettuce Following Spray Application in the Greenhouse in Germany and Italy, DACO: 7.8
1823229	2000, Determination of residues of KBR 2738 on cucumber after spray application of KBR 2738 50 WG in the greenhouse in Spain, Greece and France, DACO: 7.4.1
1823230	2000, Determination of residues of KBR 2738 on cucumber after spray application of KBR 2738 50 WG in the greenhouse in the Netherlands, Germany, Belgium and France (North), DACO: 7.4.1
1814381	1999, Determination of Residues of KBR 2738 50 WG following Spray Application in the Greenhouse in/on Cucumber in Belgium, Italy, Spain and Germany., DACO: 7.8
1814380	2009, Residue data waiver rationale for use of Decree 50 WG (Fenhexamid) for the control of grey mold Botrytis cinerea in greenhouse grown cucumbers, DACO: 7.4.1
2440073	2014, Residue report - Decree 50 WDG Fungicide (Fenhexamid) on GH pepper, DACO: 7.2.1,7.3,7.4.1,7.4.2
2748878	1999, Determination of Residues of KBR 2738 (50 WG) on Pepper in the greenhouse in Netherlands, France, Italy and Spain, DACO: 7.4.1
2748879	2000, Determination of Residues of KBR 2738 on pepper after spray application of KBR 2738 50 WG and 500 SC in the greenhouse in Italy, Portugal and France, DACO: 7.4.1
2807118	2011, Fenhexamid: Magnitude of the Residue on Onion, DACO: 7.4.1,7.4.2
1192140	1998, Magnitude of the Residue of TM-402 50 WDG on Tart Cherries, Peaches and Plums, DACO: 7.4.1
1192139	1998, Elevate 50 WDG Fungicide: Magnitude of TM-402 Residues in Peaches, Plums and Sweet Cherries from the 1996 Crop Field Trials (amended report no. 2), DACO: 7.4.1
1192332	1998, Elevate 50 WDG Fungicide: Magnitude of TM-402 Residues in Peaches from the 1997 Field Trial Conducted in Ontario, Canada, DACO: 7.4.1
2748877	2002, Magnitude of the Residue of Fenhexamid in Plum Raw Agricultural Commodities, DACO: 7.4.1
1179627	1998, Elevate 50 WDG Fungicide: Magnitude of the Residues in Strawberries from the 1997 Field Trial Conducted in Nova Scotia, Canada, DACO: 7.4.1
1179639	1997, Magnitude of TM-402 Residue in Strawberries (Amended), DACO: 7.4.1
1179650	1997, TM-402 (KBR 2738), Confined Rotational Crop Study with KBR 2738, DACO: 7.4.3
1179651	1997, Elevate 50 WDG Fungicide (Containing TM-402 (KBR 2738)): Request for a Waiver of the Requirement of Field Crop Rotation Data, DACO: 7.4.4
1179652	1996, TM-402 (KBR 2738): Determination of Residues of KBR 50 WG on Grape and Grape Processing Products in France, DACO: 7.4.5

1178078	1998, Elevate 50 WDG Fungicide: Magnitude of TM-402 Residues in Grapes and Grape Juice from the 1997 Field Trial Conducted in Washington (amended report no.1), DACO: 7.4.5
1114321	1996, Determination of Residues of KBR 2738 (50WG) in Processed Commodities of Tomato, DACO: 7.4.5

Studies Considered in the Occupational Exposure and Risk Assessment

A. Studies/Information Provided by Applicant/Registrant

PMRA Document Number	Reference
1179618, 2748875	1997, Dermal Absorption of [Phenyl-UL-14C]-TM-402 50 WP Formulation in Male Rats (Preliminary and Definitive Phases), DACO: 5.8
1179619, 2748876	1997, Dissipation of Dislodgeable Foliar Residues of TM-402 Applied to Grapes, DACO: 5.9

