Proposed Re-evaluation Decision PRVD2026-02

Famoxadone and its Associated End-use Product

Consultation Document

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Proposed re-evaluation decision for famoxadone and its associated end-use product

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 health and environmental safety standards and continue to have value. The re-evaluation considers data and information from pesticide manufacturers, incident reports and other regulatory agencies. Health Canada applies internationally accepted risk assessment methods, risk management approaches and policies to all re-evaluations.

Famoxadone is a protectant and locally systemic fungicide used to control early and late blight in potato and tomato. It is also used to control caneberry spur blight, caneberry anthracnose, cane botrytis, and preharvest fruit rot in Crop subgroup 13-07A: Caneberries (blackberry, red and black raspberry, loganberry, cultivars and hybrids of these). Famoxadone belongs to the group of fungicides classified as quinone outside inhibitors (Group 11) that target complex III of fungal respiration (ubiquinol oxidase, quinone outside site). There is one technical and one commercial class product registered in Canada. The commercial end-use product is a dry flowable that is co-formulated with cymoxanil. It is applied as a foliar spray by ground application (field sprayer or air assist sprayer) and aerial application. Registered products containing famoxadone can be found in the Pesticide Product Information Database and in Appendix I.

This document presents the proposed re-evaluation decision for famoxadone, including any proposed amendments (risk mitigation measures) to protect human health and the environment, as well as the science evaluation on which the proposed decision is based. All products containing famoxadone that are registered in Canada are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period[1], 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 after taking into consideration the comments received during the consultation period that are directly related to this proposed re-evaluation decision.

Health Canada, under the authority of the *Pest Control Products Act*, has conducted all evaluations considered necessary with respect to the health and environmental risks and value of famoxadone based on available scientific information in accordance with subsection 16(6) of the *Pest Control Products Act*. Health Canada is proposing for public consultation, pursuant to section 28 of the *Pest Control Products Act*, the continued registration of famoxadone and associated end-use product registered for sale and use in Canada under section 21 of the *Pest Control Products Act*.

Famoxadone is a quinone outside inhibitors fungicide that has value in providing a pest management solution. Based on the current use pattern, potential risks to human health (occupational, dietary and bystander) and the environment (aquatic and terrestrial organisms) are considered to be acceptable when products containing famoxadone are used according to proposed label updates (Appendix VIII).

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

Risk mitigation measures

Registered pesticide product labels include specific directions for use. Directions include risk mitigation measures to protect human health, the environment and ensure the product has acceptable value which must be followed by law. The proposed label amendments as a result of the re-evaluation of famoxadone, are summarized below. Refer to Appendix VIII for details.

Human health

- To further minimize the potential for occupational exposure for workers:
    - Add personal protective equipment for airblast application.
- Label improvements to meet current labelling standards:
    - Update spray drift and tank-mix statements.

Environment

- To protect the environment, the following proposed risk mitigation measures are proposed:
    - Standard environmental hazard statements to inform users of the potential toxic effects on aquatic organisms, birds, small wild mammals and terrestrial plants.
    - Spray buffer zones of 1–2 metres for non-target terrestrial habitats and from 1–225 metres for aquatic habitats.
    - Standard precautionary runoff statements to reduce the potential for runoff of famoxadone to adjacent aquatic habitats.

Next steps

Upon publication of this proposed re-evaluation decision, the public, including the registrants and stakeholders are encouraged to submit comments during the 90-day public consultation period.

Health Canada will accept written comments on this proposal up to 90 days from the date of publication of this document. Comments on the proposed decision can be submitted during the consultation period to the PMRA through PMRA Publications, or the Public Engagement Portal (Public Engagement Forms - Consultation Comment). For more information or if you have questions, contact the PMRA's Pest Management Information Service.

Before making a re-evaluation decision on famoxadone under section 21 of the *Pest Control Products Act*, the comments received during the consultation period that are directly related to this proposed decision, such as comments directed to the Science evaluation, will be taken into consideration in preparation of the final re-evaluation decision document. A science-based approach will be applied in making a final decision on famoxadone.

In accordance with subsection 28(5) of the *Pest Control Products Act*, Health Canada will then publish a final re-evaluation decision document, which will include the decision, the reasons for it, a summary of the comments received directly related to the proposed re-evaluation decision during the consultation period, and Health Canada's response to these comments.

Refer to Appendix I for details on specific products impacted by this proposed decision.

Other information

The relevant confidential test data on which the proposed decision is based (as referenced in Appendix IX of this document) are available for public inspection, upon application, in Health Canada's Reading Room. For more information, please contact the PMRA's Pest Management Information Service.

Additional scientific information

No additional scientific data are being requested at this time.

Science evaluation

1.0 Background

Famoxadone is a protectant and locally systemic fungicide used to control early and late blight in potato and tomato. It is also used to control caneberry spur blight, caneberry anthracnose, cane botrytis, and preharvest fruit rot in caneberries (blackberry, red and black raspberry, loganberry, cultivars and hybrids of these).

Appendix I lists all products containing famoxadone that are registered under the authority of the *Pest Control Products Act*. Appendix II lists all the uses for which famoxadone is presently registered.

In 2021, the European Union (EU) prohibited the use of famoxadone as an active substance in plant protection products (Commission Implementing Regulation (EU) 2021/1379) for health and environmental reasons. A preliminary analysis of the 2021 EU decision identified the following aspects of concern:

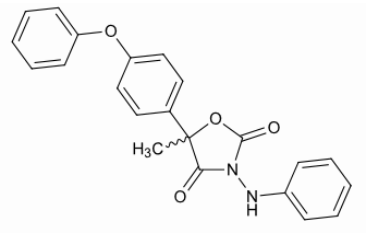
- Potential occupational postapplication risks during hand-harvesting.
- Potential chronic risk to mammals.
- Potential risk to aquatic organisms.

The present re-evaluation of famoxadone is primarily based on existing Health Canada's assessments, with targeted review for toxicology and cumulative heath assessments, and addresses the identified aspects of concern raised by the 2021 EU decision on famoxadone.

2.0 Technical Grade Active Ingredient

2.1 Identity

Common name		Famoxadone
Function		Fungicide
Chemical Family		Oxazolidinedione
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	(*RS*)-3-anilino-5-methyl-5-(4-phenoxyphenyl)oxazolidine-2,4-dione
2	**Chemical Abstracts Service (CAS)**	5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2,4-oxazolidinedione
CAS Registry Number		131807-57-3
Molecular Formula		$C_{22}H_{18}N_2O_4$

Structural Formula	
Molecular Weight	374.4 g/mol
Purity of the Technical Grade Active Ingredient	97.8%
Registration Number	27436

2.2 Physical and Chemical Properties

Property	Result
Vapour pressure at 20°C	0.00064 mPa
Ultraviolet (UV) / visible spectrum	Not expected to absorb at λ >350 nm
Solubility in water at 20–25°C	pH — Solubility (mg/L) 9 — 0.038 7 — 0.059 5 — 0.243
n-Octanol/water partition coefficient	log K_{ow}= 4.65 at pH 7
Dissociation constant	The dissociation constant could not be measured or inferred from solubility or octanol water partition coefficient.

3.0 Human health assessment

3.1 Toxicology summary

Famoxadone is an oxazolidinedione fungicide and its pesticidal mode of action involves inhibition of complex III of the mitochondrial electron transport chain, resulting in decreased ATP production. A detailed review of the toxicology database for famoxadone was previously conducted and published in REG2003-10 (Canada, 2003). The current targeted review undertook an assessment of a potential common mechanism of toxicity with famoxadone and other pesticides, and evaluated developmental and reproductive toxicity (DART) studies to determine an appropriate *Pest Control Products Act* (PCPA) factor, as one had not been previously characterized. DART points of departure, together with appropriate composite assessment factors were compared to existing toxicology reference values to determine whether existing reference values remained protective. Given the scope of the targeted evaluation, non-DART studies for famoxadone were not revisited as they were not expected to impact the hazard characterization with respect to the developing young and resulting PCPA factor. Studies that were re-considered

as part of this targeted review include an oral (dietary) 2-generation reproductive toxicity study in rats and gavage developmental toxicity studies in rats and rabbits. These DART studies were conducted according to internationally accepted protocols and Good Laboratory Practices. Preliminary dose range-finding gavage developmental toxicity studies in rats and rabbits were also available and considered. A literature search was conducted by the Health Canada Federal Science Library and then screened to identify any studies that were relevant to the scope of the targeted review. One study was determined to be relevant, offering qualitative information to the assessment of a potential common mechanism of toxicity.

The oral (dietary) 2-generation reproductive toxicity study was conducted according to OECD Test Guideline 416 (1983 version) and is currently considered acceptable with limitations.[2] At the high dose, systemic toxicity in parental animals consisted of decreased body weight and liver effects, such as changes in liver enzymes and liver weight, consistent with effects observed in the short- and long-term dietary rat toxicity studies previously summarized in REG2003-10 (Canada, 2003). Sexual maturation, ovarian follicle counts, estrous cycle length and periodicity, developmental landmarks, and sperm parameters (motility and morphology) were not examined as required by updated protocols for OECD Test Guideline 416 as of 2001. The concern for these missing parameters was considered low, given the lack of observed effects on endocrine tissues across the available toxicity database, based on study conclusions summarized in REG2003-10 (Canada, 2003).

Reproductive and offspring toxicity were noted in the 2-generation reproductive toxicity study in rats at the high dose with decreased F1 pup birth weight on postnatal day (PND) 0 which persisted through to PND 21. Similarly, F2 pups showed decreased body weight, starting on PND 4 (pre-culling) which persisted through to PND 21.

Oral (gavage) developmental toxicity studies in rats and rabbits were conducted according to OECD test guideline 414 (1981 version) and are currently considered acceptable with limitations given the shorter duration of exposure compared to updated protocols. The concern for this limitation is considered low, given the lack of observed effects on endocrine tissues across the available toxicity database, based on study conclusions summarized in REG2003-10 (Canada, 2003). Developmental toxicity was not observed in rats. In rabbits, there were abortions in 4 does between gestational days (GD) 19 to 23 at the limit dose of 1000 mg/kg bw/day. These abortions are considered to be a serious effect and suitable to characterize both maternal and developmental toxicity. However, the concern for the abortions is tempered by the presence of additional maternal toxicity, including higher body weight losses and decreased food consumption in high-dose does that did abort as compared to does that did not abort at the same dose. Abortions were not observed in an earlier preliminary rabbit gavage developmental toxicity study which tested up to the same limit dose. There was also a single incidence of hydrocephaly observed at the limit dose which was considered equivocally related to treatment. No other developmental effects were observed in either rats or rabbits.

[2] Information Note : *Determining Study Acceptability for use in Pesticide Risk Assessments*

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 of infants and children, the database contains the full complement of required studies including gavage developmental toxicity studies in rats and rabbits, and a dietary 2-generation reproductive toxicity study in rats. In addition, dose range-finding developmental toxicity studies in rats and rabbits were available.

With respect to potential prenatal and postnatal toxicity, there was indication of reproductive and offspring toxicity at the highest dose tested in the 2-generation reproductive toxicity study in rats, with decreased F1 pup birth weight on postnatal day (PND) 0, which persisted through to PND 21. Similarly, F2 pups showed decreased body weight, starting on PND 4 (pre-culling), which persisted through to PND 21. At the same dose, systemic toxicity in parental animals consisted of decreased body weight and liver effects. In the rat gavage developmental toxicity study, there were no treatment-related developmental effects up to and including the limit dose of testing. In the rabbit gavage developmental toxicity study, abortions were noted between GD 19 and 23 in 4 does at the limit dose of testing. The does that aborted had higher body weight losses and decreased food consumption compared to does that did not abort at the same dose. Abortions were not observed in an earlier preliminary rabbit gavage developmental toxicity study.

Overall, the database is adequate for determining the sensitivity of the young. The body weight effects noted in offspring in the 2-generation reproductive toxicity study in rats occurred in the presence of maternal toxicity and were not considered serious in nature. Although abortions were observed in the rabbit gavage developmental toxicity study and considered a serious effect, the level of concern was tempered by a marked decrease in food consumption and higher body weight losses in the does that aborted. On this basis, a threefold PCPA is factor is retained for scenarios for which abortions are used to establish the point of departure for risk assessment. The PCPA factor can be reduced to onefold for all other scenarios.

As published in REG2003-10, there was no evidence of carcinogenicity. The cancer assessment was not revisited as part of this targeted toxicology review. For further details, refer to REG2003-10 (Canada, 2003).

For more information, refer to Appendix III.

3.2 Dietary exposure and risk assessment

Famoxadone is registered for use on potatoes, tomatoes and caneberries. In a dietary exposure assessment, Health Canada determines how much of a pesticide residue may be ingested with the daily diet. Exposure to famoxadone from potentially treated imported foods is also included in the assessment.

3.2.1 Determination of acute reference dose (ARfD)

Based on the current targeted toxicology review, no endpoint of concern attributable to an acute exposure was identified in the DART studies and thus no change to the previous approach to the ARfD is warranted. For further details, refer to REG2003-10 (Canada, 2003).

3.2.2 Determination of acceptable daily intake (ADI)

Based on the current targeted toxicology review, no changes to the previously established toxicology reference values is warranted. The previously established ADI of 0.0014 mg/kg bw/day provides a margin of 250 000 to the NOAEL for abortions in the rabbit developmental toxicity study. For further details, refer to REG2003-10 (Canada, 2003).

3.2.3 Dietary risk assessment

As there is no endpoint of concern attributable to an acute exposure to famoxadone, an acute dietary risk assessment was not required.

As there is no evidence of carcinogenicity associated with exposure to famoxadone, a cancer risk assessment was not required.

The existing Health Canada's chronic dietary risk assessment was conducted using maximum residue limits, US tolerances, to account for imported commodities, default processing factors, and 100% of crops were assumed to be treated. Median values from US and Canadian crop field trials, experimental processing factors, and anticipated residues in livestock commodities were incorporated where available.

The refined chronic dietary exposure ranged from 19.2% to 89.2% of the ADI for all population subgroups.

Drinking water contribution to the dietary exposure was accounted for by direct incorporation of the chronic estimated environmental concentration (EEC) of 0.745 µg a.i./L.

The chronic dietary exposure from food and drinking water ranged from 22.8% to 90.9% of the ADI for all population subgroups.

