Proposed Registration Decision PRD2021-09

Flutianil and GATTEN

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Overview

Proposed registration decision for Flutianil

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of Flutianil Technical, and GATTEN, containing the technical grade active ingredient flutianil, for control of powdery mildew on cherries (Crop Subgroup 12-09A), cucurbit vegetables (Crop Group 9) and grape.

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

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of flutianil and GATTEN.

What does Health Canada consider when making a registration decision?

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

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the Health Canada regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides section of Canada.ca.

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

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

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

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

What is Flutianil?

Flutianil is a narrow spectrum, conventional fungicide that targets certain species of powdery mildew. The exact mode of action of flutianil is not known. It is applied as a foliar spray using broadcast or airblast ground equipment against certain species of powdery mildew on cherries (Crop Subgroup 12-09A), cucurbit vegetables (Crop Group 9) and grape crops.

Health considerations

Can approved uses of Flutianil affect human health?

GATTEN, containing flutianil, is unlikely to affect your health when used according to label directions.

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

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

In laboratory animals, the acute toxicity of the technical grade active ingredient flutianil was low via the oral, dermal and inhalation routes of exposure. Flutianil was non-irritating to the eyes and skin. It did not cause an allergic skin reaction.

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

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

The acute toxicity of the end-use product GATTEN, containing flutianil, was low via the oral, dermal and inhalation routes of exposure. GATTEN was moderately irritating to the eyes and mildly irritating to the skin, and caused an allergic skin reaction. Consequently, the signal word "WARNING" and the hazard statements "EYE AND SKIN IRRITANT" and "POTENTIAL SKIN SENSITIZER" are required on the label.

Registrant-supplied short- and long-term (lifetime) animal toxicity tests, as well as information from the published scientific literature, were assessed for the potential of flutianil to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment were effects on the liver, delayed bone development and the respiratory tract. There was an indication that the young were more sensitive than the adult animals. The risk assessment protects against the effects noted above and other potential effects by ensuring that the level of exposure to humans is well below the lowest dose at which these effects occurred in animal tests.

Residues in food and drinking water

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

Animal studies revealed no acute health effects. Consequently, a single dose of flutianil is not likely to cause acute health effects in the general population (including infants and children).

Aggregate chronic dietary (food plus drinking water) intake estimates for the general population and all population subgroups are expected to be less than 3% of the acceptable daily intake, and are not of health concern. Infants are the subpopulation expected to be subject to the highest exposure relative to body weight.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Given that dietary risks from the consumption of foods are shown to be acceptable when flutianil is used according to the supported label directions, MRLs are being proposed as a result of this assessment (refer to PMRL2021-31*, Flutianil*).

MRLs for flutianil determined from the acceptable residue trials conducted throughout the United States, including growing regions representative of Canada, on summer squash, cucumbers, cantaloupe, cherries, grapes, apples, and strawberries can be found in the Science Evaluation of this consultation document.

Occupational risks from handling GATTEN

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

Workers mixing, loading or applying GATTEN, and workers entering recently treated fields, orchards and vineyards can come in direct contact with flutianil residues on the skin. Therefore, the label specifies that anyone mixing, loading and applying GATTEN must wear a long-sleeved

shirt, long pants, chemical-resistant gloves, socks and shoes, and protective eyewear. The label also requires that workers do not enter or be allowed entry into treated fields, orchards or vineyards during the restricted-entry interval (REI) of 12 hours. Taking into consideration the label statements, the number of applications and the duration of exposure for handlers and postapplication workers, the risks to these individuals are not of health concern.

Health risks in residential and other non-occupational environments

Risks in residential and other non-occupational environments are not of health concern when GATTEN is used according to the proposed label directions and REIs are observed.

Residential risks from exposure to GATTEN during pick-your-own fruit activities in treated orchards and following commercial application to fruit trees in residential areas are not of health concern.

Health risks to bystanders

Bystander risks are not of health concern when GATTEN is used according to the proposed label directions and spray drift restrictions are observed.

A standard label statement to protect against drift during application is on the label. Therefore, health risks to bystanders are not of concern.

Environmental considerations

What happens when Flutianil is introduced into the environment?

When used according to label directions, the risks associated with the use of flutianil are acceptable from the viewpoint of environmental protection.

Flutianil can enter the environment when it is applied as a foliar spray to cucurbit vegetables, cherries, and grape to control powdery mildew. Flutianil is persistent under most terrestrial and aquatic conditions, except in shallow water in the presence of sunlight, where it can break down rapidly. Flutianil is not expected to be found in the atmosphere. It binds to soil, thus, it is expected to have limited mobility to groundwater. Flutianil breaks down in the field, forming three major transformation products that are expected to have very high, slight to low, and low mobility, respectively.

Flutianil presents a negligible risk to earthworms, bees, beneficial arthropods, birds, and mammals. Flutianil may, however, present a risk to non-target terrestrial plants adjacent to treated fields, which could also affect wildlife habitat. In waterbodies, flutianil may pose a risk to aquatic organisms, such as aquatic invertebrates, fish, plants, and amphibians. Precautionary measures, such as spray buffer zones and label statements, are thus required to minimize the exposure to non-target terrestrial plants and aquatic habitats. When flutianil is used in accordance with label directions, and when the required risk reduction measures are applied, the risks to the environment are considered to be acceptable.

Value considerations

What is the value of GATTEN?

The availability of GATTEN will provide Canadian users with an additional product to control powdery mildew disease on cherries (Crop Subgroup 12-09A), cucurbit vegetables (Crop Group 9) and grape.

Crops on the GATTEN label have a high susceptibility to powdery mildew and require multiple fungicide sprays over the growing season for disease management. GATTEN, applied as a spray to leaves and fruit, effectively controls powdery mildew on these economically important crops.

Measures to minimize risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the labels of Flutianil Technical and GATTEN to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Human health

To reduce the potential of workers coming into direct contact with flutianil on the skin or through inhalation of sprays, workers must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and protective eyewear during mixing, loading and applying GATTEN, as well as during cleaning and repair activities. The label also requires that workers do not enter or be allowed entry into treated fields, orchards and vineyards during the REI of 12 hours. Furthermore, standard label statements to protect against drift during application or to prevent the use of handheld airblast, misters and foggers are present on the label.

Rotational Crops

Cucurbit vegetables may be planted immediately after the last application.

For all other crops except for registered crops, **DO NOT** plant within 12 months after the last application.

Environment

Precautionary statements are required to inform users of the toxicity of flutianil to toxicity to aquatic organisms and non-target terrestrial plants.

Spray buffer zones are required to reduce the risk of spray drift to terrestrial and freshwater habitats are required.

Next steps

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

Other information

When the Health Canada makes its registration decision, it will publish a Registration Decision on flutianil and GATTEN (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room.

Science evaluation

Flutianil and GATTEN

1.0 The active ingredient, its properties and uses

1.1 Identity of the active ingredient

Active substance

Function Fungicide

Chemical name

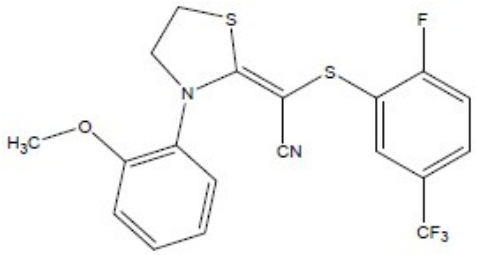
1. **International Union of Pure and Applied Chemistry (IUPAC)** (*Z*)-[3-(2-methoxyphenyl)-1,3-thiazolidin-2-ylidene](α,α,α,4-tetrafluoro-*m*-tolylthio)acetonitrile
2. **Chemical Abstracts Service (CAS)** (2*Z*)-2-[[2-fluoro-5-(trifluoromethyl)phenyl]thio]-2-[3-(2-methoxyphenyl)-2-thiazolidinylidene]acetonitrile

CAS number 958647-10-4

Molecular formula $C_{19}H_{14}F_4N_2OS_2$

Molecular weight 426.45

Structural formula



Purity of the active ingredient 99.4%

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

Technical product—Flutianil Technical

Property	Result
Colour and physical state	White to light brown crystalline powder
Odour	No characteristic odour
Melting range	178–179ºC
Boiling point or range	Decomposes prior to boiling

Property	Result
Density	1.45 g/cm^3 at 20°C
Vapour pressure at 20°C	1.530×10^{-7} Pa
Ultraviolet (UV)-visible spectrum	Methanol / λ_{max} (nm) / ε (L / (mol × cm)) Neutral / 282.0 / 1.75×10^4 244.5 / 1.69×10^4 Acidic / 283.0 / 1.71×10^4 245.0 / 1.63×10^4 Alkali / 282.0 / 1.76×10^4 245.0 / 1.67×10^4
Solubility in water at 20°C	0.0079 mg/L
Solubility in organic solvents at 20°C	Solvent / Solubility (g/L) n-hexane / <0.01 toluene / 11.2 dichloromethane / 169 acetone / 66.4 methanol / 5.62 ethyl acetate / 22.8
n-Octanol-water partition coefficient (K_{ow})	pH / log K_{ow} 4, 7, 10 / 3.1
Dissociation constant (pK_a)	No dissociable moiety at environmental pH.
Stability (temperature, metal)	The technical material was found to be stable after storage for two weeks at 54 °C.