B. Studies/Information Provided by Task Forces

PMRA Document Number	Reference
2115788	Agricultural Reentry Task Force (ARTF). 2008. Data Submitted by the ARTF to Support Revision of Agricultural Transfer Coefficients. Submission# 2006-0257.
1913109	2009, Agricultural Handler Exposure Scenario Monograph: Open Cab Groundboom Application of Liquid Sprays, DACO: 5.3,5.4
2572743	2009, Agricultural Handler Exposure Scenario Monograph: Open Cab Groundboom Application of Liquid Sprays, DACO: 5.3, 5.4
2572744	2015, Agricultural Handler Exposure Scenario Monograph: Open Pour Mixing and Loading Dry Flowable Formulations, DACO: 5.3,5.4

C. Additional Information Considered

i) Published Information

PMRA Document Number	Reference
2989335	Desert, Marine et al, 2018, Spatial and temporal distribution of current-use pesticides in ambient air of Provence-Alpes-Cote-d¿¿¿Azur Region and Corsica, France - Atmospheric Environment, Volume 192, Pages 241 to 256, DACO: 5.10
2989336	European Commission, 2013, Fenhexamid - Volume 3, Anne B.6: Toxicology and Metabolism, DACO: 12.5.5

PMRA Document Number	Reference
2989334	Tsiropoulos, Nikolaous G., 2006, Evaluation of solid sorbents for the determination of fenhexamid, metalaxyl-M, pyrimethanil, malathion and myclobutanil residues in air samples Application to monitoring malathion and fenhexamid dissipation in greenhouse air using C-18 or Supelpak-2 for sampling - Analytica Chimica Acta, Bolumes 573 to 574, Pages 209 to 215, DACO: 5.10

Studies Considered in the Environmental Assessment

A. Studies/Information Provided by Applicant/Registrant

PMRA Document Number	Reference
1179641	1998, TM-402 (KBR 2738): Dissipation Of TM-402 On Bare Soil In Canada (To Support Registration For Use On Strawberries), F. Vaughn, J. Parnell, Completed May 26, 1998 (KBR-SOIL-STBRY;97TOM01) [Elevate 50 WDG Fungicide-Fenhexamid (Proposed);SUBN.#97-1752;Volume 2 OF 2;Submitted June 15, 1998;Ring Binder 18A;Document 32B], DACO: 8.3.2.1
1179997	1997, Mobility And Degradation Of 14c-Tm-402 As Determined Using Field Lysimeters. J. Obrist. Report Completion Date: March 5, 1997.(96568;TMN-014CCC). [Fenhexamid;SUBN#97-1749;Ring-Binder#32;Volume 1 OF 4;Document#75;Submitted: October 21,1997] [*Note-Page#29 AND 32 MISFILMED], DACO: 8.2.2.1
1180000	1997, Anaerobic Aquatic (Soil) Metabolism Of KBR2738, DACO: 8.2.2.2,8.2.3.5.6
1180010	1997, Degradation And Metabolism Of KBR2738 In The System Water/Sediment, DACO: 8.2.3.5.4
1180011	1996, Adsorption/Desorption Of KBR2738 On Different Soils, DACO: 8.2.4.2
1180012	1997, Adsorption/Desorption Of [Benzoxazol-2-14C]WAK7004 On Four Different Soils, DACO: 8.2.4.2
1180026	1996, [14C]KBR2738-Uptake, Depuration And Bioconcentration In Bluegill (Lepomis macrochirus) Under Flow-Through Conditions, DACO: 9.5.6
1180041	1995, Hydrolysis Of KBR2738 In Sterile Aqueous Buffer Solutions, DACO: 8.2.3.2
1180045	1996, Photolysis Of KBR2738 On Soil Surfaces. B. Brumhard. Report Completion Date: September 26,1996.(PF-4167;TMN-014A;M1130642-7).[Fenhexamid;SUBN#97-1749;Ring-Binder#34;Volume 3 OF 4;Document#83;Submitted: October 21,1997], DACO: 8.2.3.3.1
1180047	1996, Photolysis Of KBR2738 In Aqueous Solutions, DACO: 8.2.3.3.2
1180049	1996, Aerobic Degradation And Metabolism Of KBR2738 In Soil (Including Amendment), DACO: 8.2.3.4.2
2748880	2011, [Cyclohexyl-1-14C]Fenhexamid (KBR 2738): Aerobic Degradation/Metabolism in Four European Soils, DACO: 8.2.3.4.2
2748881	2011, [Cyclohexyl-1-14C] Fenhexamid: Aerobic Aquatic Metabolism, DACO: 8.2.3.5.4
2748882	2016, Transformation and Mineralization of [14C]Fenhexamid in Two Anaerobic Aquatic Sediment Systems Following OCSPP Guideline 835.4400 and OECD Guideline 308, DACO: 8.2.3.5.6