For more information, refer to Appendix IV.

3.3 Occupational and non-occupational exposure and risk assessment

3.3.1 Toxicology reference values for occupational exposure

3.3.1.1 Short-term dermal and inhalation

Based on the current targeted review, no changes to the previously established toxicology reference values is warranted. The previously established toxicology reference values for short-term dermal and inhalation occupational exposure scenarios provide a margin of 3500 to the NOAEL for abortions in the rabbit developmental toxicity study. For further details, refer to REG2003-10 (Canada, 2003).

3.3.1.2 Intermediate-term dermal and inhalation

Based on the current targeted review, no changes to the previously established toxicology reference values is warranted. The previously established toxicology reference values for intermediate-term dermal and inhalation occupational exposure scenarios provide a margin of 75 000 to the NOAEL for abortions in the rabbit developmental toxicity study. For further details, refer to REG2003-10 (Canada, 2003).

3.3.1.3 Cancer assessment

The cancer assessment was not revisited as part of this targeted review. For further details, refer to REG2003-10 (Canada, 2003).

3.3.1.4 Dermal absorption factor

A dermal absorption value of 5.6% was determined for famoxadone based on a dermal in vivo study in rats.

3.3.2 Occupational exposure and risk assessment

There is potential for occupational exposure to famoxadone during mixing, loading and applying the pesticide, and when entering a treated site to conduct postapplication activities such as hand-set irrigation, scouting, hand weeding, pruning, tying/training, and harvesting. Occupational risk assessments were updated as part of the re-evaluation.

Occupational 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.

3.3.2.1 Mixer, loader, and applicator exposure and risk assessment

There are potential exposures to mixers, loaders, and applicators. The following scenarios were considered:

- Mixing/loading of dry flowable, and application using groundboom (caneberries, potatoes and field tomatoes).
- Mixing/loading of dry flowable, and application using airblast (caneberries).
- Mixing/loading of dry flowable for aerial application (potatoes and field tomatoes).
- Aerial application (potatoes and field tomatoes).
- Handheld application (field tomatoes).

Based on the number of applications and the timing of application, workers applying famoxadone would generally have a short-term (less than 30 days) or intermediate-term exposure (one to six months), depending on the crop.

No chemical-specific handler exposure data were available for famoxadone. Therefore, dermal and inhalation exposures were estimated using data from the Pesticide Handlers Exposure Database Version 1.1 (PHED) and the Agricultural Handlers Exposure Task Force (AHETF) studies.

Route-specific MOEs for mixers/loaders and applicators for agricultural crops are outlined in Appendix V.

Groundboom application

The short- and intermediate-term risk assessments for mixers/loaders and applicators using groundboom equipment is outlined in Appendix V, Tables 1–2.

The calculated MOEs for mixer/loaders and applicators exceeded target MOEs based on the current label personal protective equipment (PPE) consisting of chemical-resistant coveralls over a single layer of clothing, chemical-resistant gloves for mixers/loaders and applicators, plus a respirator for mixers/loaders and a limit of active ingredient handled of 35 kg a.i./day for groundboom applications. Therefore, risks were shown to be acceptable for workers mixing, loading and applying famoxadone under the current conditions of use. No additional mitigation measures are proposed.

Airblast application

The risk assessment for mixers/loaders and applicators using airblast equipment on caneberries is outlined in Appendix V, Tables 3–4.

The calculated short-term dermal and inhalation as well as intermediate-term inhalation MOEs for mixers, loaders and applicators exceeded the target MOEs based on the current label PPE requirements of chemical-resistant coveralls over a single layer of clothing, goggles or face shield, chemical-resistant gloves for mixers and loaders and applicators, plus a respirator for mixers and loaders.

The calculated intermediate-term dermal MOE for mixers, loaders and applicators is lower than the target MOE. To mitigate the potential risk to mixers, loaders and applicators, chemical-resistant headgear is proposed for applicators using open-cab airblast equipment. With the proposed mitigation measure, risks were shown to be acceptable for workers mixing, loading and applying famoxadone using airblast equipment.

Therefore, chemical-resistant headgear is proposed for applicators using open-cab airblast equipment (refer to Appendix VIII for details).

Handheld application

Handheld equipment (for example, backpack sprayer) can be used for spot treatment for controlling small outbreaks of pest, or for treating parts of the field that cannot be treated during broadcast application. A spot treatment is considered likely on high value crops like tomatoes and caneberries. Therefore, the risk during occasional spot treatment was also considered according to current Health Canada practice.

Exposure for mixers, loaders and applicators to famoxadone while wearing PPE required on the label and using handheld equipment for spot treatment applications is expected to be lower than the exposure of workers using groundboom or airblast equipment for applications to tomatoes and caneberries, respectively. Therefore, risks are considered to be acceptable for spot treatment applications.

Aerial application

The risk assessment for mixers, loaders and applicators using conventional aerial equipment to treat potatoes and tomatoes is outlined in Appendix V, Tables 5–6.

The calculated MOEs for mixers, loaders and applicators (pilots) exceeded target MOEs based on the current label PPE consisting of:

- chemical-resistant coveralls over a single layer of clothing, goggles or face shield, chemical-resistant gloves and respirator for mixers and loaders;
- single layer for the pilots; and
- a limit of active ingredient handled of 52.5 kg a.i./day.

Therefore, risks were shown to be acceptable for workers mixing, loading and applying famoxadone under the current conditions of use. No additional mitigation measures are proposed.

3.3.2.2 Postapplication 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). Based on the use pattern, there is potential for short-term (less than 30 days) or intermediate-term (one to six months) postapplication exposure to famoxadone residues for workers and would be primarily via the dermal route.

Potential exposure to postapplication workers was estimated using updated activity-specific transfer coefficients (TCs) from the Agricultural Re-entry Task Force (ARTF), standard dislodgeable foliar residue (DFR) values, and chemical-specific DFR data. 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 DFRs 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, and reflect standard agricultural work clothing worn by adult workers. Postapplication exposure activities for agricultural crops include, but are not limited to, harvesting, weeding and scouting.

A chemical-specific DFR study was considered in the postapplication risk assessment. DFRs for tomatoes and potatoes were calculated using results elicited from a tomato DFR study. For caneberries, since no acceptable chemical-specific DFR studies were available for famoxadone, standard values were used (peak DFR of 25% of the application rate for all crops, with 10% dissipation per day).

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 the treated area after application. An REI is the duration of time that must elapse before residues decline to a level where performing a specific activity results in exposures greater than the target MOE.

The aspect of concern identified in the 2021 European Commission decision on famoxadone (European Commission, 2021) for occupational postapplication risks during hand-harvesting was considered as part of the re-evaluation.

The risk assessment for workers conducting postapplication activities is summarized in Appendix VI, Table 1.

The calculated MOEs for postapplication workers exceeded the target MOE of 300 for all crops and activities based on the current label restricted-entry intervals (that is, 9 days for caneberries and 12 hours for all other crops). Therefore, risks were shown to be acceptable for workers entering agricultural sites treated with famoxadone under the current conditions of use. No additional mitigation measures are proposed.

3.3.3 Non-occupational exposure and risk assessment

Residential handler and postapplication exposures are not anticipated under the current conditions of use.

There is potential for exposure to bystanders during outdoor agricultural applications. To minimize the potential for bystander exposure, the registered commercial-class product label currently includes a spray drift statement. No additional mitigation measures are proposed. However, the spray drift statement needs to be updated to reflect current labelling standards (refer to Appendix VIII for details).

3.4 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). In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential (non-occupational) exposure pathways are assessed. A major consideration is the likelihood of co-occurrence of exposures and durations of exposures. Additionally, only exposures from routes that share common toxicological effects are aggregated.

As famoxadone is not registered for use in residential areas and exposure is expected to be minimal in residential settings, the aggregate risk assessment considered exposure from food and drinking water only (see section 3.2).

3.5 Cumulative assessment

The *Pest Control Products Act* requires that Health Canada consider the cumulative exposure to pest control products with a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pest control products was undertaken.

Famoxadone belongs to the oxazolidinedione structural class of fungicides, of which it is the only member. The fungicidal mode of action consists of famoxadone binding to the quinone outside site of complex III to inhibit mitochondrial electron transfer. Other pesticides registered in Canada with the same antifungal mode of action include fenamidone and the strobilurin fungicides (pyraclostrobin, azoxystrobin, kresoxim-methyl, trifloxystrobin, fluoxastrobin, and picoxystrobin). Common apical endpoints in animal toxicity studies include changes to body weights and organ weights, and diarrhea, which are considered indicative of more generalized toxicity. Furthermore, there are currently no molecular or mechanism of action data to establish a common mammalian mechanism of toxicity between famoxadone and other registered pest control products. While an in vitro study in cortical neuron-enriched cultures in mice by Pearson et al., (2016) provided some evidence that famoxadone may cluster transcriptionally with other pesticides with a similar fungal mode of action, famoxadone was not tested in subsequent experiments to expand upon this finding.

For the current targeted re-evaluation, the PMRA did not identify information indicating that famoxadone shares a common mammalian mechanism of toxicity with other registered pest control products, and it does not appear to produce a toxic metabolite in common with other registered pest control products. Therefore, a cumulative assessment is not required at this time.

3.6 Health incident reports

As of 28 November 2025, no human or domestic animal incident reports involving famoxadone have been reported to Health Canada.

4.0 Environmental assessment

The environmental re-evaluation of famoxadone relied upon existing fate information and toxicity endpoints reported in REG2003-10 (Canada, 2003), new data for pollinators from the registrant and information from a 2015 EFSA review (European Commission, 2015) and 2021 European Commission decision on famoxadone (European Commission, 2021). Aspects of concern related to the environment identified in the 2021 European Commission decision (aquatic organisms, chronic risks to mammals) were assed as part of the re-evaluation. The risk assessment was updated to incorporate revised Estimated Environmental Concentrations (EECs) based on the current use pattern, ecoscenario modelling, and available water monitoring data.

4.1 Fate and behaviour in the environment

The environmental fate and behaviour of famoxadone and its transformation products were summarized in REG2003-10, Appendix III, Tables 4 and 5 (Canada, 2003). As part of the re-evaluation, the degradation kinetics of famoxadone in the environment were updated to align with current standards. With the updated degradation kinetics, famoxadone is still considered to be non-persistent in soil (DT_{50} of 1.89 to 11.48 days) and non-persistent in aquatic systems (DT_{50} of 0.72 to 0.84 days). The representative half-lives in soil (83.6 days) and aquatic systems (12.73 days) (Appendix VII, Table 1) were used in the determination of updated EECs (Appendix VII, Tables 2–4).

4.2 Environmental risk characterization

Since the publication of REG2003-10 (Canada, 2003), the PMRA has moved from the use of margins of safety (MOS) to estimate the potential for adverse ecological effects on non-target organisms to the use of levels of concern (LOC) based on risk quotients (RQs).

As part of the re-evaluation, the environmental risk assessment was conducted as described in the guidance document Health Canada's Approach to Environmental Risk Assessment for Pest Control Products to estimate the potential for adverse effects on non-target species. Environmental exposure and ecotoxicology information were integrated by comparing estimated environmental concentrations (EECs) to effects-based values used to assess risk (effects metrics). EECs were estimated using standard models that consider application rate(s) and chemical and environmental fate properties, including pesticide dissipation between applications.

Acute and chronic ecotoxicological data for non-target terrestrial, freshwater and marine organisms are summarized in REG2003-10, Appendix III, Tables 8 and 9 (Canada, 2003). In the risk assessment, toxicity endpoints were adjusted via an uncertainty factor (UF) to calculate the effects metrics. The effects metrics account for potential differences in species sensitivity as well as varying protection goals (that is, protection at the community, population or individual level).

Initially, a screening-level risk assessment was performed using simple methods, conservative exposure scenarios and sensitive effects metrics. A risk quotient (RQ) was calculated by dividing the EEC by the effects metric and was then compared to the level of concern (LOC). When the screening level RQ was below the LOC, the risk was considered to be acceptable, and no further risk characterization was necessary. When the screening level RQ was equal to or greater than the LOC, a refined risk assessment was performed to further characterize the risk.

The refined risk assessment considered additional effects metrics as well as more realistic exposure scenarios, including spray drift, runoff and monitoring data. Refinements to the risk assessment continued until the risk was adequately characterized or the available data did not permit further refinements

4.2.1 Risks to terrestrial organisms

Terrestrial organisms, such as earthworms, beneficial arthropods, bees, birds, mammals, and plants may be exposed to famoxadone through direct contact with spray or spray drift, contact with sprayed surfaces, or from ingestion of contaminated food. Screening level RQs were calculated based on EECs from the maximum yearly application rate of 630 g a.i./ha (210 g a.i./ha × 3) (Appendix VII, Tables 2 and 4).

Earthworms

At the screening level, risks to earthworms were found to be acceptable as the RQs did not exceed the LOC (Appendix VII, Table 6).

Beneficial arthropods

Risks to beneficial arthropods were characterized with new information from a 2015 EFSA review (European Commission, 2015). RQs for beneficial arthropods from screening level risk assessments using the indicator species T. pyri and A. rhopalosiphi did not exceed the LOC. The risks to beneficial arthropods were found to be acceptable at the maximum application rate (Appendix VII, Tables 5 and 6).

Pollinators

Foraging bees could be exposed directly to famoxadone via spray droplets during application, to residues on the surface of leaves (acute contact exposure), and through the ingestion of contaminated pollen and nectar (oral exposure). In addition, chronic exposure to brood could be expected as foraging bees bring contaminated pollen and nectar back to the hive. New information on the toxicity of famoxadone to pollinators was provided by the registrant (Appendix VII, Table 5).

At the screening level, the RQs for acute contact, acute oral and chronic exposure to brood did not exceed the LOC at the single maximum application rate (Appendix VII, Table 7). Risks to pollinators are acceptable when famoxadone is used according to label directions.

Birds

The screening level risk assessment was conducted based on the estimated concentrations of famoxadone in various food items in the diet (Appendix VII, Table 4). The screening level RQs did not exceed the LOC for acute exposure, indicating that famoxadone does not pose acute risks to birds. The screening level RQs for chronic exposure exceeded the LOC for all bird sizes when using the most sensitive effect metrics and maximum residues (Appendix VII, Table 8).