End-use product—GATTEN

Property	Result
Colour	Yellow
Odour	Weak sweet fruity odour
Physical state	Transparent homogenous liquid
Formulation type	EC (emulsifiable concentrate)
Label concentration	50.7 g/L
Container material and description	Plastic bottle or jug, 500–2000 mL
Density	1.08 g/cm^3 at 20°C
pH of 1% dispersion in water	4.87
Oxidizing or reducing action	Oxidizing property is not expected.
Storage stability	The product is stable for 14 days when stored in plastic bottles at 54°C.

Property	Result
Corrosion characteristics	The product was demonstrated to be free of interactions with its packaging.
Explodability	The product does not contain any explosive components.

1.3 Directions for use

All uses of GATTEN require an application rate of 400-690 mL/ha (20–35 g a.i./ha) and an application interval of 7–14 days, where higher rates and shorter intervals within the rate ranges are used under conditions favouring high disease pressure. For control of powdery mildew on grape and cherries (Crop Subgroup 12-09A), GATTEN is applied as a foliar spray during fruiting a maximum of four times per year using airblast ground equipment. For control of powdery mildew on cucurbit vegetables (Crop Group 9), GATTEN is applied as a foliar spray from the seedling stage to fruiting a maximum of five times per year using broadcast ground equipment.

1.4 Mode of action

Flutianil is classified as a Group U13 fungicide by the Fungicide Resistance Action Committee (FRAC); however, the mode of action of flutianil is not definitively known. It has been observed to disrupt the formation of haustoria, which are structures that initiate powdery mildew infection. Recently, cucurbit powdery mildew strains were observed to possess cross-resistance towards flutianil and pyriofenone.

2.0 Methods of analysis

2.1 Methods for analysis of the active ingredient

The methods provided for the analysis of the active ingredient and impurities in the technical product have been validated and assessed to be acceptable.

2.2 Method for formulation analysis

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

2.3 Methods for residue analysis

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

High performance liquid chromatography methods with tandem mass spectrometric detection (LC-MS/MS; Method 181C-105 and QuEChERS; Method DFG S 19), a gas chromatography method with mass selective detection (GC/MSD; Method RM-44C-2), and a gas chromatography method with electron capture detection (GC-ECD; Method CLE 2554/019-01V) were developed and proposed for data generation and/or enforcement purposes in plant matrices. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in plant matrices. The proposed enforcement methods were successfully validated in plant matrices by an independent laboratory. Adequate extraction efficiencies were demonstrated for enforcement Method CLE 2554/019-01V using radiolabelled samples of cucumber and apple. Methods for residue analysis are summarized in Appendix I, Table 1b.

3.0 Impact on human and animal health

3.1 Hazard assessment

3.1.1 Toxicology summary

Flutianil is a thiazolidine fungicide with fungitoxic and fungistatic contact action. The details of the pesticidal mode of action have not been fully elucidated.

A detailed review of the toxicology database for flutianil was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. A number of studies assessing the toxicity of select metabolites and transformation products of flutianil were also submitted. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the toxicology data is acceptable and the database is considered adequate to characterize the potential health hazards that may result from exposure to flutianil.

Metabolism and toxicokinetics following single- and repeat-dose oral administration in the rat were investigated using flutianil radiolabelled at the methoxyphenyl ring or fluorotolyl ring. Absorption, as determined by radioactive residues in bile, urine, and tissues, was low and decreased with increasing dose level, ranging from 18% to approximately 2% of the administrated dose (AD). Maximum plasma concentrations were achieved between 3 and 13 hours post-dosing. Limited amount of flutianil absorbed was widely distributed throughout the tissues following oral administration. With the exception of the gastrointestinal tract and carcass, the liver, followed by the kidney, contained the greatest amount of radioactivity. Elimination of radioactivity was rapid and extensive, with greater than 80% of the AD recovered within 48 hours. The major route of excretion was via the feces, representing up to 98% of the AD. Recovered radiolabel represented up to 11% of the AD in bile and up to 19% of the AD in urine. Radioactivity in tissues 120 hours after a single-dose administration was low and there was no evidence of retention within tissues. The metabolic and toxicokinetic parameters measured were generally comparable between sexes. When compared with single-dose administration, repeated-dose administration resulted in slightly lower urinary excretion, but no major differences in the absorption, distribution, metabolism or excretion of flutianil.

Unchanged flutianil was the major component identified in the feces, reflecting poor absorption and low degree of metabolism. The major urinary metabolite, Met 6, accounted for up to 5.5% of the AD, and it was identified as a hydroxylated methylsulphoxy trifluoromethyl ring structure. Numerous uncharacterized metabolites were present in urine, feces and bile. None of the metabolites accounted for more than 10% of the AD.

In acute toxicity testing, the technical grade active ingredient flutianil was of low acute toxicity via the oral, dermal and inhalation routes in rats. It was non-irritating to the eyes and skin of rabbits. Flutianil was negative for skin sensitization in guinea pigs when tested using the maximization method.

The end-use product, GATTEN, was determined to be of low acute toxicity in rats via the oral, dermal and inhalation routes of exposure. It was moderately irritating to the eyes and mildly irritating to the skin of rabbits. It was positive for skin sensitization when tested in guinea pigs using the Buehler method.

Repeat-dose dietary toxicity studies with flutianil were available in mice and rats, and flutianil was administered via capsule in repeat-dose oral toxicity studies in dogs. The most sensitive species for toxicity was the rat, in which the main target of toxicity was the liver, with increased incidences of hepatic foci of cellular alteration observed in males and bile duct hyperplasia observed in females at the highest dose tested (HDT) after long-term exposure. Following both short-term and long-term dosing, increases in the incidence of hyaline droplet deposition in the kidney were observed in male rats. Immunohistochemical staining revealed that these droplets were alpha 2μ-globulin, and in the absence of any other evidence of nephropathy in the toxicology database, this finding was considered non-adverse. Given that this finding has been demonstrated to be specific to male rats with no relevance to humans (PMRA# 3227602), the dose levels administered to male rats were lowered for chronic dosing to avoid excessive kidney toxicity associated with this mode of action that could potentially confound detection of other relevant effects. Prolonged clotting time (prothrombin time and activated partial thromboplastin time) was observed after short-term exposure in rats. This effect was not observed in the long-term study. In the dietary oncogenicity study in the mouse, increased incidences of luminal dilatation in the urinary bladder, urinary bladder distended with urine, and softening/atrophy of the testis were observed in males, and decreased body weight was noted in females, all of which occurred at the HDT. With the exception of effects in males in the rat dietary combined chronic toxicity/oncogenicity study, the observed effects occurred at or above the limit dose of testing.

In a 28-day inhalation toxicity study in rats, effects were observed at the highest concentration tested. These included hepatocellular hypertrophy, atrophy of the olfactory epithelium, hyperplasia/hypertrophy of the mucous cells in the nose, and centriacinar inflammation in the lungs in both sexes, decreased body weight, inflammation of the nasal turbinates and tubular hyaline droplets in the kidneys in males, and increased liver weight in females.

No systemic toxicity occurred in rats following daily dermal application of flutianil up to the limit dose for 28 days.

Functional observation batteries were performed in the 28-d dermal and 90-d and 2-year dietary rat toxicity studies, and no effects were observed. A waiver was provided for the conditionally required acute and 90-day neurotoxicity studies. The waiver was accepted based on the absence of treatment-related findings in the functional observation batteries conducted in the short- and long-term studies.

There was no evidence of immune dysregulation in a 28-day dietary immunotoxicity study in rats.

There was no evidence of genotoxicity in a battery of in vitro and in vivo genotoxicity studies conducted with flutianil, nor was there evidence of tumourigenicity in mice or rats after long-term dietary administration.

In a 2-generation dietary reproductive toxicity study in rats, no parental offspring, or reproductive toxicity was observed up to the limit dose of testing. There was no evidence of sensitivity of the young.