PMRA Document Number	Reference
1179643	1995, KBR 2738 WG 50: Laboratory Contact Toxicity Test With The Predacious Mite, Typhlodromus pyri, Following The Method Of Louis And Hetterling (1992), DACO: 9.2.8
1179644	1996, Effects Of KBR2738 WG 50 On The Life Cycle Of The Ladybird Beetle (Coccinella septempunctata) Under Laboratory Conditions, DACO: 9.2.8
1179647	1996, Effects Of KBR 2738 WG 50 On The Life Cycle Of Rove Beetles (Aleochara bilineata) Under Laboratory Conditions, DACO: 9.2.8
1180014	1995, Toxicity Of KBR2738 (Tech.) To Earthworms. F.Heimbach. Report Completion Date: March 2,1995.(HBF/RG210;TMN-001V;E3100865-3).[Fenhexamid;SUBN#97-1749;Ring-Binder#36;Volume 1 OF 3;Document#93;Submitted: October 21,1997], DACO: 9.2.3.1
1180015	1995, Testing Toxicity To Honeybee-Apis mellifera L. (Laboratory) According To EPPO Guideline No.170: KBR2738 (Technical)., DACO: 9.2.4.1,9.2.4.2
1180028	1997, KBR2738 Technical: Acute Oral Toxicity To Bobwhite Quail. R.Grau. Report Completion Date: September 8,1995.(VB-038;TMN-001Q;E2920907-9).[Fenhexamid;SUBN#97-1749;Ring-Binder#38;Volume 3 OF 3;Document#106;Submitted: October 21,1997], DACO: 9.6.2.1
1180029	1995, KBR2738 Technical: 5-Day Dietary Lc50 To Bobwhite Quail, DACO: 9.6.2.4
1180031	1995, KBR2738 Technical: 5-Day Dietary Lc50 To Mallard Duck, DACO: 9.6.2.5
1180032	1997, Effects Of A Subchronic Dietary Exposure Of KBR2738 (Technical) On Bobwhite Quail Including Effects On Reproduction And Health (Including Amendment). R.Schmuck. Report Completion Date: Issued January 24, 1997. Amended JUNE 4,1997. (SXR/REP06;TMN-001N;E2931027-9).[Fenhexamid;SUBN#97-1749;Ring-Binder#38;Volume 3 OF 3;Document#109;Submitted: October 21,1997], DACO: 9.6.3.1
2748883	2015, Fenhexamid - 10-Day Toxicity Test Exposing Midge (Chironomus dilutus) to a Test Substance Applied to Sediment Under Static-Renewal Conditions, DACO: 9.3.4
2748884.	2015, Fenhexamid - 10-Day Toxicity Test Exposing Freshwater Amphipods (Hyalella azteca) to Sediment Under Static Renewal Conditions, DACO: 9.3.4
2748885	2015, Elevate(R) 50 WDG - Acute Toxicity to Mysids (Americamysis bahia) Under Static Conditions, Following OCSPP Draft Guideline 850.1035, DACO: 9.4.2
2748886	2015, Fenhexamid TGAI - Acute Toxicity to Eastern Oyster (Crassostrea virginica) Under Flow-Through Conditions, DACO: 9.4.2
2748887	2015, Fenhexamid - Life-Cycle Toxicity Test with Mysids (Americamysis bahia), DACO: 9.4.5
2748888	2015, Elevate(R) 50 WDG - 96-Hour Toxicity Test with the Freshwater Diatom, Navicula pelliculosa, DACO: 9.8.2
2748889	2015, Elevate(R) 50 WDG - 96-Hour Toxicity Test with the Freshwater Cyanobacterium, Anabaena flos-aquae, DACO: 9.8.2
2748890	2015, Elevate(R) 50 WDG - 96-Hour Toxicity Test with the Marine Diatom, Skeletonema costatum, DACO: 9.8.3
2748891	2015, Elevate(R) 50 WDG - Seedling Emergence Test, DACO: 9.8.4
2748892	2015, Elevate(R) 50 WDG - Vegetative Vigor Test, DACO: 9.8.4
2748893	2015, Fenhexamid - 22-Day Survival of Honey Bee Larvae, Apis mellifera L., During An In Vitro Exposure, DACO: 9.2.4.3