The risks were further characterized by considering additional feeding guilds (frugivores and granivores in addition to insectivores), off-field spray deposition and mean residues on dietary items potentially consumed by birds (Appendix VII, Table 9). Chronic RQs for insectivores (up to 3.6) still exceeded the LOC for small and medium sized birds. All other RQs were below the LOC.

Conservative assumptions were made in the estimation of chronic exposure to birds. The risk assessment assumes 100% of the bird's diet is composed of contaminated food items (arthropods) directly sprayed without consideration of foliar interception, movement and new insect emergence. For the chronic risk assessment, these worst-case scenarios are unlikely to impact a sizeable fraction of an entire bird population. Actual chronic exposure for birds is expected to be much lower than assumed in the risk assessment.

Label statements are proposed to be added on products to warn users of the toxicity of famoxadone to birds. Risks to birds are considered acceptable when famoxadone is used according to label directions.

Small wild mammals

The screening level risk assessment was conducted based on the estimated concentrations of famoxadone in various food items in the diet (Appendix VII, Table 4). The screening level RQs did not exceed the LOC for acute exposure, indicating that famoxadone poses acceptable acute risks to small wild mammals. The screening level RQs for chronic exposure exceeded the LOC for small insectivores (1.3) and for medium and large herbivores (2.4 and 1.3, respectively).

The risks were further characterized by considering additional feeding guilds (frugivore and granivore in addition to insectivores), off-field spray deposition, and mean residues on dietary items potentially consumed by mammals. Chronic RQs were below the LOC for mammals (Appendix VII, Table 9).

Label statements are proposed to be added on products to warn users of the toxicity of famoxadone to small wild mammals.

Although the EU identified potential long-term effects of famoxadone to mammals as an aspect of concern in their 2015 review (European Commission, 2015) and 2021 decision (European Commission, 2021), Health Canada's assessment (using the same toxicological endpoints as the EU) has concluded that chronic risks to mammals are acceptable when famoxadone is used according to Canadian label directions.

Non-target terrestrial plants

Risk to non-target terrestrial plants from off-field spray deposition, RQs (<1.9) exceeded the LOC. (Appendix VII, table 6).

To mitigate risks associated with spray drift, spray buffer zones of up to 2 metres are proposed. A label statement indicating that famoxadone is toxic to plants is also proposed. When used according to the proposed updated label directions, risks to non-target plants are acceptable.

4.2.2 Risks to aquatic organisms

Aquatic organisms could be exposed to famoxadone through spray drift or runoff that enters aquatic habitats. A screening level risk assessment for aquatic organisms was conducted using existing toxicity data and direct overspray of a water body with famoxadone at the maximum yearly application rate of 630 g a.i./ha. Water bodies of two different depths were evaluated: 15-cm (seasonal water body for amphibians) and 80-cm (permanent water body for all other aquatic organisms). At the screening level, RQs (up to 470) exceeded the LOC (Appendix VII, Table 10).

The aquatic risk assessment was further characterized to consider exposure from spray drift, runoff and available water monitoring data.

Assessment of potential risk from spray drift

To assess the risks to aquatic organisms from spray drift of famoxadone from a treated field to a water body, EECs were calculated for different methods of application. The maximum percent drift deposition for field sprayer application using an ASABE "Medium" droplet size is 6% of

the application rate. The maximum percent drift deposition for early and late season airblast application is 74% and 59% of the application rate, respectively. The maximum percent drift deposition for aerial application on agricultural crops with a "Medium" spray droplet size is 23% of the application rate. The EECs were calculated for water bodies 15-cm deep for amphibians and 80-cm deep for all other aquatic organisms. For marine organisms, RQs from spray drift were determined based on acute effect metrics at the maximum single application rate (210 g a.i./ha) to reflect the lower potential of chronic exposure due to higher water renewal rates in tidal/estuarine areas.

The refined RQs for freshwater and marine habitats (maximum 347 and 28, respectively) indicate that the LOCs from exposure to famoxadone due to spray drift are exceeded for all application methods (Appendix VII, Table 11). To mitigate risks to aquatic organisms from spray drift of famoxadone, spray buffer zones ranging from 1 to 225 m, depending on the crop and method of application, are proposed to protect freshwater and marine habitats. When used according to the proposed label directions, risks to aquatic organisms associated with spray drift are considered acceptable.

Assessment of potential risk from runoff

Water modelling

Aquatic organisms can also be exposed to famoxadone from runoff that enters a body of water from a treated field. The Pesticide in Water Calculator (PWC version 1.52) was used to generate EECs. PWC calculates the amount of pesticide entering the water body by runoff alone, and the subsequent transformation of the pesticide in the water system. EECs are calculated by modelling a total land area of 10 ha draining into a 1 ha pond of two different depths (15 and 80 cm). The model was run for 50 years for different regions of Canada at two application rates, 3 × 210 g a.i./ha for caneberries and potatoes; and 3 × 140 g a.i./ha for field tomatoes with re-application intervals of 12 days between the 1st and 2nd applications and 24 days between the 2nd and 3rd applications. Modelled runoff EECs are presented in Appendix VII, Table 3.

To assess acute risks based on modelled EECs, the 90th percentile of 24- or 96-hour EECs were compared to the acute effects metrics to generate acute RQ values. To assess chronic risks based on modelling, 21- or 60-day EECs were compared to the chronic effects metrics to generate chronic RQ values. The acute and chronic RQs from exposure to famoxadone based on modelled runoff EECs are presented in Appendix VII, Table 12. Acute and chronic RQs exceeded the LOC (up to 16.5).

The risks were further characterized by considering water monitoring data as outlined below.

Water monitoring

Canadian water monitoring data from 2009–2025 were considered in the aquatic risk assessment. Water monitoring data were available from many sources across Canada including Health Canada's Canadian Water Monitoring Program for Pesticides (CWMPP), PEI Department of Communities, Land and Environment database, Ontario Ministry of the Environment, Conservation and Parks, and Alberta Agriculture and Forestry: Irrigation and Farm Water Branch (Water Quality Section).

Data from the USA were available from the US Environmental Protection Agency's Storage and Retrieval (STORET) data warehouse, available through the National Water Quality Monitoring Council's Water Quality Portal (WQP) and the California Department of Pesticide Regulation's Surface Water Database.

The Canadian data were analysed and assessed for reliability, relevancy and robustness for consideration in aquatic risk assessment. To assess the relevancy of the water monitoring data, geospatial analysis was conducted to determine if crops with registered uses of famoxadone were grown where samples were collected.

A total of 5154 Canadian surface water samples were considered in the aquatic risk assessment. These samples came from canals, streams, brooks, creeks, ditches/drains, lakes, wetlands, and rivers within all Canadian provinces (Appendix VII, Table 13). Famoxadone was not detected in any of the available Canadian surface water samples.

In the US, famoxadone is applied on more agricultural crops and at higher application rates as compared to Canada. Water monitoring data from the US was also considered in the aquatic risk assessment. A total of 8842 surface water samples analyzed for famoxadone were available in US databases from 2009–2023. There was insufficient information to fully assess the relevancy of the sites at which the samples were collected. From the 8842 US surface water samples, there were eight detections of famoxadone in 4 replicates sampled at a site in Sacramento, California in 2012. The maximum concentration detected was 0.022 µg a.i./L.

Overall, there were 8 detections of famoxadone in 13 996 surface water samples in Canada and the US. The limit of detection in these samples ranged from 0.001 to 1.54 µg a.i./L.

Runoff assessment risk conclusions

Water modelling inputs and assumptions are conservative. The EECs generated through modelling are likely higher than actual concentrations present in water bodies. Famoxadone dissipates rapidly in water by hydrolysis, photolysis and aerobic degradation and is non-persistent in aquatic environments.

The availability of highly relevant Canadian water monitoring data and a large amount of data from the US allows for further refinement of the aquatic risk assessment. This water monitoring data indicates that residues of famoxadone in Canadian surface water are not expected. The eight detections from the US (California) were at levels below the most sensitive acute and chronic effects metrics for aquatic organisms. The use pattern in the US has additional crops and higher maximum yearly application rates as compared to Canada.

A label statement is proposed to warn users of the toxicity of famoxadone to aquatic organisms. Best management practices to reduce runoff entering sensitive aquatic habitats are proposed to be added on product labels. Risks to aquatic organisms from runoff are acceptable when the end-use product is used according to the proposed label directions.

Although the EU identified potential risks of famoxadone to aquatic organisms as an aspect of concern in their 2021 decision (European Commission, 2021), Health Canada's assessment (using the same or more sensitive endpoints than the EU) has concluded that risks to aquatic organisms are acceptable when following proposed Canadian label directions.

4.2.3 Environmental incident reports

As of 28 November 2025, no environmental incident reports involving famoxadone have been submitted to Health Canada.

5.0 Value assessment

Famoxadone is a protectant and locally systemic broad-spectrum fungicide that is compatible with a number of disease management practices and fits well into integrated pest management strategies due to its strong activity on diseases. For further details, refer to REG2003-10 (Canada, 2003).

6.0 Pest Control Product Policy considerations

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

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, that is, 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, famoxadone was assessed in accordance with the PMRA Regulatory Directive DIR99-03[3] and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that famoxadone and its transformation products do not meet all of the TSMP Track 1 criteria.

Please refer to Appendix VII, Table 14, for further information on the TSMP assessment.

6.2 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.[4] The list is used as described in the PMRA Science Policy Note SPN2020-01[5] and is based on existing policies and regulations, including the *Toxic Substances Management Policy* and *Formulants Policy*,[6] and taking into consideration the *Ozone-depleting Substances and Halocarbon*

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

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

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

[6] DIR2006-02, *Formulants Policy and Implementation Guidance Document*

Alternatives Regulations under the *Canadian Environmental Protection Act, 1999* (substances designated under the *Montreal Protocol*).

The PMRA has reached the conclusion that famoxadone Technical does not contain any formulants or contaminants 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.

List of abbreviations

♀	female
♂	male
↑	increased
↓	decreased
%	percent
≥	equal to or greater than
>	greater than
°C	degrees Celsius
a.i.	active ingredient
abs	absolute
ADI	acceptable daily intake
AHETF	Agricultural Handlers Exposure Task Force
AOPWIN	Atmospheric Oxidation Program for Microsoft Windows
AR	applied radioactivity
ASABE	American Society of Agricultural and Biological Engineers
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
AD	administered dose
AGD	anogenital distance
ALT	alanine aminotransferase
AP	alkaline phosphatase
AST	aspartate aminotransferase
BAF	bioaccumulation factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bwg	body weight gain
bw	body weight
CAF	composite assessment factor
CEPA	*Canadian Environmental Protection Act*
CF	conversion factor
cm	centimetre(s)
cm^3	cubic centimetre(s)
CO_2	carbon dioxide
CWMPP	Canadian Water Monitoring Program for Pesticides
d	day(s)
DART	developmental and reproductive toxicity
DFOP	double first-order in parallel
DFR	Dislodgeable foliar residue
DT_{50}	dissipation time 50%
dw	dry weight
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure
EEC	estimated environmental concentration
ER_{25}	effective rate on 25% of the population
ER_{50}	effective rate on 50% of the population
F0	parental generation

F1	first filial generation
F2	second filial generation
fc	food consumption
FIR	food ingestion rate
g	gram(s)
GD	gestation day
GLP	Good Laboratory Practice
h	hour(s)
ha	hectare(s)
IORE	Indeterminate Order Rate Equation
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{ow}	octanol-water partition coefficient
L	litre(s)
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LD	lactation day
LOAEL	lowest adverse effect level
LOC	level of concern
LOEC	lowest observed effect concentration
LOED	lowest observed effect dose
LOEL	lowest observed effect level
LOER	lowest observed effect rate
LR_{50}	lethal rate 50%
MECP	Ministry of the Environment, Conservation and Parks
MOE	margin of exposure
mg	milligram
mL	millilitre(s)
MW	molecular weight
N/A	not applicable
ND	not detected
NZW	New Zealand White
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NOER	no observed effect rate
OMAFRA	Ontario Ministry of Agriculture, Food and Rural Affairs
Pa	Pascal
PCPA	Pest Control Products Act
pH	measure of the acidity or basicity of an aqueous solution
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
PND	postnatal day
PPE	personal protective equipment
PWC	Pesticide Water Calculator
REI	restricted-entry interval
rel	relative

RQ	risk quotient
SDH	sorbitol dehydrogenase
SFO	single first-order
SPN	science policy note
$t_{1/2}$	half-life
t_R	representative half-life
TC	transfer coefficients
TP	transformation product
TSMP	Toxic Substances Management Policy
UF	uncertainty factor
UK	United Kingdom
US	United States
USEPA	United States Environmental Protection Agency
µg	microgram
wt	weight

Appendix I Registered products containing famoxadone

Table 1 Registered products containing famoxadone as of 2 July 2025

Registration number	Marketing class	Registrant	Product name	Formulation type	Guarantee
27436	Technical	Corteva Agriscience Canada Company	Famoxadone Technical	Solution	97.8%
27435	Commercial	Corteva Agriscience Canada Company	Tanos™ Fungicide	Dry Flowable	25% Famoxadone 25% Cymoxanil

Appendix II Registered uses of famoxadone in Canada

Table 1 Registered commercial uses of famoxadone in Canada

Crop	Single application rate (g a.i./ha)	Maximum cumulative rate (g a.i./ha/year)	Number of application per year	RTI (days)	REI	Application method
Caneberries	210	630	3	12 days between 1st and 2nd application. 24 days between 2nd and 3rd application.	9 days	Ground
Field Tomatoes	140	420	3	12 days between 1st and 2nd application. 24 days between 2nd and 3rd application.	12 hours	Ground Aerial
Potatoes	140–210	630	3	12 days between 1st and 2nd application. 24 days between 2nd and 3rd application.	24 hours	Ground Aerial

Appendix III Toxicology risk assessment

Table 1 Toxicity profile of technical famoxadone

Effects observed in both sexes are presented first, followed by sex-specific effects in males, then females, each separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to body weights unless otherwise noted.

Given the current targeted review, only developmental and reproductive toxicity studies were revisited and summarized in Table 1. For a summary of the other toxicology studies conducted with technical famoxadone, refer to REG2003-10 (Canada, 2003).