In the gavage developmental toxicity studies, there was no evidence of sensitivity of the young in rabbits. Maternal rabbits were tested up to the limit dose and no treatment-related maternal or developmental effects were observed. In the rat developmental toxicity study, there was evidence of sensitivity of the young, as increased incidences of incomplete ossification or non-ossification of the sternal centra were observed in fetuses in the absence of maternal toxicity at the limit dose of testing. This developmental effect is not considered a serious effect, reflecting a delay in fetal development.

The toxicity of select metabolites and transformation products of flutianil were investigated. There was no evidence of genotoxicity when OC 53276 (environmental transformation product) and OC 56635 (environmental transformation product and intermediate metabolite in the rat) were tested in in vitro bacterial reverse mutation and mammalian forward gene assays, or in in vivo micronucleus assays. In an acute oral toxicity study in rats, treatment with OC 56635 resulted in mortality at the limit dose, and was considered of moderate acute toxicity via the oral route. Due to the highly acidic nature of OC 56635, the sodium salt form (OC 63421) was used to evaluate the subchronic toxicity of OC 56635. OC 63421 did not cause mortality in rats at the limit dose in acute toxicity testing, and was considered of low acute toxicity via the oral route. In a 28-day dietary study with OC 63421 in rats, no effects were observed above the limit dose of testing. Based on the available information, metabolites OC53276 and OC 56635 were considered of equivalent toxicity to flutianil.

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

3.1.2 *Pest Control Products Act* hazard characterization

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

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database contains the full complement of required studies including oral gavage developmental toxicity studies in rats and rabbits, and a dietary 2-generation reproductive toxicity study in rats.

With respect to potential prenatal and postnatal toxicity, no evidence of sensitivity of the young was observed in the 2-generation reproductive toxicity study in rats or in the developmental toxicity study in the rabbit. In a developmental toxicity study in rats, a delay in ossification of fetuses was noted in the absence of maternal toxicological effects. This developmental effect is not considered serious in nature, and occurred only at the limit dose of testing.

Overall, endpoints in the young were well-characterized and not considered serious in nature. On the basis of this information, the PCPA factor was reduced to onefold.

3.2 Toxicology reference values

3.2.1 Route and duration of exposure

Occupational exposure to GATTEN is expected to occur predominantly via the dermal and inhalation routes for mixers, loaders and applicators (M/L/As), and through the dermal route for postapplication workers and residents. Exposure is expected to be intermittent over a short-term duration for farmers and intermediate-term duration for custom applicators as there are four applications made 7–14 days apart and various postapplication activities occurring during that time period (which can result in exposure for greater than 30 days). Exposure duration for residents is expected to be less than that of postapplication workers.

3.2.2 Occupational and residential toxicology reference values

Short- and intermediate-term dermal

For short- and intermediate-term dermal risk assessment, a NOAEL of 333 mg/kg bw/day from the developmental toxicity study in rats was selected. Toxicity was observed in the form of delayed bone ossification at a LOAEL of 1000 mg/kg bw/day. Worker populations could include pregnant or lactating women and therefore this endpoint was considered appropriate for the occupational risk assessment. The available 28-day dermal toxicity study did not assess the relevant endpoints of concern (that is, developmental effects following prenatal exposure).

The target MOE for all dermal scenarios is 300, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. Furthermore, a threefold uncertainty factor was applied to account for residual uncertainty with respect to differences in absorption when extrapolating from an oral toxicity study to the dermal route of exposure. This uncertainty stems from the fact that the oral absorption of flutianil was demonstrated to be quite low at the dose levels tested in the oral toxicity studies, while absorption via the dermal route is not known, and therefore assumed to be 100% (default value). For residential scenarios, the PCPA factor was reduced to onefold, for the reasons outlined in the *Pest Control Products Act* Hazard Characterization section. The selection of this study and target MOE is considered protective of all populations, including nursing infants and the unborn children of exposed female workers.

Short- and intermediate-term inhalation

For short- and intermediate-term occupational inhalation risk assessment, a NOAEC of 0.1 mg/L (equivalent to a dose level of 26 mg/kg bw/day) from the 28-day inhalation toxicity study in rats was selected. Toxicity was observed in the form of effects on the respiratory tract, liver and body weight at the LOAEC of 1 mg/L (261 mg/kg bw/day).

The target MOE for all inhalation scenarios is 100, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The selection of these studies and target MOE is considered protective of all populations, including nursing infants and the unborn children of exposed female workers.

3.2.3 Acute reference dose (ARfD)

Establishment of an acute reference dose is not required, as an endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies.

3.2.4 Acceptable daily intake (ADI)

To estimate risk following repeated dietary exposure, the NOAEL of 82 mg/kg bw/day from the 2-year dietary chronic toxicity/oncogenicity study in the rat was selected. At the LOAEL of 249 mg/kg bw/day, increased incidence of hepatic foci of cellular alteration were observed in males. This study provides the lowest oral NOAEL in the database. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the PCPA factor was reduced to onefold.

The composite assessment factor (CAF) is thus 100.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{82 \text{ mg/kg bw/day}}{100} = 0.8 \text{ mg/kg bw/day of flutianil}$$

3.2.5 Cancer assessment

There was no evidence of tumourigenicity and, therefore, a cancer risk assessment was not necessary.

3.2.6 Aggregate toxicology reference values

Aggregate exposure is the total exposure to a single pesticide that may occur from dietary (food and drinking water), residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation). Acute aggregate exposure to flutianil may be comprised of food, drinking water and residential exposure via the dermal route.

No endpoints were selected for the acute aggregate risk assessment as no endpoints of concern attributable to a single exposure were identified. The most relevant toxicology endpoint and assessment factor for the chronic oral aggregate exposure is the same as that selected for the ADI (see Section 3.2.4).

3.3 Dermal absorption

A chemical-specific dermal absorption study was not submitted and is not on file for flutianil. Therefore, the default dermal absorption value of 100% was used in the occupational and residential exposure assessments.

3.4 Occupational and residential exposure assessment

3.4.1 Occupational exposure and risk assessment

3.4.1.1 Mixer, loader and applicator exposure and risk assessment

Individuals have the potential to be exposed to GATTEN during mixing, loading and application. Exposure estimates were derived for mixers, loaders and applicators applying GATTEN to cherries (Crop Subgroup 12-09A), grape and cucurbit vegetables (Crop Group 9) using groundboom, airblast and handheld equipment (backpack, manually-pressurized handwand and mechanically-pressurized handgun equipment).

The unit exposure estimates in the risk assessment are based on mixers/loaders/applicators wearing a single layer and chemical-resistant gloves (unless inside a closed-cab tractor).

As chemical-specific data for assessing human exposure were not submitted, dermal and inhalation exposures for workers were estimated using data from the Agricultural Handlers Exposure Task Force (AHETF), of which the applicant is a member and has full access to the data, or the Pesticide Handlers Exposure Database (PHED). Both are compilations of generic mixer/loader and applicator passive dosimetry data, which facilitate the generation of scenario-specific exposure estimates (Appendix I, Table 6).

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

The exposure estimates were compared to the selected flutianil toxicology reference values (dermal NOAEL = 333 mg/kg bw/day and inhalation NOAEL= 26 mg/kg bw/day) to obtain the margin of exposure (MOE). The target MOEs are 300 for dermal exposure and 100 for inhalation exposure. Dermal and inhalation MOEs were not combined since the dermal and inhalation endpoints are based on different toxicological effects. The calculated MOEs are greater than the target MOEs (Appendix I, Table 7) when using groundboom, airblast and handheld equipment (backpack, manually-pressurized handwand and mechanically-pressurized handgun equipment) and are therefore not of health concern for mixers, loaders and applicators.

3.4.1.2 Exposure and risk assessment for workers entering treated areas

Flutianil has a vapour pressure of 1.530×10^{-10} k*P*a (at 20°C). This is lower than the North American Free Trade Agreement (NAFTA) criterion for a non-volatile product at 1×10^{-4} kPa for outdoor uses at 20–30°C. Inhalation risk is not of health concern for postapplication workers as flutianil is considered non-volatile and the REI of 12 hours will allow residues to dry, suspended particles to settle and vapours to dissipate.

Chemical-specific dislodgeable foliar residue (DFR) study on apples, grapes and cantaloupe was reviewed and used for assessing human exposure during postapplication activities specific to cherries, grapes and cucurbits. The study was conducted at three locations on three different crops (apples in New York, grapes in California and cantaloupe in Texas). At all three sites, the application rate corresponded to the maximum rate proposed on the label (45.9 g a.i./ha) and, therefore, is not expected to underestimate exposure. Applications were done at seven-day intervals with a maximum of five applications (only four applications on apples in New York). Sampling was conducted before and after each application as well as spanning 35 days after the last application. Data were not corrected for recovery as all field fortification samples were above 95% (Appendix I, Table 8).