PMRA Document Number	Reference
2833712	2015, Fenhexamid -10-Day Toxicity Test Exposing Estuarine Amphipods (Leptocheirus plumulosus) to a Test Substance Applied to Sediment under Static Conditions, DACO: 9.3.4
2860312	2018, Fenhexamid WG 50 - Assessment of Effects on the Adult Honey Bee, Apis mellifera L., in a 10 Days Chronic Feeding Test under Laboratory Conditions, DACO: 9.2.4.4

B. Additional Information Considered

i) Published Information

PMRA Document Number	Reference
2988073	2016, Battaglin, W.A. et al., Sci. Tot. Environ. 566-567: 320-332, Potential interactions among disease, pesticides, water quality and adjacent land cover in amphibian habitats in the United States, DACO: 12.5.9
2988086	2012, Reilly, T.J. et al., Chemosphere 89: 228-234, Occurrence of boscalid and other selected fungicides in surface water and groundwater in three targeted use areas in the United States., DACO: 12.5.9
2982480	2017, United States Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention, Registration Review: Preliminary environmental fate and ecological risk assessment for fenhexamid, DACO: 12.5.8,12.5.9
2983491	2013, EFSA, European Food Safety Authority, Fenhexamid Volume 3, Annex B.8: Environmental Fate and Behaviour, DACO: 12.5.8
2985335	2013, EFSA, European Food Safety Authority, Fenhexamid Volume 3, Annex B.9: Ecotoxicology, DACO: 12.5.9
2859046	2013, EFSA (European Food Safety Authority), Draft Assessment Report for Fenhexamid (http://dar.efsa.europa.eu/dar-web/download?h=2A6B390B6A715F98AC494138C78D9AE9&d=4228&da=24/01/2018%2020:15:24), Fenhexamid Volume 3, Annex B.8: Environmental Fate and Behaviour, DACO: 12.5.8

ii) Unpublished Information

PMRA Document Number	Reference
2872993	2017, Data Evaluation Record Acute LC50 Test With An Estuarine/Marine Shrimp OCSPP 850.1035 - Citation: Elevate 50 WDG- Acute Toxicity to Mysids (Americamysis bahia) Under Static Conditions, Following OCSPP Draft Guideline 850.1035, DACO: 12.5.9
2872995	2017, Data Evaluation Record on the Toxicity of Fenhexamid to Terrestrial Vascular Plants: Seedling Emergence - Elevate 50 WDG - Seedling Emergence Test. Unpublished study performed by Smithers Viscient, Wareham, Massachusetts. Laboratory Project Number: 14080.6107. Study sponsored by Arysta LifeScience North America, LLC, Cary, North Carolina. Study completed April 20, 2015., DACO: 12.5.9