Note: unless otherwise specified, studies listed in this table are considered Acceptable according to Information Note: Determining Study Acceptability for use in Pesticide Risk Assessments

Study type/ Animal/PMRA No.	Study results
Developmental/Reproductive Toxicity Studies – Famoxadone technical	
2-Generation Reproductive Toxicity (diet) (1 litter/generation) Sprague-Dawley rats PMRA No. 1018824, 1018825, 1018826, 1018835, 1018844	**Acceptable with limitations** **Parental Toxicity** NOAEL = 11/14 mg/kg bw/day (♂/♀) **45/53 mg/kg bw/day:** ↑ AP (F0: (♂); F1: (♂/♀)), ↑ AST (F0: (♂); F1: (♂/♀)), ↑ SDH (F0: (♂) ; F1: (♂/♀)), ↓ triglycerides (F0/F1 (♂/♀), ↓ globulin (F0: (♀); F1: (♂/♀)) (♂/♀), ↑ peroxisomal β-oxidation (F0/F1: (♂/♀)) (♂/♀); ↓ bw (F0), ↓ bwg (F0), ↓ fc (F0), ↑ ALT (F0/F1), ↑ bilirubin (F0/F1), ↑ BUN (F1), ↓ abs/rel liver weights (F0) (♂); ↓ premating bw (F0/F1), ↓ premating bwg (F0/F1), ↓ gestation bw (F0/F1: GD 0-21), ↓ gestation bwg (F0/F1: GD 0-7), ↓ lactation bw (F0/F1: LD 0-14), ↓ lactation bwg (F0/F1: LD 0-21), ↓ premating fc (F0/F1), ↓ gestation fc (F0/F1: GD 0-14), ↑ alopecia during premating (F1), ↑ alopecia during gestation (F0/F1), ↑ alopecia during lactation (F0), ↑ cholesterol (F0/F1), ↑ abs/rel liver weight (F0/F1), dilation of kidneys (F1) (♀) **Offspring Toxicity** NOAEL = 14 mg/kg bw/day (♀) **53 mg/kg bw/day:** ↓ pup bw (F1/F2: PND 0-21; F2: LD 4-21), ↑ alopecia (F1), sparse fur (F2) **Reproductive Toxicity** NOAEL = 11/14 mg/kg bw/day (♂/♀)

Study type/ Animal/PMRA No.	Study results
	45/53 mg/kg bw/day: ↓ pup birth wt (F1: PND 0) **No evidence of sensitivity of young** **Limitations:** study did not measure estrus cyclicity in females, sperm parameters in males, developmental landmarks (vaginal opening, preputial separation in F1 offspring and AGD in F2 offspring, organ weights (except liver and testes).
Range-finding Developmental Toxicity Study (gavage) Sprague-Dawley rats PMRA No. 3191377	**Acceptable with limitations** **Maternal Toxicity** No maternal toxicity noted up to the highest dose tested of 400 mg/kg bw/day **Developmental Toxicity** No developmental toxicity noted up to the highest dose tested of 400 mg/kg bw/day in the limited parameters assessed **Limitations:** small group size, limited number of parameters assessed. Study designed to determine dose range for definitive study.
Range-finding Developmental Toxicity Study (gavage) Sprague-Dawley rats PMRA No. 3191378	**Acceptable with limitations** **Maternal Toxicity** **1000 mg/kg bw/day:** ↓ bw (GD 9-17), ↓ bwg (GD 7-9), ↓ fc (GD 7-17), tan stool (GD 7-16; GD 17-22) **Developmental Toxicity** No developmental toxicity noted at a limit-dose of 1000 mg/kg bw/day in the limited parameters assessed **Limitations**: small group size, limited number of parameters assessed. Study designed to determine dose range for definitive study.
Developmental Toxicity (gavage) Sprague-Dawley rats PMRA No. 1018845,	**Acceptable with limitations** **Maternal Toxicity** NOAEL = 250 mg/kg bw/day **≥ 500 mg/kg bw**: ↓ bwg (GD 7-9) and food consumption (GD 7-9)

Study type/ Animal/PMRA No.	Study results
1018846	**Developmental Toxicity** NOAEL = 1000 mg/kg bw/day (limit dose) **No evidence of treatment-related malformations** **No evidence of sensitivity of the young** **Limitations:** Treatment was limited to days 7–16 of gestation. Missing some parameters given older protocol.
Range-finding Developmental Toxicity Study (gavage) NZW rabbits PMRA No. 3191379	**Acceptable with limitations** **Maternal Toxicity** **1000 mg/kg bw/day:** ↑ diarrhea (GD 7-19), ↑ stained tail (GD 7-19), ↑ tan stool (GD 7-19) **Developmental Toxicity** No developmental toxicity noted at a limit-dose of 1000 mg/kg bw/day in the limited parameters assessed. **Limitations**: small group size, limited number of parameters assessed. Study designed to determine dose range for definitive study.
Developmental Toxicity (gavage) NZW rabbits PMRA No. 1018847, 1018848	**Acceptable with limitations** **Maternal Toxicity** NOAEL = 350 mg/kg bw/day **1000 mg/kg bw/day**: ↑ abortion (GD 19-23), ↓ bw, bw losses, and ↓ fc in dams that aborted, ↑ number of does with abnormal or little or no stool **Developmental Toxicity** NOAEL = 350 mg/kg bw/day **1000 mg/kg bw/day**: ↑ abortion (GD 19-23), single incidence of hydrocephaly (equivocal) **Equivocal evidence of treatment-related malformations**

Study type/ Animal/PMRA No.	Study results
	No evidence of sensitivity of the young **Limitations:** Treatment was limited to days 7–19 of gestation. Missing some parameters given older protocol
In vitro transcriptional changes Pearson et al. (2016) PMRA No. 3713520 Cortical neuron-enriched cultures in mice	**Acceptable with limitations** Famoxadone appeared to cluster with other pesticides with a similar fungal mode of action (quinone outside inhibitors) that may produce transcriptional changes in vitro which may be similar to those seen in humans with various neurological conditions. **Limitations:** Famoxadone was not tested further in the study to determine specific in vitro effects and provides no quantitative endpoints specific for famoxadone.

Table 2 Toxicology reference values for use in human health risk assessment for famoxadone

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or target MOE
ARfD (all populations)	No endpoint of concern attributable to an acute exposure was identified in the toxicology database; therefore, an ARfD was not established.		
	ARfD = not applicable		
Repeated Dietary (all populations)	90-day toxicity in dogs	LOAEL = 1.4 mg/kg bw/day Treatment-related microscopic eye lesions in females (cataracts).	1000 (includes 10-fold UF for use of a LOAEL and duration extrapolation)
	ADI = 0.0014 mg/kg bw/day		
Short-term dermal[2] and inhalation[3]	90-day toxicity in dogs	NOAEL = 10 mg/kg bw/day Treatment-related myotonic twitches in both sexes starting on day 21	100
Intermediate -term dermal[2] and inhalation[3]	90-day toxicity in dogs	LOAEL = 1.4 mg/kg bw/day Treatment-related microscopic eye lesions in females (cataracts).	300 (includes threefold UF for use of LOAEL)
Cancer	A cancer risk assessment was not required		

1 CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments; MOE (margin of exposure) refers to a target MOE for occupational and residential assessments.

2 Since an oral NOAEL was selected, a dermal absorption factor of 5.6% was used in a route-to-route extrapolation.

3 Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Appendix IV Dietary risk assessment

Table 1 Chronic dietary exposure and risk for famoxadone

Population subgroup	Food alone		Food plus drinking water[2]	
	Exposure (mg/kg bw/day)	% ADI[1]	Exposure (mg/kg bw/day)	% ADI[1]
General Population	0.000912	65.2	0.000928	66.3
All Infants (<1 year old)	0.000268	19.2	0.000320	22.8
Children 1–2 years old	0.001249	89.2	0.001272	90.9
Children 3–5 years old	0.001114	79.6	0.001136	81.1
Children 6–12 years old	0.000750	53.6	0.000765	54.7
Youth 13–19 years old	0.000597	42.6	0.000608	43.4
Adults 20–49 years old	0.001052	75.1	0.001066	76.2
Adults 50+ years old	0.000814	58.2	0.000830	59.3
Females 13–49 years old	0.000710	50.7	0.000725	51.8

1 Acceptable daily intake (ADI) of 0.0014 mg/kg bw/day based on a LOAEL of 1.4 mg/kg bw/day and composite assessment factor of 1000.

2 Drinking water was assessed using Level 1 estimated environmental concentration of 0.745 µg a.i./L

Table 2 Level 1 estimated environmental concentration of famoxadone in drinking water*

Crop and annual application rate	Compound	Groundwater (µg a.i./L)		Surface water (µg a.i./L)			
				Reservoir		Dugout	
		Acute[1]	Chronic[2]	Acute[3]	Chronic[4]	Acute[3]	Chronic[4]
Caneberry, potato, tomato	Famoxadone	0	0	17.4	**0.745**	4.98	0.197

* Expected concentrations using different initial application dates and assuming an application rate of 210 g a.i./ha, 6 times with 7 days intervals.

1 90th percentile of daily average concentrations

2 90th percentile of yearly average concentrations

3 90th percentile of yearly peak concentrations

4 90th percentile of yearly average concentrations

Appendix V Occupational mixer/loader/applicator risk assessment

Table 1 Short-term risks to workers mixing/loading and applying famoxadone using groundboom equipment

Crop	M/L and application type	M/L UEs (µg/kg a.i.)		Applicator UEs (µg/kg a.i.)		AR (kg a.i./ha)	ATPD (ha)	Amount Handled per day (kg a.i./day)[1]	Dermal exposure (mg/kg bw/day)[2]	Dermal MOE[3]	Inhalation exposure (mg/kg bw/day)[4]	Inhalation MOE[3]	Combined MOE[5]
		Dermal	Inhalation	Dermal	Inhalation								
Potato (custom and farmer)	**Open mix/load of dry flowable (AHETF) and application using groundboom (AHETF)**												
	M/L/A CR coveralls + CR gloves + Respirator												
	Open M/L + open cab	39.13	2.18	11.77	1.680	0.21	107	22.47	0.0009	11111	0.0011	9091	5000
	Open M/L + open cab	39.13	2.18	11.77	1.680	0.21	165	34.56	0.0013	7692	0.0017	5882	3333
Tomato	**M/L/A CR coveralls + CR gloves + Respirator**												
	Open M/L + open cab	39.13	2.18	11.77	1.680	0.14	26	3.64	0.0002	50 000	0.0002	50000	25000
Caneberries	**M/L/A CR coveralls + CR gloves + Respirator**												
	Open M/L + open cab	39.13	2.18	11.77	1.680	0.21	26	5.46	0.0002	17 272	0.0003	3744	3077

M/L = Mixer/Loader; A = Applicator; UE = Unit Exposure; MOE = margin of exposure; AHETF = Agricultural Handlers Exposure Database; CR = chemical-resistant; AR = Maximum Application Rate; ATPD = Area Treated Per Day

1 Amount Handled Per Day = Maximum Application Rate (kg a.i./ha) × Area Treated Per Day (ha)

2 Dermal exposure (mg/kg bw/day) = Dermal unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha) × 5.6% dermal absorption/average worker body weight (80 kg)

3 Based on a dermal and inhalation NOAEL of 10 mg/kg bw/day; target MOE of 100 (Appendix III).

4 Inhalation exposure (mg/kg bw/day) = Inhalation unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha)/average worker body weight (80 kg)

5 Combined MOE = NOAEL / (Exp_{dermal} + $Exp_{inhalation}$); target MOE = 100

Table 2 Intermediate-term risks to workers mixing/loading and applying famoxadone using groundboom equipment

Crop	M/L and application type	M/L UEs (µg/kg a.i.)		Applicator UEs (µg/kg a.i.)		AR (kg a.i./ha)	ATPD (ha)	Amount Handled per day (kg a.i./day)[1]	Dermal exposure (mg/kg bw/day)[2]	Dermal MOE[3]	Inhalation exposure (mg/kg bw/day)[4]	Inhalation MOE[3]	Combined MOE[5]
		Dermal	Inhalation	Dermal	Inhalation								
Potato (custom and farmer)	**Open mix/load of dry flowable (AHETF) and application using groundboom (AHETF)**												
	M/L/A CR coveralls + CR gloves + Respirator												
	Open M/L + open cab	39.13	2.18	11.77	1.680	0.21	107	22.47	0.0009	1556	0.0011	1273	700
	Open M/L + open cab	39.13	2.18	11.77	1.680	0.21	165	34.56	0.0013	1077	0.0017	824	467
Tomato	**M/L/A CR coveralls + CR gloves + Respirator**												
	Open M/L + open cab	39.13	2.18	11.77	1.680	0.14	26	3.64	0.0002	7000	0.0002	7000	3500
Caneberries	**M/L/A CR coveralls + CR gloves + Respirator**												
	Open M/L + open cab	39.13	2.18	11.77	1.680	0.21	26	5.46	0.0002	7000	0.0003	4667	2800

M/L = Mixer/Loader; A = Applicator; UE = Unit Exposure; MOE = margin of exposure; AHETF = Agricultural Handlers Exposure Database; CR = chemical-resistant; AR = Maximum Application Rate; ATPD = Area Treated Per Day

1 Amount Handled Per Day = Maximum Application Rate (kg a.i./ha) × Area Treated Per Day (ha)

2 Dermal exposure (mg/kg bw/day) = Dermal unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha) × 5.6% dermal absorption/average worker body weight (80 kg)

3 Based on a dermal and inhalation NOAEL of 1.4 mg/kg bw/day; target MOE of 300 (Appendix III).

4 Inhalation exposure (mg/kg bw/day) = Inhalation unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha)/average worker body weight (80 kg)

5 Combined MOE = NOAEL / (Exp_{dermal} + $Exp_{inhalation}$); target MOE = 300

Table 3 Short-term risks to workers mixing/loading and applying famoxadone using airblast equipment