For the purpose of this risk assessment, the peak grape DFR value (0.193 µg/cm^2) was deemed the most appropriate for estimating postapplication exposure to grapes and the peak apple DFR value (0.083 µg/cm^2) was deemed the most appropriate for estimating exposure to cherries (crop subgroup 12-09A). The peak values were chosen since the r^2 of the regression equations were below 0.85 and, therefore, the regression equation could not be used to estimate a dissipation rate. For the cantaloupe data, the r^2 was above 0.85 (0.91) and, therefore, the regression equation from the cantaloupe DFR analysis was used to estimate a dissipation rate for cucurbit vegetables (crop group 9). When the actual values from the study were used, they were adjusted for the difference in application rate between the study rate and the label rate (35 g a.i./ha vs. 45.9 g a.i./ha).

Postapplication dermal exposure may occur when workers enter treated cherry orchards, grape vineyards and cucurbit vegetable fields to perform various activities. Dermal exposure to workers entering treated areas is estimated by combining chemical-specific DFR values and a 100% dermal absorption (default value) with activity-specific transfer coefficients (TCs). Activity-specific TCs are based on data from the Agricultural Re-entry Task Force (ARTF).

The exposure estimates were compared to the flutianil dermal toxicology reference value (NOAEL = 333 mg/kg bw/day) to obtain the MOE. The target MOE is 300. Since the calculated MOEs are greater than the target MOE of 300 (Appendix I, Table 9), the postapplication exposure is not of health concern and the REI of 12 hours is adequate.

3.4.2 Residential exposure and risk assessment

3.4.2.1 Handler exposure and risk assessment

GATTEN is not a domestic class product; therefore, a residential handler risk assessment is not required.

3.4.2.2 Postapplication exposure and risk assessment

GATTEN is proposed for use on cherries where pick-your-own activities are possible, as well as, there is the potential for trees in residential settings to be treated. As such, a residential postapplication risk assessment is required.

3.4.2.2.1 Pick-Your-Own (PYO) activities

Given that cherries can be treated with flutianil, there is potential for exposure during pick-your-own activities. The postapplication occupational risk assessment is protective of the risk associated with dermal exposure to the public in a pick-your-own facility and, therefore, a quantitative risk assessment is not required.

3.4.2.2.2 Trees in residential areas treated with GATTEN

When a commercial applicator is hired to treat orchard trees in a residential area or a farmer treats orchard trees adjacent to residential areas, there is potential for postapplication dermal exposure to residents.

The residential postapplication dermal risk assessment was conducted for adults (16 years old and over) and children (6 to less than 11 years old) when contacting treated fruit trees to perform activities such as hand harvesting, thinning, pruning, etc. The maximum application rate, maximum number of applications per season and minimum retreatment interval (RTI) were used. As mentioned previously, a chemical-specific DFR study was submitted and the peak apple DFR value (0.083 $\mu g/cm^2$) was deemed the most appropriate for estimating exposure to the cherries (crop subgroup 12-09A). This value was adjusted for the difference in application rate between the study rate and the label rate (35 g a.i./ha vs 45.9 g a.i./ha).

Dermal exposure was estimated using the DFR value, the TCs, durations of exposure and body weights from the 2012 United States Environmental Protection Agency Residential Standard Operating Procedures. Using the dermal toxicology reference value, calculated MOEs were greater than the target MOE of 300 (Appendix I, Table 10) for all residential postapplication exposure scenarios on Day zero. As such, health risks are not of concern and the individuals can enter the treated area once the sprays have dried.

3.4.3 Bystander exposure and risk assessment

Bystander exposure should be negligible since the potential for drift is expected to be minimal. Application is limited to agricultural crops only when there is low risk of drift to areas of human habitation or activity such as houses, cottages, schools and recreational areas, taking into consideration wind speed, wind direction, temperature, application equipment and sprayer settings.

3.5 Dietary exposure and risk assessment

3.5.1 Exposure from residues in foods of plant and animal origin

The residue definition for risk assessment in plant products is flutianil and the metabolite OC 56635 [2-fluoro-5-(trifluoromethyl)benzenesulfonic acid] for fruits (cherries, grapes, apples, strawberries) and flutianil only for cucurbit vegetables. The residue definition for enforcement in plant products is flutianil. The data gathering/enforcement analytical methods are valid for the quantitation of flutianil and metabolite OC 56635 residues in crop matrices. The residues of flutianil are stable in apples for up to 18 months, in grapes, grape juice, and raisins for up to 14.6 months, in summer squash for up to 13 months, in cucumber for up to 15 months, in cantaloupe for up to 11 months, in cherries and strawberries for up to 12 months, in radish and spinach for up to 7.3 months, in wheat forage for up to 8.2 months, in wheat hay for up to 8.9 months, and in wheat straw and grain for up to 4.4 months when stored in a freezer at -20°C. The residues of metabolite OC 56635 are stable in grapes, grape juice, and raisins for up to 6 months, in radish and spinach for up to 7.3 months, in wheat forage for 8.2 months, in wheat hay for up to 8.9 months, and in wheat straw and grain for up to 4.4 months when stored in a freezer at -20°C.

Flutianil residues concentrated in the following processed commodities: apple wet pomace (3.3×) and raisins (1.2×). Crop field trials conducted throughout the United States, including growing regions representative of Canada, using end-use products containing flutianil at equivalent or at slightly exaggerated rates in or on summer squash, cucumbers, cantaloupe, cherries, grapes, apples, and strawberries are sufficient to support the proposed maximum residue limits. Field rotational crop studies were conducted in/on radish, wheat, lettuce, and spinach. The data are adequate to demonstrate that a 12-month plant-back interval is appropriate for non-labelled crops.

3.5.2 Exposure from residues in drinking water

3.5.2.1 Modelling estimates

Environmental concentrations of flutianil in potential drinking water sources were estimated using numerical models for the human health risk assessment. Modelling was conducted using the Pesticides in Water Calculator (PWC) version 1.52, using standard PMRA scenarios which take into account regional weather and soil characteristics as well as relevant plant properties.

3.5.2.2 Application information and model inputs

A conservative use pattern was modelled consisting of five applications of 35 g a.i./ha with an interval of 7 days, yearly applications not exceeding 175 g a.i./ha, with application dates between early April and mid-September. Modelling inputs for drinking water estimated environmental concentrations (EEC) differ from environmental fate parameters given the residue definition (Table 1).

Table 1 Major fate input parameters for the drinking water modelling assessment

Fate parameter	Flutianil	Flutianil + OC 56635 + OC 56574	Unit
K_d	451	0.024	L/kg
Water $t_{1/2}$ at 20ºC	579	693	d
Sediment $t_{1/2}$ at 20ºC	1.98×10^3	1.35×10^3	d
Aquatic Photolysis $t_{1/2}$ at latitude 40ºN	1.03	494	d
Hydrolysis $t_{1/2}$ (pH=7)	stable	stable	d
Soil $t_{1/2}$ at 20ºC	2.41×10^3	2.09×10^3	d
Foliar $t_{1/2}$	stable	stable	d
MWT	426	426	g/mol
Vapor Pressure (20ºC)	1.94×10^{-9}	1.94×10^{-9}	torr
Solubility (pH = 7)	0.0079	0.0079	mg/L
Henry's law constant (20ºC)	1.3×10^{-7}	1.3×10^{-7}	unitless
Air Diffusivity	3.4×10^3	3.4×10^3	cm^2/day
Heat of Henry	5.25×10^4	5.25×10^4	J/mol

3.5.2.3 Estimated environmental concentrations in drinking water

For surface water, PWC calculates the amount of pesticide entering the water body by run-off and drift, and the subsequent degradation of the pesticide in the water system. Estimated drinking water concentrations were calculated by modelling a total land area of 173 ha draining into a 5.3 ha reservoir with a depth of 2.7 m. Ground water EECs are calculated by simulating leaching through a layered soil profile and reporting the average concentration in the top 1 m of the water table.

The Level 1 EECs for the combined residue of flutianil and the transformation products OC 56635 and OC 56574 in potential sources of drinking water are provided in Table 2. Level 1 EECs are conservative values intended to screen out pesticides that are not expected to pose any concern related to drinking water. These are calculated using conservative inputs with respect to application rate, application timing, and geographic scenario. Level 1 EECs cover all regions of Canada.

Table 2 Level 1 Estimated environmental concentrations of the combined residue of Flutianil + OC 56635 + OC 56574 in potential sources of drinking water, reported as parent equivalent

Use pattern	Groundwater (µg a.i./L)		Surface water (µg a.i./L)		
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]	Overall[5]
5 applications of 35 g a.i./ha at 7-day intervals	244	244	8.1	1.7	1.2

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

3.5.3 Dietary risk assessment

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

3.5.3.1 Acute dietary exposure results and characterization

No appropriate toxicological reference value attributable to a single dose for the general population (including children and infants) was identified.