PMRA Document Number	Reference
2872996	2017, Data Evaluation Record on the Toxicity of Fenhexamid to Terrestrial Vascular Plants: Vegetative Vigor - Citation: Elevate 50 WDG Vegetative Vigor Test. Unpublished study performed by Smithers Viscient, Wareham, Massachusetts. Laboratory Project Number: 14080.6109. Study sponsored by Arysa LifeScience North America, LLC. Cary, North Carolina. Study completed April 16, 2015., DACO: 12.5.9
2872997	2017, Data Evaluation Report on the Toxicity of Fenhexamid TEP (Elevate 50 WDG) to Algae, Navicula pelliculosa - Citation: Elevate 50 WDG: 96-Hour Toxicity Test with the Freshwater Diatom, Navicula pelliculosa, Following OCSPP Guideline 850.4500. Study performed by Smithers Viscient, Wareham, MA. Smithers Viscient Study No. 14080.6101. Study sponsored by Arysta LifeScience North America, LLC, Cary, NC. Study initiated 26 August 2014 and completed 14 April 2015, DACO: 12.5.9
2872998	2017, Data Evaluation Report on the Toxicity of Fenhexamid Technical End Product Elevate 50 WDG to Algae, Skeletonema costatum - Elevate 50 WDG: 96-Hour Toxicity Test with the Marine Diatom, Skeletonema costatum, Following OCSPP Guideline 850.4500. Study performed by Smithers Viscient, Wareham, MA. Smithers Viscient Study No. 14080.6102. Study sponsored by Arysta LifeScience North America, LLC, Cary, NC. Study initiated 26 August 2014 and completed 17 March 2015, DACO: 12.5.9
2872999	2017, Data Evaluation Report on the Toxicity of Formulated Fenhexamid (Elevate 50 WDG) to Algae, Anabaena flos-aquae - Elevate 50 WDG: 96-Hour Toxicity Test with the Freshwater Cyanobacterium, Anabaena flos-aquae, Following OCSPP Guideline 850.4550. Study performed by Smithers Viscient, Wareham, MA. Smithers Viscient Study No. 14080.6103. Study sponsored by Arysta LifeScience North America, LLC, Cary, NC. Study initiated 26 August 2014 and completed 24 April 2015, DACO: 12.5.9
2873000	2017, Data Evaluation Record 72-3(B) -- Acute EC50 Test With An Estuarine/Marine Mollusk Shell Deposition Study - Citation: Fenhexamid TGAI - Acute Toxicity to Eastern Oyster (Crassostrea virginica) Under Flow-Through Conditions, Following OCSPP Guideline 850.1025, DACO: 12.5.9
2873001	2016, Data Evaluation Record Mysid Chronic Toxicity Test Guideline OCSPP 850.1350 - Citation: Fenhexamid: Life-Cycle Toxicity Test with Mysids (Americamysis bahia), DACO: 12.5.9
2873002	2017, Data Evaluation Record Chronic (Repeat Dose) Toxicity Tests With The Honey Bee (Apis mellifera) Larvae Non-Guideline - Citation: Fenhexamid 22-Day Survival of Honey Bee Larvae, Apis mellifera L., during an In Vitro Exposure, DACO: 12.5.9
2873003	2017, Data Evaluation Record Whole Sediment Acute Toxicity Invertebrates, Freshwater OPPTS Guideline 850.1735 - Citation: Fenhexamid - 10-Day Toxicity Test Exposing Midge (Chironomus dilutus) to a Test Substance Applied to Sediment Under Static-Renewal Conditions, DACO: 12.5.9
2873004	2017, Data Evaluation Record Whole Sediment Acute Toxicity Invertebrates, Freshwater OPPTS Guideline 850.1735 - Citation: Fenhexamid - 10-Day Toxicity Test Exposing Freshwater Amphipods (Hyalella azteca) to Sediment Under Static-Renewal Conditions., DACO: 12.5.9
2873005	2017, Data Evaluation Record Whole Sediment Acute Toxicity Invertebrates, Marine OPPTS Guideline 850.1740 - Citation: Fenhexamid - 10-Day Toxicity Test Exposing Estuarine Amphipods (Leptocheirus plumulosus) to a Test Substance Applied to Sediment Under Static Conditions, DACO: 12.5.9