Crop	M/L and application type	M/L UEs (µg/kg a.i.)		Applicator UEs (µg/kg a.i.)		AR (kg a.i./ha)	ATPD (ha)	Amount handled per day (kg a.i./day)[1]	Dermal exposure (mg/kg bw/day)[2]	Dermal MOE[3]	Inhalation exposure (mg/kg bw/day)[4]	Inhalation MOE[3]	Combined MOE[5]
		Dermal	Inhalation	Dermal	Inhalation								
Caneberries	**Open mix/load of dry flowable (AHETF) and application using airblast (AHETF)**												
	M/L/A CR coveralls + CR gloves + Respirator												
	Open M/L + open cab	39.13	2.18	3323.5	0.910	0.21	20	4.2	0.0099	1010	0.0002	50000	990

M/L = Mixer/Loader; A = Applicator; UE = Unit Exposure; MOE = margin of exposure; AHETF = Agricultural Handlers Exposure Database; CR = chemical-resistant; AR = Maximum Application Rate; ATPD = Area Treated Per Day

1 Amount Handled Per Day = Maximum Application Rate (kg a.i./ha) × Area Treated Per Day (ha)

2 Dermal exposure (mg/kg bw/day) = Dermal unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha) × 5.6% dermal absorption/average worker body weight (80 kg)

3 Based on a dermal and inhalation NOAEL of 10 mg/kg bw/day; target MOE of 100 (Appendix III).

4 Inhalation exposure (mg/kg bw/day) = Inhalation unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha)/average worker body weight (80 kg)

4 Combined MOE = NOAEL / (Exp_{dermal} + $Exp_{inhalation}$); target MOE = 100

Table 4 Intermediate-term risks to workers mixing/loading and applying famoxadone using airblast equipment

Crop	M/L and application type	M/L UEs (µg/kg a.i.)		Applicator UEs (µg/kg a.i.)		AR (kg a.i./ha)	ATPD (ha)	Amount Handled per day (kg a.i./day)[1]	Dermal exposure (mg/kg bw/day)[2]	Dermal MOE[3]	Inhalation exposure (mg/kg bw/day)[4]	Inhalation MOE[3]	Combined MOE[5]
		Dermal	Inhalation	Dermal	Inhalation								
Caneberries	**Open mix/load of dry flowable (AHETF) and application using airblast (AHETF)**												
	M/L/A CR coveralls + CR gloves + Respirator												
	Open M/L + open cab	39.13	2.18	3323.5	0.910	0.21	20	4.2	0.0099	**141**	0.0002	7000	**139**
	M/L/A CR coveralls + CR gloves + hat												
	Open M/L + open cab	39.13	2.18	106.77	9.080	0.21	20	4.2	0.0005	2800	0.0006	2333	1273

Bolded cells indicate risks that are not considered to be acceptable (MOEs that are less than the target MOE of 300).

M/L = Mixer/Loader; A = Applicator; UE = Unit Exposure; MOE = margin of exposure; AHETF = Agricultural Handlers Exposure Database; CR = chemical-resistant; AR = Maximum Application Rate; ATPD = Area Treated Per Day

1 Amount Handled Per Day = Maximum Application Rate (kg a.i./ha) × Area Treated Per Day (ha)

2 Dermal exposure (mg/kg bw/day) = Dermal unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha) × 5.6% dermal absorption/average worker body weight (80 kg)

3 Based on a dermal and inhalation NOAEL of 1.4 mg/kg bw/day; target MOE of 300 (Appendix III).

4 Inhalation exposure (mg/kg bw/day) = Inhalation unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha)/average worker body weight (80 kg)

5 Combined MOE = NOAEL / (Exp_{dermal} + $Exp_{inhalation}$); target MOE = 300

Table 5 Short-term risks to workers mixing/loading and applying famoxadone using aerial equipment

Crop	M/L and application type	M/L UEs (µg/kg a.i.)		Applicator UEs (µg/kg a.i.)		AR (kg a.i./ha)	ATPD (ha)	Amount Handled per day (kg a.i./day)[1]	Dermal exposure (mg/kg bw/day)[2]	Dermal MOE[3]	Inhalation exposure (mg/kg bw/day)[4]	Inhalation MOE[3]	Combined MOE[5]
		Dermal	Inhalation	Dermal	Inhalation								
Potato (custom and farmer)	**Open mix/load of dry flowable (AHETF)**												
	M/L CR coveralls + CR gloves + Respirator												
	Open M/L	39.13	2.18	-	-	0.21	107	22.47	0.0005	20000	0.0005	20000	10000
	Open M/L	39.13	2.18	-	-	0.21	250	52.5	0.0012	8333	0.0012	8333	4167
Tomato	**M/L CR coveralls + CR gloves + Respirator**												
	Open M/L	39.13	2.18	-	-	0.14	26	3.64	0.0001	100000	0.0001	100000	50000
Potato (pilot)*	**Application using aerial equipment (AHETF)**												
	Single layer, no gloves	-	-	2.67	0.010	0.21	250	52.5	0.0001	100000	0.0001	100000	50000

*Aerial application scenario for potato encompasses famoxadone use on tomato.

M/L = Mixer/Loader; UE = Unit Exposure; MOE = margin of exposure; AHETF = Agricultural Handlers Exposure Database; CR = chemical-resistant; AR = Maximum Application Rate; ATPD = Area Treated Per Day

1 Amount Handled Per Day = Maximum Application Rate (kg a.i./ha) × Area Treated Per Day (ha)

2 Dermal exposure (mg/kg bw/day) = Dermal unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) x ATPD (ha) × Maximum AR (kg a.i./ha) × 5.6% dermal absorption/average worker body weight (80 kg)

3 Based on a dermal and inhalation NOAEL of 10 mg/kg bw/day; target MOE of 100 (Appendix III).

4 Inhalation exposure (mg/kg bw/day) = Inhalation unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) x ATPD (ha) × Maximum AR (kg a.i./ha)/average worker body weight (80 kg)

5 Combined MOE = NOAEL / (Exp_{dermal} + $Exp_{inhalation}$); target MOE = 100

Table 6 Intermediate-term risks to workers mixing/loading and applying famoxadone using aerial equipment

Crop	M/L and application type	M/L UEs (µg/kg a.i.)		Applicator UEs (µg kg a.i.)		AR (kg a.i./ha)	ATPD (ha)	Amount Handled per day (kg a.i./day)[1]	Dermal exposure (mg/kg bw/day)[2]	Dermal MOE[3]	Inhalation exposure (mg/kg bw/day)[4]	Inhalation MOE[3]	Combined MOE[5]
		Dermal	Inhalation	Dermal	Inhalation								
Potato (custom and farmer)	**Open mix/load of dry flowable (AHETF)**												
	M/L CR coveralls + CR gloves + Respirator												
	Open M/L	39.13	2.18	-	-	0.21	107	22.47	0.0002	7000	0.0002	7000	3500
	Open M/L	39.13	2.18	-	-	0.21	250	52.5	0.0004	3500	0.0004	3500	1750
Tomato	**M/L CR coveralls + CR gloves + Respirator**												
	Open M/L	39.13	2.18	-	-	0.14	26	3.64	0.0001	14000	0.0001	14000	7000
Potato (pilot)*	**Application using aerial equipment (AHETF)**												
	Single layer, no gloves	-	-	2.67	0.010	0.21	250	52.5	0.0001	14000	0.0001	14000	7000

*Aerial application scenario for potato encompasses famoxadone use on tomato.

M/L = Mixer/Loader; UE = Unit Exposure; MOE = margin of exposure; AHETF = Agricultural Handlers Exposure Database; CR = chemical-resistant; AR = Maximum Application Rate; ATPD = Area Treated Per Day

1 Amount Handled Per Day = Maximum Application Rate (kg a.i./ha) × Area Treated Per Day (ha)

2 Dermal exposure (mg/kg bw/day) = Dermal unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha) × 5.6% dermal absorption/average worker body weight (80 kg)

3 Based on a dermal and inhalation NOAEL of 1.4 mg/kg bw/day; target MOE of 300 (Appendix III).

4 Inhalation exposure (mg/kg bw/day) = Inhalation unit exposure (µg/kg a.i.) × CF (1 mg/1000µg) × ATPD (ha) × Maximum AR (kg a.i./ha)/average worker body weight (80 kg)

5 Combined MOE = NOAEL / (Exp_{dermal} + $Exp_{inhalation}$); target MOE = 300

Appendix VI Postapplicator exposure and risk assessment

Table 1 Dermal postapplication exposure and risk assessment of famoxadone

Crop	Use pattern[1]			Peak DFR (µg/cm²)[2]	Activity	TC (cm²/hr)[3]	Dermal exposure (mg/kg bw/day)[4]	Dermal MOE[5]	REI[6]
	Max. AR (kg a.i./ha)	No. of application	RTI (days)						
Field Tomatoes	0.14	3	12 (1st-2nd application) 24 (2nd-3rd application)	0.230	Hand-set irrigation	1750	0.00196	713	12 hours
					Tying/training, hand harvesting	1100	0.0040	350	12 hours
					Scouting	210	0.00076	1835	12 hours
					Hand weeding/ pruning	70	0.00025	5505	12 hours
Potatoes	0.21	3	12 (1st-2nd application) 24 (2nd-3rd application)	0.649	Hand-set irrigation	1750	0.00553	**253**	3 days
					Roguing	1100	0.0040	350	12 hours
					Scouting	210	0.00076	1835	12 hours
Caneberries	0.21	3	12	0.3206	Hand-set irrigation	1750	0.0033	419	12 hours
					Hand harvesting, tying/training	1400	0.0027	527	12 hours
					Hand pruning/weeding, scouting	640	0.0012	1147	12 hours
					Transplanting	230	0.0004	3192	12 hours

Bolded cell indicates a risk that is not considered to be acceptable (the MOE is less than the target MOE of 300).

Max. AR = maximum application rate; RTI = re-treatment interval; DFR = dislodgeable foliar residue; TC = transferable residues; MOE = margin of exposure; REI = Restricted-entry interval

1 Use directions as per currently registered product labels

2 Peak DFR (µg/cm²) – For field tomatoes and potatoes, DFR levels are based on the chemical-specific tomato DFR study. For caneberries, a standard DFR value was estimated assuming 25% of the application rate and a dissipation rate of 10% per day.

3 TC (cm²/hr) - highest TC value for a given crop (ARETF, 2015)

4 Dermal exposure = Peak DFR (µg/cm²) × 1000 µg/mg × TC (cm²/hr) × 8 hours / average worker body weight of 80 kg

5 Dermal MOE based on a NOAEL of 1.4 mg/kg bw/day; target MOE = 300 (Appendix III)

6 Previously established REIs for Tanos Fungicide end-use product (Reg. No. 27435) are based on co-formulant: Potatoes = 1–18-day REI; Tomatoes = 0.5–8-day REI; Caneberries = 9–11-day REI

Appendix VII Environmental risk assessment

Table 1 Updated half-lives (days) of famoxadone in aerobic soil and aquatic systems used in determination of EECs

	Reported in (REG2003-10) DT_{50} (d)	DT_{50}	Representative half-life (d)	Kinetic model	Comments	Remark
Soil						
Speyer sandy loam, Germany	6	5.16	30.75	IORE	Non-persistent	
Madison loamy sand soil, Ohio	9	8.87	116.81	DFOP	Non- persistent	
Milton sandy loam, UK	11	11.48	80.42	DFOP	Non-persistent	
Matapeake silt loam, Delaware	3	3.56	29.50	IORE	Non-persistent	
Nambsheim silt loam, France	2	1.89	9.41	IORE	Non-persistent	
90^{th} percentile confidence bound on the mean of five values	N/A	N/A	83.60		Moderately persistent	Used in determination of terrestrial EECs
Aquatic system						
Ohio whole system at pH 7.1	0.68	0.84	2.79	IORE	Non-persistent	
Ohio water phase at pH 7.1	N/A	0.03	0.20	IORE		
Ohio whole system at pH 7.7	2.05	0.72	12.73	DFOP	Non-persistent	Longer representative half-life used in the determination of aquatic EECs.
Ohio water phase at pH 7.7	N/A	0.02	5.63	DFOP		

EEC = Estimated environmental concentration. N/A = not available
DFOP = Double first-order in parallel
IORE = Indeterminate-order rate equation

Table 2 Screening level EECs of famoxadone in soil, foliar and water bodies (80 cm and 15 cm)

Use scenario	Terrestrial habitat		Aquatic habitat	
	EEC in 0-15 cm depth soil (µg a.i./kg)	Foliar EEC (g a.i./ha)	EEC in 15 cm depth (µg a.i./L)	EEC in 80 cm depth (µg a.i./L)
Maximum app. rate on potatoes and caneberries (3 × 210 g a.i./ha)	239.1	301.4	212.8	39.9
Maximum app. rate on field tomatoes (3 × 140 g a.i./ha)	159.4	200.9	141.9	26.6

EEC = Estimated environmental concentration.

EECs in soil, water and foliage were calculated using half-lives of 83.6 days for soil, 12.73 days for aquatic systems and 10 days for foliar; soil density and depth equal to 1.5g/cm^3 and 15 cm, respectively; and seasonal and permanent water body depths equal to 15 and 80 cm, respectively; with application intervals of 12 days between 1st and 2nd applications and 24 days between 2nd and 3rd applications.

Table 3 Runoff EECs (in µg a.i./L) for ecological risk assessment of famoxadone

Use	Water depth	Water column (µg a.i./L)				Pore water (µg a.i./L)	
		24 hour	96 hour	21 day	60 day	Peak	21 day
3 × 210 g a.i./ha for potatoes and caneberries	15 cm	9.94	5.18	2.56	1.63	N/A	N/A
	80 cm	4.98	3.02	1.40	0.76	0.89	0.80
3 × 140 g a.i./ha for field tomatoes	15 cm	6.63	3.46	1.71	1.09	N/A	N/A
	80 cm	3.32	2.02	0.93	0.51	0.59	0.53

EEC = Estimated environmental concentration. N/A = not applicable

Table 4 Screening level EECs in vegetation and insects after direct over-spray for birds and mammals

Matrix	EEC (mg a.i./kg fw)		Fresh/dry weight ratios	EEC (mg a.i./kg dw)	
	Maximum residues	Mean residues		Maximum residues	Mean residues
Short range grass	65	23	3.3	212.87	75.60
Long grass	30	10	4.4	129.97	42.44
Broadleaf plants	36	12	5.4	196.95	65.11
Insects (Small and large)	25	17	3.8	96.21	66.43
Grain and seeds	4	2	3.8	14.89	7.10
Fruit	4	2	7.6	29.78	14.20

EEC = Estimated environmental concentration.