3.5.3.2 Chronic dietary exposure results and characterization

The following criteria were applied to the basic chronic analysis for flutianil: 100% crop treated, default processing factors (where available), the proposed Canadian MRLs, and the American tolerances for imported commodities. The basic chronic dietary exposure from all supported flutianil food uses (alone) for the total population, including infants and children, and all representative population subgroups is less than 1% of the acceptable daily intake (ADI), which is not of health concern. Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that chronic dietary exposure to flutianil from food and drinking water is 0.7% (0.006 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for all infants (< 1 year) at 2.5% (0.020 mg/kg bw/day) of the ADI.

3.6 Aggregate exposure and risk assessment

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

Aggregation of acute dietary (food and drinking water) and dermal exposure to flutianil from pick-your-own activities is not required, as no dietary acute reference value was identified for the general population, including infants and children.

Aggregation of chronic dietary (food and drinking water) and dermal exposure to flutianil from harvesting, pruning, thinning of trees in residential settings is not required, as the dietary and dermal endpoints are based on different toxicological effects.

3.7 Cumulative assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative effects of pest control products that have a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pesticides was undertaken for flutianil. Based on its chemical structure, flutianil has been classified as a thiazolidine fungicide. Currently, flutianil and thiadifluor are the only members of that class. Thiadifluor is not currently registered in Canada or the United States. For the current evaluation, the PMRA did not identify information indicating that flutianil shares a common mechanism of toxicity with other pest control products. Therefore, no cumulative health risk assessment is required at this time.

3.8 Maximum residue limits

Table 3.8-1 Recommended maximum residue limits

MRL (ppm)	Food commodity
0.7	Small fruits vine climbing, except fuzzy kiwifruit (Crop subgroup 13-07F)
0.5	Low growing berries (Crop subgroup 13-07G)
0.4	Cherries (Crop subgroup 12-09A)
0.2	Squash/Cucumber (Crop subgroup 9B)
0.15	Apples
0.07	Melons (Crop subgroup 9A)

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

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

The nature of the residues in plant matrices, analytical methodologies, field trial data, and chronic dietary risk estimates are summarized in Appendix I, Tables 1b, 11and 12.

3.9 Health incident reports

Flutianil is a new active ingredient pending registration for use in Canada, and as of 12 March 2021, no incident reports have been submitted to the PMRA.

4.0 Impact on the environment

The environmental assessment was conducted based on data and information from the registrant, as well as other regulatory agencies, such as the United States Environmental Protection Agency and the European Food Safety Authority.

4.1 Fate and behaviour in the environment

A summary of the environmental fate properties of flutianil and its transformation products are summarized in Appendix I, Tables 13 and 14 .

4.1.1 Terrestrial environment

In the terrestrial environment, hydrolysis is not expected to contribute significantly to the dissipation of flutianil as it is stable to hydrolysis under all conditions (half-life > 365 days at pH 4, 7, and 9).

In soil, phototransformation of flutianil is slow (half-life = 110 days). Phototransformation may, however, be a transformation pathway for flutianil due to the formation of a single major transformation product; OC 56635, reaching a high of 10.7% of the applied radioactivity (AR) at study termination (37 days). Two identified minor transformation products were also produced, OC 56574, and OC 53276.

Flutianil is persistent in terrestrial biotic transformation processes in both the laboratory (aerobic half-life = 1114 to 2855 days; anaerobic half-life = 1460 to 13191 days) and field (DT_{50} = 312 to 398 days). Under laboratory conditions, no major transformation products were produced, yet OC 56635, OC 53276, OC 56574, and OC 53279 were observed in both the aerobic and anaerobic studies in minor quantities. Under field conditions, three of these transformation products were identified as major transformation products, OC 56635, OC 56574, and OC 53276 (maximum of 29.8, 11.4, and 14.4% AR, respectively). Based on information from the field dissipation study; OC 53276 was considered to be persistent (half-life = 259 days), while OC 56635 was considered to be slightly persistent (half-life = 42.2 days). The maximum concentration of flutianil residues observed during field trials was 34.6% AR after 460 days in one replication at the New York site, yet it was not detected after 271 days in the other two replications in New York or at the Iowa site. As such, flutianil may have the potential to carry-over under field conditions. A label statement pertaining to carry-over, however, is not required as flutianil is strongly bound to soil, is a non-leacher, and, generally, is not toxic to terrestrial organisms or aquatic organisms from runoff.

Flutianil is expected to be immobile in soil (K_{oc} = 11779 to 47320 L/kg) and was not detected below 8 cm depth in the field dissipation study, except at one sampling point where it was detected at 15 cm. The three main soil transformation products are all expected to have higher mobility than flutianil. Based on the adsorption information, OC 56574 and OC 53276 are expected to have slight to low mobility (K_{oc} = 1278 to 2090 L/kg) and low mobility (K_{oc} = 821 to 919 L/kg), respectively, and were not detected below 8 cm in the field dissipation study. Based on the information available, flutianil, OC 53276, and OC 56574 are not expected to reach groundwater sources according to the criteria of Cohen et al. (1984) and Gustafson (1989). The third transformation product, OC 56635, is expected to be very mobile in soil, due to the lack of adsorption (no K_{oc} calculation possible due to minimal adsorption) and its high water solubility (> 1000 g/L at 20°C). Consequently, it is classified as a leacher according to the criteria of Cohen et al. (1984) and Gustafson (1989). This transformation product, however, was detected at a maximum depth of between 8 and 15 cm in the field dissipation study and was transient in nature. Even though the physicochemical parameters of OC 56635 suggest that it has the potential to reach groundwater, the persistance of the parent along with the limited mobility demonstrated in the field dissipation study indicates that a leaching statement on the label is not required for flutianil or its transformation products.

4.1.2 Aquatic environment

In the aquatic environment, hydrolysis is not expected to contribute significantly to the dissipation of flutianil as it is stable to hydrolysis under all conditions (half-life > 365 days at pH 4, 7, and 9).

Aquatic phototransformation of flutianil is rapid (half-life = 1 to 1.1 day), transforming to OC 56635, and unidentified transformation products, Unk AP5A and Unk AP1B, at up to 71% (7 days), 30% (1 day), and 26% (2 days) AR, respectively. The estimated half-lives of the major transformation products Unk AP5A and Unk AP1B (half-life = 3.8 to 4.4 and 3.8 to 6.0 days, respectively) indicate that they are transient, whereas OC 56635 is likely to be present in the environment for longer periods of time based on the estimated extrapolated half-life of 62 to 71 days. Phototransformation usually only occurs when the compound is at or near the surface of the water and light can penetrate through. Therefore, even though aquatic phototransformation is rapid, it is unlikely to be a major breakdown pathway of flutianil.

Under laboratory conditions, flutianil is persistent in aquatic aerobic biotransformation systems (whole system DT_{50} = 236 to 699 days). Two major transformation products were produced, OC 56574 (up to a maximum of 13.7% AR after 272 days) and OC 53279 (up to a maximum of 3.7% AR after 61 days). In aquatic anaerobic systems, flutianil is persistent (whole system DT_{50} = 766 to 2280 days). No major transformation products were observed in the laboratory under anaerobic conditions.

4.1.3 Air transformation

Flutianil has low solubility in water (0.0079 mg/L), low vapour pressure (1.53×10^{-7} Pa at 20°C), and a low Henry's law constant (4.853×10^{2} Pa at 20°C). The intrinsic physio-chemical properties suggest that flutianil is not likely to volatilize from moist soil or water surfaces under field conditions. Flutianil, therefore, has a low potential for transport in the atmosphere.

The rate of the gas-phase reaction between photochemically produced hydroxyl radicals and flutianil in the atmosphere is expected to be rapid, with an estimated half-life of 0.285 days.

4.1.4 Bioaccumulation

The *n*-octanol/water partitioning coefficient of flutianil (log K_{ow} = 3.1) indicates that it has the potential to bioaccumulate. However, the measured bioconcentration in rainbow trout (*Oncorhynchus mykiss*) was low (whole body kinetic bioconcentration factor, $BCF_k \leq 380$ L/kg). Flutianil had a depuration half-life of < 2 days in rainbow trout, and nearly all residues (~ 95%) were eliminated rapidly from fish tissues after 6.5 days. Flutianil is, therefore, not expected to bioaccumulate.

The transformation product OC 56635 was identified as a possible hydrophobic ionogenic organic compound that may be expected to bioaccumulate. It was thus modelled using the Bioconcentration for Ionizable Organics (BIONIC V2) model and yielded a range of BCFs from 1 to 2, implying that there is a low potential for bioaccumulation.