Table 5 Toxicity effects of famoxadone to beneficial arthropods and pollinators updated for re-evaluation (not reported in REG2003-10)

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA Number
Aphidius rhopalosiphi	Acute 48-h Glass plate	DPX-KP481 (23.9% famoxadone)	ER_{50} > 534.4 (g a.i./ha) [2]	N/A	3555927
		DPX-KX007 (22.5% famoxadone)	ER_{50} > 303.8 (g a.i./ha) [2]		
Typhlodromus pyri	Acute 7-d Glass plate	DPX-KP481 (23.9% famoxadone)	LR_{50} = 521.5(g a.i./ha) [2]		
		DPX-KX007 (22.5% famoxadone)	LR_{50} > 302.4 (g a.i./ha) [2]		
Honey bee *Apis mellifera* L.	48-h Acute Contact	Famoxadone (DPX-JE874-133; purity 97.7%)	48-h LD_{50} > 25 µg a.i./bee (nominal)	Practically non-toxic	1018722
	48-h Acute Oral	Famoxadone (purity: 97.3 % w/w)	48-h LD_{50} > 0.92 µg a.i./bee (nominal)	Practically non-toxic up to Highly toxic	3191449
	48-h Acute Contact		48-h LD_{50} > 97.3 µg a.i./bee (nominal)	Practically non-toxic	
	48-h Acute Contact	Famoxadone 10 EC (purity 9.2% a.i.)	48-h LD_{50} = 11.9 µg a.i./bee (nominal)	Practically non-toxic	3191451
	48-h Acute Oral		48-h LD_{50} > 63.5 µg a.i./bee (actual consumption of test substance)	Practically non-toxic	3555927
	72-h Acute Contact	DPX-KX007 DF (purity: 30% cymoxanil and 22.5% famoxadone)	72-h LD_{50} > 45 µg famoxadone/bee		
	72-h Acute Oral		72-h LD_{50} > 41.9 µg famoxadone/bee (based on actual consumption of test substance)		
	10-d Chronic Oral	Famoxadone (purity of 99.1 %)	10-d NOED ≥ 7.21 µg a.i./bee/ day	N/A	3191454
	22-d Chronic larva (adult emergence)	Famoxadone Technical (98.2% purity)	22-d NOED ≥7.51 µg a.i./larva/day	N/A	3191453

[1] USEPA classification, where applicable
[2] Corrected to % famoxadone in the product. N/A = not applicable
ER_{50}= Effective rate on 50% of the population
LD_{50} = lethal dose causing 50% mortality
LR_{50} = Lethal rate on 50% of the population
NOAEL = No observed adverse effect level.
NOEC = No observed effect concentration.

Table 6 Screening level and refined risk assessment for arthropods and terrestrial plants at the maximum yearly application rate of 210 g a.i./ha × 3

Organism	Exposure	Test Substance	Endpoint reported in REG2003-10	Effect metric[1]	Screening EEC	Screening RQ	LOC	Screening LOC exceeded (Yes or No)	Drift EEC[2]	Drift RQ	Drift LOC exceeded?
Earthworm (*Eisenia fetida*)	Chronic	Famoxadone (97.4%)	NOEC = 62.5 (mg a.i./kg soil)	NOEC/1 = 62500 (µg a.i./kg)	239 (µg a.i./kg/soil)	0.003	1	No	N/A	N/A	N/A
Predatory mite (*Typhlodromus pyri*)	Acute 7-d Glass plate	DPX-KP481 (23.9% famoxadone, 25.3% cymoxanil)	N/A	LR_{50}/1 = 521.5(g a.i./ha)	301.424 (g a.i./ha)	0.58	2	No	N/A	N/A	N/A
Parasitic wasp (*Aphidius rhopalosiphi*)	Acute 48-h Glass plate		N/A	ER_{50}/1 > 534.4 (g a.i./ha)	301.424 (g a.i./ha	< 0.56	2	No	N/A	N/A	N/A
Parasitic wasp (*Aphidius rhopalosiphi)*	Acute 48-h Glass plate	DPX-KX007 (22.5% famoxadone, 30.1% cymoxanil)	N/A	ER_{50}/1 > 303.8 (g a.i./ha)	301.424 (g a.i./ha	< 0.99	2	No	N/A	N/A	N/A
Predatory mite (*Typhlodromus pyri)*	Acute 7-d Glass plate		N/A	LR_{50}/1 > 302.4 (g a.i./ha)	301.424 (g a.i./ha	< 1	2	No	N/A	N/A	N/A
Various plants (terrestrial)	Vegetative vigour	DPX-JE874 10EC (famoxadone 9.2%)	EC_{25} > 2.28 kg/ha	ER_{25}/1 > 210 (g a.i./ha)	537.9 (g a.i./ha	< 2.6	1	Yes	398 g a.i./ha)	<1.9	Yes
Various plants (terrestrial)	Seedling emergence		EC_{25} > 2.28 kg/ha	ER_{25}/1 > 93 (µg a.i./kg)	239 (µg a.i./kg)	< 2.6	1	Yes	176.9 (µg a.i./kg/soil)	<1.9	Yes

N/A= Not available

[1] Uncertainty factors of 1 applied to the acute and reproductive endpoints, respectively.

[2] Refined EEC off-field = screening EEC × 74% maximum spray drift deposition from early airblast application

EC_{25} = effective concentration causing 25% effect

NOEC = No observed effect concentration

LR_{50} = Lethal rate on 50% of the population

ER_{50} = Effective rate on 50% of the population

RQ = Risk quotient

LOC = Level of concern

Table 7 Screening level risk assessment for pollinators at the single maximum application rate 210 g a.i./ha

Organism	Exposure	Test substance	Endpoint reported in REG2003-10	Effect metrics[1]	EEC	RQ	LOC	Level of Concern exceeded ?
Bee adult *Apis mellifera*	48-h contact	Famoxadone (DPX-JE874-133; purity 97.7%)	LC_{50} > 25 mg a.i./bee	LD_{50} /1 >25 µg a.i./bee	0.504 µg a.i./bee	<0.02	0.4	No
		Famoxadone (purity: 97.3 % w/w)	N/A	LD_{50} /1 > 97.3 µg a.i./bee		<0.01		No
		Famoxadone 10 EC (purity 9.2% a.i.)	N/A	48-h LD_{50} / 1= 11.9 µg a.i./bee		0.04		No
	72-h contact	DPX-KX007 DF (purity: 30% cymoxanil and 22.5% famoxadone)	N/A	LD_{50}/1 > 45 µg a.i./bee		<0.01		No
	48-h oral	Famoxadone 10 EC (purity 9.2% a.i.)	N/A	LD_{50} > 63.5 µg a.i./bee	6.009 µg a.i./bee	<0.09	0.4	No
	72-h oral	DPX-KX007 DF (purity: 30% cymoxanil and 22.5% famoxadone)	N/A	LD_{50} /1 > 41.9 µg a.i./bee		<0.1		No
	10-d chronic oral	Famoxadone (purity of 99.1 %)	N/A	NOED/1 ≥ 7.21 µg a.i./bee		≤0.8	1	No
Bee larva *Apis mellifera*	22-d chronic larva (adult emergence)	Famoxadone Technical (98.2% purity)	N/A	NOED/1 ≥ 7.51 µg a.i./larva/day	2.552 µg a.i./bee	≤0.3	1	No

[1] Uncertainty factor of 1 applied to the acute and reproduction endpoints, respectively.
LD_{50} = lethal dose causing 50% mortality
LOC = Level of concern
NOED = No observed effect dose
N/A = Not available

Table 8 Screening level risk assessment for birds and mammals at the maximum yearly application rate (210 g a.i./ha × 3)

Study type	Endpoint reported in REG2003-10	Effects metric[1] (mg a.i./kg bw/d)	Feeding guild (food item)	EDE[2] (mg a.i./kg bw)	RQ	LOC	LOC exceeded?
Small bird (0.02 kg)							
Acute oral	LD_{50} > 2250 mg a.i./kg bw	LD_{50}/10 > 225	Insectivore	24.53	0.11	1	No
Reproduction	NOEC = 46 mg a.i./kg diet	NOED/1 = 4.74	Insectivore	24.53	**5.18**	1	Yes
Medium-sized bird (0.1 kg)							
Acute oral	LD_{50} > 2250 mg a.i./kg bw	LD_{50}/10 > 225	Insectivore	19.15	0.09	1	No
Reproduction	NOEC = 46 mg a.i./kg diet	NOED/1 = 4.74	Insectivore	19.15	**4.04**	1	Yes
Large-sized bird (1 kg)							
Acute oral	LD_{50} > 2250 mg a.i./kg bw	LD_{50}/10 > 225	Herbivore (short grass)	12.37	0.05	1	No
Reproduction	NOEC = 46 mg a.i./kg diet	NOED/1 = 4.74	Herbivore (short grass)	12.37	**2.61**	1	Yes
Small mammal (0.015 kg)							
Acute oral	LD_{50} = 3100 mg a.i./kg diet	LD_{50}/10 = 310	Insectivore	14.11	0.05	1	No
Dietary	NOAEL = 50 mg a.i./kg diet	N/A					
Reproduction	NOED = 11.3 mg a.i./kg bw/d	NOED/1 = 11.3	Insectivore	14.11	**1.25**	1	Yes
Medium-sized mammal (0.035 kg)							
Acute oral	LD_{50}= 3100 mg a.i./kg diet	LD_{50}/10 = 310	Herbivore (short grass)	27.37	0.09	1	No
Dietary	NOAEL = 50 mg a.i./kg diet	N/A					
Reproduction	NOED = 11.3 mg a.i./kg bw/d	NOED/1 = 11.3	Herbivore (short grass)	27.37	**2.42**	1	Yes
Large-sized mammal (1 kg)							
Acute oral	LD_{50}= 3100 mg a.i./kg diet	LD_{50}/10 = 310	Herbivore (short grass)	14.62	0.05	1	No
Dietary	NOAEL = 50 mg a.i./kg diet	N/A					
Reproduction	NOED = 11.3 mg a.i./kg bw/d	NOED/1 = 11.3	Herbivore (short grass)	14.62	**1.29**	1	Yes

[1] Uncertainty factors of 10 and 1 were applied to the acute oral (or acute dietary) and reproduction endpoints, respectively.

[2] EDE = Estimated dietary exposure. EDEs were calculated using the following formula: (FIR/body weight) × EEC, where: FIR: Food Ingestion Rate (Nagy, 1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used:

Passerine Equation (body weight < or =200 g): FIR (g dry weight/day) = 0.398 (body weight in g) $^{0.850}$

All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648 (body weight in g) $^{0.651}$
For small wild mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235 (body weight in g) $^{0.822}$
EEC: Concentration of pesticide on food item based on Hoerger and Kenaga (1972) and Kenaga (1973) and modified according to Fletcher et al. (1994). At the screening level, relevant food items representing the most conservative EEC for each feeding guild are used. The EECs for birds and mammals were calculated based on 210 g a.i./ha × 3 with a 12-day first re-application interval] and 24-day second re-application interval and a default foliar half-life of 10 days.
LD_{50} = lethal dose causing 50% mortality; RQ = Risk quotient; LOC = Level of concern; LC_{50} = lethal concentration causing 50% mortality; NOED = No observed effect dose, N/A = not applicable.
Bold values indicate that the LOC is exceeded.

Table 9 Further characterization of risk to birds and mammals from drift from early season airblast at the maximum yearly application rate of 210 g a.i./ha × 3

Exposure type			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off-Field		On-field		Off-Field	
	Effects metric (mg a.i./kg bw/d)	Feeding guild (food item)	EDE (mg a.i./kg bw)	RQ	EDE[1] (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ
Small bird (0.02 kg)										
Reproduction	4.74	Insectivore	24.53	5.18	18.16	3.83	16.94	3.57	12.54	2.64
	4.74	Granivore (grain and seeds)	3.80	0.80	2.81	0.59	1.81	0.38	1.34	0.28
	4.74	Frugivore (fruit)	7.59	1.60	5.62	1.19	3.62	0.76	2.68	0.57
Medium-sized bird (0.1 kg)										
Reproduction	4.74	Insectivore	19.15	4.04	14.17	2.99	13.22	2.79	9.78	2.06
	4.74	Granivore (grain and seeds)	2.96	0.63	2.19	0.46	1.41	0.30	1.05	0.22
	4.74	Frugivore (fruit)	5.93	1.25	4.39	0.93	2.83	0.60	2.09	0.44
Large-sized bird (1 kg)										
Reproduction	4.74	Insectivore	5.59	1.18	4.14	0.87	3.86	0.81	2.86	0.60
	4.74	Granivore (grain and seeds)	0.87	0.18	0.64	0.14	3.86	0.81	0.31	0.06
	4.74	Frugivore (fruit)	1.73	0.37	1.28	0.27	0.83	0.17	0.61	0.13
	4.74	Herbivore (short grass)	12.37	2.61	9.15	1.93	4.39	0.93	3.25	0.69

Exposure type			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off-Field		On-field		Off-Field	
	Effects metric (mg a.i./kg bw/d)	Feeding guild (food item)	EDE (mg a.i./kg bw)	RQ	EDE[1] (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ
	4.74	Herbivore (long grass)	7.55	1.59	5.59	1.18	2.47	0.52	1.82	0.38
	4.74	Herbivore (Broadleaf plants)	11.44	2.41	8.47	1.79	3.78	0.80	2.80	0.59
Small mammal (0.015 kg)										
Reproduction	11.30	Insectivore	14.11	1.25	10.44	0.92	9.74	0.86	7.21	0.64
	11.30	Granivore (grain and seeds)	2.18	0.19	1.62	0.14	1.04	0.09	0.77	0.07
	11.30	Frugivore (fruit)	4.37	0.39	3.23	0.29	2.08	0.18	1.54	0.14
Medium-sized mammal (0.035 kg)										
Reproduction	11.30	Insectivore	12.37	1.09	9.15	0.81	8.54	0.76	6.32	0.56
	11.30	Granivore (grain and seeds)	1.91	0.17	1.42	0.13	0.91	0.08	0.68	0.06
	11.30	Frugivore (fruit)	3.83	0.34	2.83	0.25	1.83	0.16	1.35	0.12
	11.30	Herbivore (short grass)	27.37	2.42	20.25	1.79	9.72	0.86	7.19	0.64
	11.30	Herbivore (long grass)	16.71	1.48	12.37	1.09	5.46	0.48	4.04	0.36
	11.30	Herbivore (Broadleaf plants)	25.32	2.24	18.74	1.66	8.37	0.74	6.19	0.55
Large-sized mammal (1 kg)										
Reproduction	11.30	Insectivore	6.61	0.58	4.89	0.43	4.56	0.40	3.38	0.30
	11.30	Granivore (grain and seeds)	1.02	0.09	0.76	0.07	0.49	0.04	0.36	0.03

Exposure type			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off-Field		On-field		Off-Field	
	Effects metric (mg a.i./kg bw/d)	Feeding guild (food item)	EDE (mg a.i./kg bw)	RQ	EDE[1] (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ
	11.30	Frugivore (fruit)	2.05	0.18	1.51	0.13	0.98	0.09	0.72	0.06
	11.30	Herbivore (short grass)	14.62	1.29	10.82	0.96	5.19	0.46	3.84	0.34
	11.30	Herbivore (long grass)	8.93	0.79	6.61	0.58	2.92	0.26	2.16	0.19
	11.30	Herbivore (Broadleaf plants)	13.53	1.20	10.01	0.89	4.47	0.40	3.31	0.29

[1] EDEs for birds and small wild mammals were calculated based on the application rate of 210 g a.i./ha with a 12-day first re-application interval and 24-day second re-application interval and a foliar half-life of 10 days.