4.2 Environmental risk characterization

The environmental risk assessment integrates environmental exposure and ecotoxicology information to estimate the potential for adverse effects to non-target species. This integration is achieved by comparing EECs in various environmental media (food, water, soil, and air) with the concentrations at which adverse effects occur. The EECs are estimated using standard models that take into consideration the application rate(s), and chemical and environmental fate properties, including the dissipation of the pesticide between applications.

Ecotoxicology information includes acute and chronic toxicity data for organisms (invertebrates, vertebrates, and plants) from both terrestrial and aquatic habitats. Effects metrics are the toxicity study endpoints that have been adjusted by an uncertainty factor to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level). A summary of the terrestrial and aquatic endpoints available and the effects metrics used in the risk assessment are presented in Appendix 1, Tables 15, 16, and 17, respectively.

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing

the EEC by the appropriate effects metric and is then compared to the level of concern (LOC; Appendix I, Table 17). If the screening level risk quotient is below the LOC, the risk is considered negligible, and no further risk characterization is necessary. If the screening level RQ is equal to or greater than the LOC, further characterization of the risk is conducted by taking into consideration more realistic exposure scenarios and effects metrics. These considerations may include additional exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods.

One end-use product, GATTEN, is proposed for registration. The potential risk from the use of this product was assessed at the following application rates:

- five applications of 35 g a.i./ha (175 g a.i./ha total) with a 7-day re-application interval.

The screening level risk assessment and further characterization of risk for flutianil and its end-use product is summarized in in Appendix I, Tables 18 to 24.

4.2.1 Risks to terrestrial organisms

Terrestrial organisms, such as earthworms, honey bees, beneficial arthropods, birds, small mammals, and terrestrial non-target vascular plants can be exposed to flutianil through direct contact with spray, spray drift, run-off, contact with sprayed surfaces, or from ingestion of contaminated food. A risk assessment of flutianil, its transformation products, and the associated end-use product, GATTEN, was undertaken based on available toxicity data for earthworms, honey bees and other beneficial arthropods, birds, small wild mammals, and terrestrial plants. A summary of the toxicity of flutianil to terrestrial organisms is provided in Appendix I, Table 15. The terrestrial effects metrics used in the risk assessment are provided in Appendix I, Table 17.

When used according to the proposed label directions, risks associated with the use of flutianil are acceptable for the following terrestrial organisms:

- Earthworms,
- Pollinators,
- Beneficial arthropods, and
- Birds and mammals.

The LOC was exceeded for the following organisms and further characterization of the risk was completed:

- Terrestrial vascular plants.

With the observance of mitigation measures (in other words, buffer zones) to reduce exposure, the risks towards terrestrial vascular plants associated with the use of flutianil are acceptable.

4.2.1.1 Screening level risk assessment

The screening level risk assessment determines the potential risk to non-target terrestrial organisms assuming they are within the area that will receive direct application of the pesticide.

The calculated EECs were compared to the most sensitive effect metric for each group of terrestrial organisms. EECs for the transformation products were assumed to be a 100% conversion (molecular w/w) from flutianil. When the LOC was exceeded, further characterization of the risks was completed and presented in Section 4.2.1.2.

Earthworms and soil-dwelling arthropods

Earthworms and soil-dwelling arthropods may be exposed to flutianil through contact with residues in soil. Soil EECs were calculated based on a direct overspray, considering the maximum cumulative application rate of five applications of 35 g a.i./ha (175 g a.i./ha total) with a 7-day re-application interval and a soil half-life of 2410 days. Soil EECs were converted from g a.i./ha to mg a.i./kg soil using the assumption that flutianil was homogeneously mixed in the top 15-cm soil layer, and the soil had a bulk density of 1.5 g/cm^3.

Effects metrics were compared to the screening level soil EEC of 0.077 mg a.i./kg. The resulting RQs did not exceed the LOC for flutianil or its transformation products (RQs ≤ 0.01; Appendix I, Table 18), indicating that risks to earthworms and soil-dwelling arthropods are acceptable when flutianil is used according to the label.

Foliar-dwelling beneficial arthropods

The main route of exposure of flutianil to foliar-dwelling beneficial arthropods is via contact to surface residues as a result of a spray application. For direct overspray to plant surfaces in the field, the maximum cumulative application rate was considered with a default foliar dissipation half-life of 10 days.

Effects metrics were compared to the screening level foliar EEC of 83.01 g a.i./ha. The RQs did not exceed the LOC for the end-use product, GATTEN, or the transformation product, OC 53276 (RQs ≤ 0.35; Appendix I, Table 18), indicating that risks to foliar-dwelling arthropods are acceptable when flutianil is used according to the label.

Bees

Foraging bees could be exposed directly to flutianil 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, brood may be exposed to flutianil as foraging bees bring contaminated pollen and nectar back to the hive. For the screening level risk assessment, it was conservatively assumed that flutianil is systemic, although it is not expected to move through plants to the pollen and nectar. The estimated contact and oral exposure for bees is compared to the toxicity endpoints (expressed in µg a.i./bee) derived from laboratory studies. As such, a conversion of the application rate from kg a.i./ha to µg a.i./bee is required for both contact and oral studies.

The LOC was not exceeded for all bee studies with either flutianil or the end-use product, GATTEN (RQs ≤ 0.05; Appendix I, Table 18), indicating that risks to pollinators are acceptable when flutianil is used according to the label.

Terrestrial vertebrates

Birds and small mammals could be exposed directly to flutianil via spray droplets during application or to residues on the surface of leaves (acute contact exposure). Foraging birds and small mammals could also be exposed to flutianil through the ingestion of a contaminated diet (oral exposure). To assess the risk to birds and mammals, the estimated concentration of flutianil on various food items was used to determine the amount of pesticide in the diet (the estimated daily exposure (EDE)). Exposure is dependent on the body weight of the organism, and the amount and type of food consumed. As such, a set of generic body weights was used to represent a range of species (20, 100, and 1000 g for birds and 15, 35, and 1000 g for mammals) and specialized feeding guilds (in other words, herbivore, frugivore, insectivore, and granivore) were considered for each category of animal weights (Appendix I, Table 19).

The LOC was not exceeded for all feeding guilds of birds and mammals (RQs < 0.04 and < 0.02 for birds and mammals, respectively; Appendix I, Table 19), indicating that risks to birds and mammals are acceptable when flutianil is used according to the label.

Non-target terrestrial plants

The screening level risk assess the direct exposure of plants to the pesticide. This assessment was conducted for seedling emergence, using the soil half-life of 2410 days, and for vegetative vigour, using the default foliar dissipation half-life of 10 days. The highest rate tested (a single nominal application rate of GATTEN at 44.8 g a.i./ha) was below the maximum proposed annual application rate. At this rate, a 25% effect level was not established, suggesting that effects to 25% will be observed at higher application rates.

This right-censored endpoint was used as the effect metric and resulted in RQs that slightly exceed the LOC (RQs of < 4.09 and < 1.95 for seedling emergence and vegetative vigour, respectively; Appendix I, Table 18), indicating a potential risk to non-target terrestrial plants. The risk was thus further characterized in Section 4.2.1.2.

4.2.1.2 Further risk characterization

The LOC was exceeded for terrestrial plants in the screening level assessment. Therefore, further risk characterization was completed. The further characterization considered applications to cucurbits, and cherries and grape separately, using the following proposed rates:

- Cucurbits: five applications of 35 g a.i./ha (175 g a.i./ha total) with a 7-day re-application interval; and
- Cherries and grape: four applications of 35 g a.i./ha (140 g a.i./ha total) with a 7-day re-application interval.

4.2.1.2.1 Spray drift

Further characterization of exposure was conducted considering off-target spray drift. The amount of spray drift depends on the type of equipment used and the size of the spray droplets, as well as the type of crop. To calculate off-field EECs, spray drift factors were applied to the in-field EECs. The spray drift factor is defined as the maximum percentage of spray drift deposition at 1 m downwind from the point of application. For flutianil, the product should be applied using an ASAE fine[5] spray quality. The corresponding spray drift factors of 11% for field sprayers using a fine spray, and 74 and 59% for early- and late-season airblast sprayers, respectively, were used to determine estimated exposure due to spray drift.

Non-target terrestrial plants

Based on the RQs using the off-field EECs from drift, the level of concern is not exceeded for applications to cucurbits via field sprayer (RQ < 0.45; Appendix I; Table 18). However, the off-field RQs for application to cherries and grape via airblast exceed the LOC (RQs of < 1.08 to < 2.43), indicating that risks to non-target terrestrial plants are possible when flutianil is used according to the label.