Table 10 Screening level risk assessment for aquatic organisms at the maximum yearly application rate (210 g a.i./ha × 3)

Organism	Exposure	Endpoint reported in REG2003-10 (µg a.i./L)	Effect metric[1] (µg a.i./L)	Screening EEC (µg a.i./L)	Screening RQ	Screening LOC Exceeded ?
Freshwater organisms						
Water flea (*Daphnia magna)*	Acute 48-h	NOEC = 3.5 EC_{50} = 11.8	EC_{50}/2 = 5.9	39.91	6.8	Yes
	Chronic 21-d	NOEC = 0.085	NOEC/1 = 0.085	39.91	470	Yes
Midge *Chironomus riparius*	Chronic 28-d	NOEC = 10	NOEC/1 = 0.085	39.91	4.0	Yes
Rainbow trout *(Oncorhynchus mykiss*)	Acute 96-h	NOEC = 5.2 LC_{50} = 12	LC_{50}/10 = 1.2	39.91	33	Yes
	Chronic 90-d	NOEC = 1.4	NOEC/1 = 1.4	39.91	29	Yes
Rainbow trout (*Oncorhynchus mykiss*) as surrogate for amphibians	Acute 96-h	N/A	LC_{50}/10 = 1.2	212.85	177	Yes
	Chronic 90-d	N/A	NOEC/1 = 1.4	212.85	152	Yes
Green alga (*Raphidocelis*	Acute 5-d	NOEC = 3.9 LC_{50} = 23	EC_{50}/2 = 11.5	39.91	3.5	Yes

Organism	Exposure	Endpoint reported in REG2003-10 (µg a.i./L)	Effect metric[1] (µg a.i./L)	Screening EEC (µg a.i./L)	Screening RQ	Screening LOC Exceeded ?
subcapitata, reported as *Selenastrum capricornutum*)						
Marine organisms						
Atlantic oyster (*Crassostrea virginica*)	Acute 96-h	NOEC < 1.1 EC_{50} = 1.4	EC_{50}/2 = 0.705	39.91	57	Yes
Mysid shrimp (*Americamysis bahia*, reported as *Mysidopsis bahia)*	Chronic 28-d	NOEC = 0.83	NOEC/1 = 0.83	39.91	48	Yes
Sheepshead minnow (*Cyprinodon variegatus*)	Acute 96-h	NOEC = 27.7 LC_{50} = 49.4	LC_{50}/10 = 4.94	39.91	8.1	Yes
	Chronic 30-d	NOEC = 5.58	NOEC/1 = 5.58	39.91	7.2	Yes
Diatom (*Skeletonema costatum*)	Acute 48-h	NOEC = 9.09 LC_{50} = 41.5	EC_{50}/2 = 20.75	39.91	1.9	Yes

[1] Uncertainty factors of 2, 10 and 1 were applied to the acute and reproduction endpoints, respectively. EECs for were calculated for seasonal and permanent water bodies based on 210 g a.i./ha × 3 with a 12-day first re-application interval and 24-day second re-application interval and aquatic half-life of 12.73 days.

EC_{50} = effective concentration causing 50% effect
LC_{50} = lethal concentration causing 50% mortality
NOEC = No observed effect concentration.
LOC = Level of concern

Table 11 Spray drift risk assessment for aquatic organisms at the maximum cumulative application rate (210 g a.i./ha × 3) on caneberries and potatoes using different application methods and on minimum cumulative application rate (140 g a.i./ha × 3) on field tomatoes.

Organism	Exposure	Effect metrics[1]	Early airblast – Caneberries		Late airblast – Caneberries		Field sprayer – Potatoes		Aerial spray – Potatoes		Field sprayer – Tomatoes	
		(µg a.i./L)	EEC[2]	RQ	EEC[3]	RQ	EEC[4]	RQ	EEC[5]	RQ	EEC[6]	RQ
Freshwater organisms												
Water flea (*Daphnia magna*)	Acute 48-h	EC_{50}/2 5.9	30	5	24	4	2	0.4	9	1.6	2	0.27
	Chronic 21-d	NOEC/1 0.085	30	347	24	277	2	28	9	108	2	19
Rainbow trout (*Oncorhynchus mykiss*)	Acute 96-h	LC_{50}/10 1.2	30	25	24	20	2	2	9	7.6	2	1.3
	Chronic 90-d	NOEC/1 1.4	30	21	24	17	2	1.7	9	6.6	2	1.1
Rainbow trout (*Oncorhynchus*	Acute 96-h	LC_{50}/10 1.2	158	131	126	105	13	11	49	41	9	7.1

Organism	Exposure	Effect metrics[1]	Early airblast – Caneberries		Late airblast – Caneberries		Field sprayer – Potatoes		Aerial spray – Potatoes		Field sprayer – Tomatoes	
		(µg a.i./L)	EEC[2]	RQ	EEC[3]	RQ	EEC[4]	RQ	EEC[5]	RQ	EEC[6]	RQ
mykiss) as surrogate for amphibians	Chronic 90-d	NOEC/1 = 1.4	158	113	126	90	13	9.1	49	35	9	6.1
Green alga (*Raphidocelis subcapitata*, reported as *Selenastrum capricornutum*)	Acute 5-d	EC_{50}/2 11.5	30	2.6	24	2	2	0.21	9	0.8	2	0.14
Marine organisms												
Atlantic oyster (*Crassostrea virginica*)	Acute 96-h	EC_{50}/2 0.705	19	28	15	22	2	2.2	6	8.6	1	1.5
Mysid shrimp (*Americamysis bahia*, reported as *Mysidopsis bahia*)	Chronic 28-d	NOEC/1 = 0.83	19	23	15	19	2	1.9	6	7.3	1	1.3
Sheepshead minnow (*Cyprinodon variegatus*)	Acute 96-h	LC_{50}/10 = 4.94	19	3.9	15	3.1	2	0.32	6	1.2	1	0.21
	Chronic 30-d	NOEC/1 = 5.58	19	3.5	15	2.8	2	0.28	6	1.1	1	0.19

[1] Uncertainty factors of 2, 10 and 1 were applied to the acute and reproduction endpoints, respectively.
LOC = Level of concern
[2] Refined EEC off-field = screening EEC × 74% maximum spray drift deposition from early airblast application
[3] Refined EEC off-field = screening EEC × 59% maximum spray drift deposition for late airblast application on caneberries
[4] Refined EEC off-field = screening EEC × 6% maximum spray drift deposition for field application on potatoes
[5] Refined EEC off-field = screening EEC × 23% maximum spray drift deposition for aerial application on potatoes
[6] Refined EEC off-field = screening EEC × 6% maximum spray drift deposition for field application on field tomatoes

Table 12 Runoff risk assessment of famoxadone to aquatic organisms

Organism	Exposure	Effect metrics (µg a.i./L)	Max, 3 × 210 g a.i./ha		Max, 3 × 140 g a.i./ha	
			EEC	RQ	EEC	RQ
Freshwater organisms						
Water flea (*Daphnia magna*)	Acute 48-h	EC_{50}/2 = 5.9	4.98	0.84	3.32	0.56
Water flea (*Daphnia magna*)	Chronic 21-d	NOEC/1 = 0.085	1.4	16.5	0.93	10.9
Rainbow trout (*Oncorhynchus mykiss*)	Acute 96-h	LC_{50}/10 = 1.2	3.02	2.5	2.02	1.7
Rainbow trout (*Oncorhynchus mykiss*)	Chronic 90-d	NOEC/1 = 1.4	0.76	0.54	0.51	0.36
Rainbow trout (*Oncorhynchus mykiss*) as surrogate for amphibians	Acute 96-h	LC_{50}/10 = 1.2	5.18	4.3	3.46	2.9

Organism	Exposure	Effect metrics (µg a.i./L)	Max, 3 × 210 g a.i./ha		Max, 3 × 140 g a.i./ha	
			EEC	RQ	EEC	RQ
Rainbow trout (*Oncorhynchus mykiss*) as surrogate for amphibians	Chronic 90-d	NOEC/1 = 1.4	1.63	1.2	1.09	0.78
Marine organisms						
Atlantic oyster (*Crassostrea virginica*)	Acute 96-h	EC_{50}/2 = 0.705	3.02	4.3	2.02	2.9
Mysid shrimp (*Americamysis bahia*, reported as *Mysidopsis bahia*)	Chronic 28-d	NOEC/1 = 0.83	1.4	1.7	0.93	1.1
Sheepshead minnow (*Cyprinodon variegatus*)	Acute 96-h	LC_{50}/10 = 4.94	3.02	0.61	2.02	0.41
Sheepshead minnow (*Cyprinodon variegatus*)	Chronic 30-d	NOEC/1 = 5.58	1.4	0.25	0.93	0.17
Diatom (*Skeletonema costatum*)	Acute 48-h	EC_{50}/2 = 20.75	4.98	0.24	3.32	0.16

*EECs representing the 90th percentile of 48-hour, 96-hour concentration (acute assessment), 21-day and 60-day concentrations (chronic assessment) as predicted by PWC.
EEC = Estimated environmental concentration.
EC_{50} = effective concentration causing 50% effect
LC_{50} = lethal concentration causing 50% mortality
NOEC = No observed effect concentration.
LOC = Level of concern
PWC = Pesticide in water calculator

Table 13 Summary of available water monitoring data in Canada and USA for assessment of famoxadone in surface water sources relevant to eco-scenario from 2009 to 2025

Source	Number of samples	Number of sample detects	% Detection	LOD (µg/L)	Max. concentration (µg/L)	PMRA Number
Water suitable for the aquatic risk assessment						
Ambient surface water						
Alberta						
2016 Prov Data	308	0	0%	0.1401	ND	3580937
2022–2024	132	0	0%	0.085–1.2	ND	3583716
2024–2025	99	0	0%	0.06–0.085	ND	3583717
British Columbia						
2022–2024	133	0	0%	1.2	ND	3583716
2024–2025	75	0	0%	0.06–0.085	ND	3583717
Manitoba						
2022–2024	324	0	0%	0.085–1.2	ND	3583716
2024–2025	119	0	0%	0.06	ND	3583717
Nova Scotia	466		0%	1.2	ND	3583716

Source	Number of samples	Number of sample detects	% Detection	LOD (µg/L)	Max. concentration (µg/L)	PMRA Number
2022–2024 2024–2025	14	0 0	0%	0.06–0.085	ND	3583717
Ontario 2022 Prov Data 2023 Prov Data 2022–2024 2024–2025	 10 128 1501 284	 0 0 0 0	 0% 0% 0% 0%	 0.08 0.08 0.085–1.2 0.06	 ND ND ND ND	 3577875 3577875 3583716 3583717
Prince Edward Island 2018 Prov Data 2022–2024 2024–2025	 9 680 13	 0 0 0	 0% 0% 0%	 0.154 1.2 0.06	 ND ND ND	 3580938 3583716 3583717
Quebec 2022–2024 2024–2025	 567 0	 0 0	 0% 0%	 0.085–1.2 N/A	 ND N/A	 3583716 3583717
New Brunswick 2022–2024 2024–2025	 116 3	 0	 0% 0%	 0.085 0.06	 ND ND	 3583716 3583717
Newfoundland and Labrador 2022–2024 2024–2025	 102 10	 0 0	 0% 0%	 1.2 0.06	 ND ND	 3583716 3583717
Sasketchewan 2022–2024 2024–2025	 38 21	 0 0	 0% 0%	 0.085–1.2 0.06	 ND ND	 3583716 3583717
Northwest Territories 2022–2024 2024–2025	 0 2	 0 0	 0% 0%	 N/A 0.085	 ND ND	 3583716 3583717
Canada – Total						
Canada surface water (2016, 2018, 2022 - 2025)	**5154**	**0**	**0%**	**0.06–1.54**	ND	
USA						
United States Geological Survey 2009–2023	 7499	 0	 0%	 0.0017	 ND	 3580939
California Department of Pesticide Regulation 2009–2023	 1343	 8	 0.60	 0.001–0.0025	 0.0216	 3582232
USA - Total						
USA surface water (2009–2023)	8842	8	0.09	0.001–0.0025	0.0216	
Surface water total for aquatic risk assessment	**13996**	**8**	**0.06**	**0.001–1.54**	**0.0216**	

ND – not detected

Table 14 Toxic Substances Management Policy considerations - comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active ingredient endpoints	Transformation product 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, DT_{50} values of 1.9 to 11.5 days in aerobic soils.	N/A
	Water	Half-life ≥ 182 days	No, DT_{50} values of 0.72 to 0.84 days in aerobic Whole System	N/A
	Sediment	Half-life ≥ 365 days		
	Air	Half-life ≥ 2 days, or evidence of atmospheric transport to remote regions such as the Arctic	No, the AOPWIN (v1.92) predicted half-life in the gas phase in the atmosphere is 0.09 days (2.263 hours) based on the hydroxyl (OH) radical reaction (1.5×10^6 molecules OH/cm^3) during 12 hours of daylight.	N/A
Bioaccumulation[4]	Log $K_{ow} \geq 5$		No, Log $K_{ow} = 4.7$	N/A
	BCF ≥ 5000		No, 3425	N/A
	BAF ≥ 5000		N/A	N/A
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet all of the TSMP Track 1 criteria.	N/A

[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 (that is, 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] The pesticide and/or the transformation product(s) is considered persistent when the criterion is met in any one medium.