Overall conclusion about potential risks to non-target terrestrial plants

There may be potential risks to non-target terrestrial plants from the use of flutianil. To inform users of the potential risk to non-target terrestrial plants, label statements pertaining to the toxicity of flutianil towards non-target terrestrial plants are required on the label of GATTEN.

Additionally, spray buffer zones of 1 to 3 m are required to mitigate the risk to non-target terrestrial habitats. With the implementation of these proposed mitigation measures, the risks are considered acceptable.

4.2.2 Risks to aquatic organisms

Aquatic organisms, such as invertebrates, fish, amphibians, and aquatic plants can be exposed to flutianil via spray drift or through runoff entering aquatic habitats. The aquatic risk assessment was conducted following a tiered approach, with a conservative screening assessment followed by refinements for spray drift and runoff if concerns were identified at the screening level. A summary of the effects on aquatic organisms considered in the selection of toxicity endpoints is provided in Appendix I, Table 16. The most sensitive aquatic endpoints used in the risk assessment are provided in Appendix I, Table 17.

[5] Droplet size classification system of the American Society of Agricultural Engineers (ASAE) based on the volume median diameter (VMD) of spray droplets.

When used according to approved label directions, the risks associated with flutianil are acceptable for the following aquatic organisms:

- Marine plants.

The level of concern was exceeded for the following organisms:

- Freshwater and marine invertebrates,
- Freshwater and marine fish,
- Amphibians, and
- Freshwater plants.

With the observance of preventative measures and use-restrictions to reduce exposure, the risks towards aquatic organisms associated with the use of flutianil are acceptable.

4.2.2.1 Screening level risk assessment

Flutianil is classified as very highly toxic to practically non-toxic to freshwater organisms (Appendix I, Table 16). However, most endpoints were empirically estimated to be higher than the highest concentration tested, as test concentrations were capped at the limit of solubility of flutianil (0.0079 mg/L). As such, many of the calculated RQs in the screening level risk assessment are a conservative representation of the potential risk.

The screening level EECs in surface waters were calculated considering a direct overspray of flutianil at the maximum cumulative application rate of five application of 35 g a.i./ha with a 7-day re-treatment interval. Water bodies of two different depths were evaluated: EECs in surface water of 0.115 and 0.022 mg a.i./L for 15- and 80-cm depth were used to determine the risks to amphibians and all other aquatic organisms, respectively, aside from sediment-dwelling organisms, where the soil EEC of 0.077 mg a.i./kg was conservatively used for sediment concentrations. When the level of concern was exceeded, further characterization of the risk was completed and presented in Section 4.2.2.2.

For the purposes of the screening level risk assessment, the EECs for the transformation products were assumed to be a 100% conversion (molecular w/w) from flutianil.

Aquatic invertebrates

Freshwater

In the screening level risk assessment, the LOC was exceeded for both acute and chronic flutianil exposure to the water flea, *Daphnia magna* (RQ < 6.62 and 3.03, respectively, Appendix I, Table 20). However, acute exposures to GATTEN and the transformation products OC 56635, OC 56574, and OC 53276 did not exceed the LOC (RQs of < 0.01 to 0.98) nor did chronic exposure to OC 56635 (RQ < 0.01).

The concentration of flutianil in sediment did not pose a chronic risk to the sediment-dwelling amphipod, *Hyallela azteca* (RQ = 0.01), yet the RQs for *H. azteca* exceeded the LOC based on overlying and pore water concentrations (RQ = 3.84 and 1.02, respectively). Risks to freshwater invertebrates will be further characterized.

Marine

The risk quotients for marine invertebrates resulting from acute and chronic exposures to flutianil exceeded the LOC in two cases (Appendix I, Table 20); flutianil and GATTEN pose a potential acute risk to eastern oysters, *Crassostrea virginica* (RQs of < 2.26 and < 1.20, respectively), but is not expected to pose a chronic risk to saltwater mysids, *Americamysis bahia* (RQ = 0.47) or to the sediment dwelling amphipod, *Leptocheirus plumulosus*, based on sediment concentration (RQ = 0.01). Acute risks to marine invertebrates will be further characterized.

Fish

Freshwater

The screening level RQs for freshwater fish were exceeded in three out of seven instances (RQs of < 0.01 to < 41.2; Appendix I, Table 20). The risk quotients for fathead minnow, *Pimephales promelas*, resulting from acute exposure to flutianil (RQ < 41.2), rainbow trout, *Oncorhynchus mykiss*, resulting from acute exposure to GATTEN (RQs = 4.12), and fathead minnow resulting from chronic exposure to flutianil (RQ = 8.96) exceeded the LOC. There were no effects of acute or chronic exposure to the transformation products on freshwater fish (RQs < 0.07). Risks to freshwater fish will be further characterized.

Marine

The risk quotients for the marine fish, sheepshead minnow (*Cyprinodon variegatus*), resulting from acute exposure to the end-use product, GATTEN, exceeded the LOC (RQ < 2.79; Appendix I, Table 20). Flutianil alone is not expected to pose an acute or chronic risk to sheepshead minnow (RQs of < 0.25 and 0.31, respectively). Risks to marine fish will be further characterized.

Amphibians

When rainbow trout and fathead minnows were used as surrogates for amphibians, the LOC was exceeded, with RQs of < 220 for acute and 47.8 for chronic exposures to flutianil, and 22.0 for acute exposures to GATTEN (Appendix I, Table 20). There were no effects of acute or chronic exposure to the transformation products on amphibians (RQs < 0.34). Risks to amphibians will be further characterized.

Algae and vascular plants

Freshwater

The LOC was not exceeded for freshwater vascular plants exposed to GATTEN (duckweed, *Lemna gibba*, RQ < 0.20; Appendix I, Table 20). However, the LOC was exceeded for green algae, *Pseudokirchneriella subcapitata*, exposed to flutianil (RQ ≤ 3.14). There were no effects of the transformation products on freshwater plants (RQs ≤ 0.02). Risks to freshwater plants will be further characterized.

Marine

The LOC was not exceeded for the marine diatom, *Skeletonema costatum* (RQ = 0.33; Appendix I, Table 20). Risks to marine plants are acceptable when flutianil is used according to the label.

4.2.2.2 Further risk characterization

Due to the insoluble nature of flutianil, the majority of the screening level risk assessment for aquatic organisms is based on non-definitive endpoints with an additional uncertainty factor applied. Applying an uncertainty factor to non-definitive endpoints in studies where no effects were observed is overly conservative. To further characterize the risk, a more representative effect metric was used; either the lowest non-definitive endpoint without the uncertainty factor applied or the lowest endpoint from a study that did display effects with the uncertainty factor still applied, whichever is lowest.

4.2.2.2.1 Spray drift

Non-target aquatic organisms can also be exposed to flutianil via spray drift. The refinement parameters for freshwater organisms and amphibians were the same as for the terrestrial spray drift refinement. For marine organisms, spray buffer zones are determined based on acute endpoints and the maximum single application rate only to reflect the lower potential of chronic exposure due to higher water renewal rates in tidal/estuarine areas.

Cucurbit vegetables

The further risk characterization resulted in RQs of ≤ 0.01 to 5.26 (Appendix I, Table 21). Only acute and chronic exposure of flutianil to amphibians (RQs of < 2.42, and 5.26, respectively), and acute exposures of GATTEN to amphibians (rainbow trout; RQ = 2.42) resulted in an exceedance of the LOC. The LOC for all other aquatic organisms was not exceeded (RQs of ≤ 0.99). In the absence of mitigative measures, risks to amphibians remains possible from spray drift of flutianil applied to cucurbit vegetables. Therefore, mitigation is required.

Cherries and grape

Taking early- and late-season airblast into account, the consideration of spray drift resulted in RQs ranging from ≤ 0.04 to 28.4 and ≤ 0.03 to 22.7, respectively (Appendix I, Table 21). Chronic exposure of flutianil to sediment-dwelling amphipods in pore water (RQs of 0.61 and 0.49 for early- and late-season airblast, respectively) and acute marine exposures (RQs ≤ 0.18) did not result in an exceedance of the LOC.

In the absence of mitigative measures, risks to aquatic invertebrates, fish, amphibians, and freshwater plants remain possible from spray drift of flutianil applied to cherries and grape. Therefore, mitigation is required.

Summary of spray drift risk to aquatic organisms

There is a potential risk to aquatic organisms from the use of flutianil when taking spray drift into account. To protect these organisms, standard label statements pertaining to aquatic organisms are required on the label of GATTEN. Freshwater spray buffer zones of up to 25 m will be required on GATTEN product labels to protect freshwater organisms from the potential effects of spray drift from the use of flutianil on cucurbit vegetables, and cherries and grape fruit. Marine spray buffer zones are based on the maximum single application rate, not the cumulative, and are thus not required. With implementation of these proposed mitigation measures, the risks from the use of GATTEN are considered acceptable.