[4] The AOPWIN (v1.92) predicted half-life in the gas phase in the atmosphere is 0.09 days based on the hydroxyl (OH) radical reaction (1.5×10^6 molecules OH/cm^3) during 12 hours of daylight. (AEROWIN, v1.00).

[5] Bioaccumulation describes the process by which a substance accumulates in a living organism, either from the surrounding medium or through food containing the substance. A substance's potential to bioaccumulate can be expressed by the bioaccumulation factor (BAF), the bioconcentration factor (BCF), or the octanol-water partition coefficient (Log K_{ow}). The BAF and the BCF measure the concentration of a substance in a living organism relative to its concentration in the surrounding medium. The BAF accounts for substance intake from both food and the surrounding medium, while the BCF accounts for intake from the surrounding medium only. The Log K_{ow} estimates a substance's tendency to partition from water to organic media, such as lipids present in living organisms. In the absence of BAF or BCF data, the log K_{ow} may be used.

N/A = Not available.

Appendix VIII Proposed label updates for products containing famoxadone

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

1.0 Label amendments for famoxadone technical product (Reg. No. 27436)

A. **Replace** the ENVIRONMENTAL HAZARDS section and contents with:

"ENVIRONMENTAL PRECAUTIONS
Toxic to aquatic organisms."

B. Under DIRECTIONS FOR USE:

1. **Add:**

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

2. **Replace** the DISPOSAL statement**:**

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

With:

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

2.0 Label amendments for famoxadone commercial end-use product (Reg. No. 27435):

A. Under PRECAUTIONS:

1. **Add:**

"**For airblast application**
Wear chemical resistant coveralls over long-sleeved shirt and long pants, goggles or face shield and chemical resistant gloves during mixing, loading, application, cleanup and repair. In addition, wear chemical-resistant headgear during open cab airblast application. Chemical-resistant headgear includes Sou'Wester hat, chemical-resistant rain hat or large brimmed waterproof hat and hood with sufficient neck protection. Gloves are not required during application within a closed cab."

2. **Replace:**

"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."

With:

"Apply only when the potential for drift beyond the area to be treated is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings."

B. Under ENVIRONMENTAL PRECAUTIONS:

1. **Replace:**

"• TOXIC to aquatic organisms. Observe spray buffer zones specified under DIRECTIONS FOR USE
- To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.
- Avoid application when heavy rain is forecast.
- Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body."

With:

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

Toxic to birds and small wild mammals.

To reduce runoff from treated areas into aquatic habitats, avoid application to areas with a moderate to steep slope, compacted soil, or clay. Avoid application when heavy rain is forecast. Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative filter strip between the treated area and the edge of the water body. Additional guidance can be found on the Runoff Mitigation portion of the Canada.ca website."

C. Under DIRECTIONS FOR USE update with:

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

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

Field sprayer application: DO NOT apply when wind speed is less than 1 km/h. Avoid application of this product when winds are gusty. DO NOT apply with sprays finer than the American Society of Agricultural and Biological Engineers (ASABE) S572 (572.1 to 572.3) Medium classification. Boom height must be 60 cm or less above the crop or ground.

Airblast application: DO NOT apply when wind speed is less than 1 km/h. 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.

Conventionally piloted aircraft application: DO NOT apply when wind speed is less than 1 km/h. Avoid application of this product when winds are gusty. DO NOT apply when wind speed is greater than 16 km/h at flying height at the site of application. DO NOT apply with sprays finer than the American Society of Agricultural and Biological Engineers (ASABE) S572 (572.1 to 572.3) Medium classification. Reduce drift caused by turbulent wingtip vortices. Nozzle distribution along the spray boom length MUST NOT exceed 65% of the wing- or rotorspan.

Apply only by aircraft equipment which has been functionally and operationally calibrated for the atmospheric conditions of the area and the application rates and conditions of this label.

Label rates, conditions and precautions are product specific. Read and understand the entire label before opening this product. Apply only at the rate specified for aerial application on this label. Where no rate for aerial application appears for the specific use, this product cannot be applied by any type of aerial equipment.

Ensure uniform application. To avoid streaked, uneven or overlapped application, use appropriate marking devices or a Global Positioning System (GPS).

Use Precautions
Apply only when meteorological conditions at the treatment site allow for complete and even crop coverage. Applicators must meet all requirements for aerial application as outlined in the relevant manuals, as specified by the provincial or territorial pesticide regulatory authority where the pesticide application is to occur.

Product Specific Precautions
Read and understand the entire label before opening this product. If you have questions, call the registrant at *[(XXX)YYY-ZZZZ]* or obtain technical advice from the distributor or your provincial or territorial agricultural representative. Application of this specific product must meet and/or conform to the following:
Volume: Apply the specified rate in a minimum spray volume of 50 litres per hectare for conventionally piloted aircraft.

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

Method of Application	Crop/Site		Spray Buffer Zones (metres) Required for the Protection of:				
			Freshwater Habitat of Depths:		Estuarine/Marine Habitat of Depths:		Terrestrial Habitat:
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m	
Field sprayer	Potatoes, Caneberries		15	5	2	1	1
	Field tomatoes		10	5	1	1	1
Airblast	Caneberries	Early growth stage	50	40	25	15	2
		Late growth stage	40	30	15	5	1
Aerial	Potatoes	Fixed wing	225	95	10	1	1
		Rotary wing	175	55	10	1	1

When tank mixes are permitted, consult the labels of the tank mix partners and observe the largest (most restrictive) spray buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASABE) category indicated on the labels for those tank mix partners."

D. Under DISPOSAL

1. **Replace:**

"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."

With:

"1.Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.
2. Follow provincial or territorial instruction for any required additional cleaning of the container prior to its disposal.
3. Make the empty, rinsed container unsuitable for further use.
4. Dispose of the container in accordance with provincial or territorial requirements.
5. For information on disposal of unused, unwanted product, contact the registrant or the provincial or territorial regulatory agency. Contact the registrant and the provincial or territorial regulatory agency in case of a spill, and for cleanup of spills."

E. Under STORAGE:

1. **Add:** "Store this product away from food or feed."

References

A. Information considered for re-evaluation

Published information

PMRA Document Number	Reference
651144	Canada, 2003. Regulatory Note, REG2003-10, Famoxadone/Tanos 50DF

B. Information considered in the chemistry assessment

Studies/information submitted by registrant

PMRA Document Number	Reference
3054096	2012. Description and validation of the analytical methods for determination of impurities in technical grade famoxadone (DPX-JE874), DACO: 2.13.3 CBI
3054097	2012, Batch analysis of famoxadone (DPXDPX-JE874) technical, DACO: 2.13.3 CBI
3054098	2012. Batch chromatograms from the analysis of famoxadone (DPX-JE874)
3054099	2012. Batch analysis of famoxadone (DPX-JE874) technical, DACO: 2.13.3 CBI
3054100	Batch chromatograms from the analysis of famoxadone (DPX-JE874)
3054101	2011. Determination of famoxadone (DPX-JE874) in technical grade famoxadone, DACO: 2.13.3 CBI
2468081	2014. DuPont - 40041: Technical grade famoxadone (DPX-JE874) manufacturing description and formation of impurities- confidential, DACO: 2.11.1,2.11.2,2.11.3,2.11.4 CBI
2468088	2014. Batch analysis of famoxadone (DPX-JE874) technical - confidential, DACO: 2.13 CBI
2118331	2011. Batch analysis of famoxadone (DPX-JE874) technical, DACO: 2.13.3 CBI
2118333	2011. Batch analysis of famoxadone (DPX-JE874) technical, DACO: 2.13.3 CBI
2491003	2011. Determination of [CBI removed] in famoxadone technical [CBI removed], DACO: 2.13.1 CBI
2490999	2011. Determination of [CBI Removed] in famoxadone technical [CBI removed], DACO: 2.13.1 CBI
2491000	2011. Determination of [CBI Removed] in famoxadone technical [CBI removed], DACO: 2.13.1 CBI
2118325	2011. Technical grade famoxadone (DPX-JE874) manufacturing description and formation of impurities, DACO: 2.11.1,2.11.2,2.11.3,2.11.4 CBI

C. Information considered in the toxicology assessment

Studies/information submitted by registrant

PMRA Document Number	Reference
1018824, 1018825, 1018826, 1018835, 1018844	1995. Reproductive and fertility effects with DPX-JE874-221; multigeneration reproduction study in rats. DACO 4.5.1
3191377	1998. DPX-JE874-133: Pilot developmental toxicity study in rats. DACO 4.5.2
3191378	1998. DPX-JE874-221: Pilot developmental toxicity study in rats. DACO 4.5.2
1018845, 1018846	1994. Developmental toxicity of DPX-JE874-221 in rats. DACO 4.5.2
3191379	1998. DPX-JE874-221: Pilot developmental toxicity study in rabbits. DACO 4.5.2
1018847, 1018848	1994. Developmental toxicity of DPX-JE874-221 in rabbits. DACO 4.5.3

Additional information considered

Published information

PMRA Document Number	Reference
3713520	Pearson, B. L., Simon, J. M., McCoy, E. S., Salazar, G., Fragola, G., & Zylka, M. J. (2016). Identification of chemicals that mimic transcriptional changes associated with autism, brain aging and neurodegeneration. *Nature communications*, *7*(1), 11173.

D. Information considered in occupational assessment

Studies/information submitted by registrant

PMRA Document Number	Reference
922467	Hinderliter, P.M., 2004. Cymoxanil/Famoxadone (DPX-KP481) 50WG (1:1): In Vivo Dermal Kinetics of Cymoxanil in the Rat, 2004.
1028035	Jones and Howell, 1999. Dissipation of Dislodgeable Foliar Famoxadone and Cymoxanil Residues from Tomatoes treated with DPX KP481, 1999.

List of Studies/Information Provided by Task Force

PMRA Document Number	Reference
2115788	Agricultural Reentry Task Force (ARTF). 2008. Data Submitted by the ARTF to Support Revision of Agricultural Transfer Coefficients. Submission Number 2006-0257.
1913109	AHETF, 2009. Agricultural Handler Exposure Scenario Monograph: Open Cab Groundboom

PMRA Document Number	Reference
	Application of Liquid Sprays. Report Number AHE1004. December 23, 2009.
2572744	AHETF, 2015. Agricultural Handler Exposure Scenario Monograph: Open Pour Mixing and Loading Dry Flowable Formulations. Report Number AHE1001-1. March 31, 2015.

E. Information considered in Environmental Assessment

Studies/information submitted by registrant

PMRA Document Number	Reference
1018722	Beavers, J.B, Palmer, SJ, 1994.DPX-JE874-133: an acute contact toxicity study with the honey bee. Final report. DACO 9.2.4.1
3191449	Vinall, S. 1998. AMR 5165-98 Acute oral and contact toxicity to the honeybee, *Apis mellifera*. DACO 9.2.4.1, 9.2.4.2
3191451	Hoxter, K; Palmer, S; Krueger, H. 1997. AMR 4609-97 An acute oral toxicity study with the honey bee. DACO 9.2.4.2
3191454	Ming Hua Huang, 2015. DuPont-40438 technical Assessment of chronic effects to the honeybee, Apis mellifera. DACO 9.2.4.4
3560876	Haupt, S. 2017. DuPont-46745 technical Honey bee (*Apis mellifera* L.) larval toxicity test (repeated feeding exposure). DACO 9.2.4.4

Additional information considered

Published information

PMRA Document Number	Reference
3555927	European Commission, 2015. Famoxadone Annex B (volume 3) B.9 Ecotoxicology. DACO 12.5.9
3583716	Health Canada Year 1 Pilot Program for National Water Monitoring Program for Pesticides (NWMPP) Data - Open Government Portal (canada.ca) (2022-2024)
3580938	Prince Edward Island Department of Land and Environment pesticide analysis for famoxadone in stream water (2018)
3582232	California Department of Pesticide Regulation data on Famoxadone in surface water. Downloaded in March 2024. https://www.cdpr.ca.gov/docs/emon/surfwtr/surfdata.htm
3580939	US Environmental Protection Agency's Storage and Retrieval (STORET) data warehouse for famoxadone. Downloaded March 2024. Water Quality Data Home
3801246	European Commission, 2021. Targeted risk assessment for famoxadone. DACO 12.5.9

Unpublished information

PMRA Document Number	Reference
3577875	Monitoring Data for Pesticides in Ontario Stream Water for 2023. Ontario Ministry of the Environment, Conservation and Parks (MECP) and Ontario Ministry of Agriculture, Food and Rural Affairs (OMAFRA).
3583717	Health Canada Year 2 Pilot Program for National Water Monitoring Program for Pesticides (NWMPP) Data - Open Government Portal (canada.ca) (2022-2023)
3580937	Alberta Agriculture and Forestry unpublished water monitoring data for famoxadone in irrigation surface water samples (2006-2007; 2011-2016).
1018722	Beavers, J.B, Palmer, SJ, 1994.DPX-JE874-133: an acute contact toxicity study with the honey bee. Final report. DACO 9.2.4.1
3191449	Vinall, S. 1998. AMR 5165-98 Acute oral and contact toxicity to the honeybee, *Apis mellifera*. DACO 9.2.4.1, 9.2.4.2
3191451	Hoxter, K; Palmer, S; Krueger, H. 1997. AMR 4609-97 An acute oral toxicity study with the honey bee. DACO 9.2.4.2
3191454	Ming Hua Huang, 2015. DuPont-40438 Technical Assessment of chronic effects to the honeybee, Apis mellifera. DACO 9.2.4.4
3560876	Haupt, S. 2017. DuPont- 46745 technical Honey bee (*Apis mellifera* L.) larval toxicity test (repeated feeding exposure). DACO 9.2.4.4