4.2.2.2.2 Runoff

Given the high K_{oc} and low solubility of flutianil, it is not expected to be mobile in soils. Flutianil can, however, travel to waterbodies bound to soil particles in runoff, resulting in exposure to aquatic organisms.

Refined EECs from surface runoff of flutianil were based on the parent only (no combined residues) and were modelled based on a 10-ha watershed adjacent to a 1-ha water body of 15-cm depth (amphibian habitat) or 80-cm depth (shallow pond; for model inputs see Appendix I, Table 22). The model simulates pesticide application over a 50-year period, during which time, the maximum acute and chronic EECs are generated based on the amount of pesticide entering the water body by runoff and the subsequent degradation of the pesticide in the aquatic systems. Deposition of pesticide on the water body due to spray drift is not included. The risk quotients for the refined assessment from run-off are presented in Appendix I, Table 24.

Cucurbit vegetables

Based on the modelling EECs, acute and chronic risk quotients were calculated using the 24-hour run-off EEC of 0.0029 mg a.i./L and 21-d EEC of 0.0019 mg a.i./L, respectively (Appendix I, Table 23). The 21-day pore water EEC was 0.0018 mg a.i./L.

The refined risk assessment, taking runoff into account, results in RQs of 0.09 to 0.85 (Appendix I, Table 24). Therefore, the LOC for all aquatic organisms was not exceeded. Risk to aquatic organisms is thus acceptable from runoff of flutianil applied to cucurbit vegetables.

Cherries and grape

Acute and chronic risk quotients were calculated using the 24-hour run-off EEC of 0.0019 mg a.i./L and 21-d EEC of 0.0009 mg a.i./L, respectively (Appendix I, Table 23). The 21-day pore water EEC was 0.00078 mg a.i./L.

The refined risk assessment results in RQs ranging from 0.04 to 0.42 (Appendix I, Table 24). Therefore, the LOC for all aquatic organisms was not exceeded. Risk to aquatic organisms is thus acceptable from runoff of flutianil applied to cherries and grape.

Summary of surface runoff risk to aquatic organisms

The risk to aquatic organisms from the use of flutianil when taking runoff into account is acceptable. However, standard label statements pertaining to runoff are required on the label of GATTEN. Vegetative filter strips are recommended as a best management practice to protect aquatic habitats from runoff. When used according to label directions, the risks from the use of flutianil are considered acceptable from the viewpoint of environmental protection.

5.0 Value

The results of field efficacy trials were submitted that demonstrated control of certain species of powdery mildew on cherries (Crop Subgroup 12-09A), cucurbit vegetables (Crop Group 9) and grape by application of GATTEN according to label directions. GATTEN was shown to protect leaves and fruits of cherry and grape crops and leaves of cucurbit crops from powdery mildew infection under conditions of moderate to high disease pressure. No adverse effects, including phytotoxicity, to treated crops were observed in any of the trials.

Effective powdery mildew management must be enacted preventatively and may require multiple fungicide applications over the growing season. As the active ingredient in GATTEN, flutianil, has been shown to effectively control certain species of powdery mildew on cucurbits, cherry and grape at application rates that are lower than those of registered alternatives, the availability of GATTEN may help to reduce the amount of pesticide active ingredient entering the environment. Because flutianil is a narrow spectrum active ingredient that specifically targets certain species of powdery mildews, use of GATTEN may reduce pressure on non-target species of fungi that have beneficial effects on the agro-ecosystem.

Because the risk of fungicide resistance is elevated for powdery mildews, particularly in crops such as cherry and grape in which crop rotation is not possible to break the cycle of infection, GATTEN will constitute an effective alternative product for use in fungicide rotation programs that serve to mitigate resistance development.

Details of the supported uses are provided in Appendix I, Table 26.

6.0 Pest control product policy considerations

6.1 Toxic substances management policy considerations

The *Toxic Substances Management Policy* (TSMP)[6] is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, in other words, those that meet all four criteria outlined in the policy: persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity, and toxic as defined by the *Canadian Environmental Protection Act*. The PCPA requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, flutianil and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03 and evaluated against the Track 1 criteria. The PMRA has reached the following conclusion:

- Flutianil and its transformation products do not meet all of the TSMP Track 1 criteria.

Please refer to Appendix I, Table 25 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.*[7] The list is used as described in the PMRA Science Policy Note SPN2020-01[8] and is based on existing policies and regulations, including the *Toxic Substances Management Policy* and *Formulants Policy,*[9] and taking into consideration the *Ozone-Depleting Substance Regulations*, 1998, of the *Canadian Environmental Protection Act* (substances designated under the *Montreal Protocol*).

The PMRA has reached the conclusion that flutianil and its end-use product, GATTEN, do not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

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

7 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.*

8 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.*

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

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

7.0 Proposed regulatory decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of Flutianil Technical and GATTEN, containing the technical grade active ingredient flutianil, for control of powdery mildew on cherries (Crop Subgroup 12-09A), cucurbit vegetables (Crop Group 9) and grape.

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

List of abbreviations

↑	increased
↓	decreased
♂	male
♀	female
µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
AHETF	Agricultural Handlers Exposure Task Force
ALS	acetolactate synthase
APTT	activated partial thromboplastin time
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
atm	atmosphere
ATPD	area treated per day
AUC	area under the curve
BAF	bioaccumulation Factor
BBCH	Biologishe Bundesanstalt, Bundessortenamt and Chemical industry
BCF	bioconcentration Factor
bw	body weight
bwg	body weight gain
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CG	Crop Group
cm	centimetres
Cmax	maximum plasma concentration
CR	chemical-resistant
CSG	Crop Subgroup
DF	dry flowable
DFR	dislodgeable foliar residue
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
dw	dry weight
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure
EEC	estimated environmental exposure concentration
ER_{25}	effective rate for 25% of the population
ER_{50}	effective rate on 50% of the population
FIR	food ingestion rate
FRAC	Fungicide Resistance Action Committee

g	gram
GC-ECD	gas chromatography with electron capture detection
GC/MSD	gas chromatography with mass selective detection
ha	hectare(s)
HAFT	highest average field trial
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
HPLC-MS	high performance liquid chromatography with mass spectroscopy
hr(s)	hour(s)
ILV	independent laboratory validation
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
k*P*a	kiloPascal
L	litre
LC_{50}	concentration estimated to be lethal to 50% of the test population
LD_{50}	dose estimated to be lethal to 50% of the test population
LC-MS/MS	liquid chromatography with tandem mass spectrometry
LAFT	lowest average field trial
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
mg	milligram
M/L/A	Mixer/Loader/Applicator
mL	millilitre(s)
MAS	maximum average score
MIS	maximum irritation score
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
NAFTA	North American Free Trade Agreement
ND	not detected
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required

NZW	New Zealand white
OC 53276	(Z)-2-[fluoro-5-(trifluoromethyl)phenyl sulfinyl]-2-[3-(2-methoxyphenyl) thiazolidinylidene]acetonitrile
OC 53279	(2Z)-{[2-fluoro-5-(trifluoromethyl)phenyl]sulfanyl}[4-hydroxy-3-(2-methoxyphenyl)-1,3-thiazolidin-2-ylidene]acetonitrile
OC 56574	(Z)-2-[2-fluoro-5-(trifluoromethyl)phenylthio]-2-[3-(2-methoxyphenyl)-1-oxo-1,3-thiaolidin-2-ylidene]acetonitrile
OC 56635	2-fluoro-5-(trifluoromethyl)bensenesulfonic acid
OC	organic carbon content
OM	organic matter content
PBI	plant-back interval
PCPA	*Pest Control Product Act*
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	Personal protective equipment
ppm	parts per million
PT	prothrombin time
RAC	raw agricultural commodity
REI	Restricted-entry interval
RQ	risk quotient
RSD	relative standard deviation
SC	soluble concentrate
SRBC	sheep red blood cells
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TC	Transfer coefficient
TDAR	T-dependent antibody response
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution
wt	weight

Appendix I Tables and figures

Table 1a Residue analysis

Analyte	Matrix	Method type	LOQ (ppm)	Reference
OK-5203 (flutianil)	Soil/sediment*	HPLC-MS/MS	0.01	PMRA# 2962226
	Soil/sediment*	GC-ECD	0.01	PMRA# 2962050
	Surface water	HPLC-MS/MS	0.0100 mg/L	PMRA# 2961044, 2961920
	Ground water	HPLC-MS/MS	0.0100 mg/L	PMRA #2961044, 2961920
OC 53276	Soil/sediment*	HPLC-MS/MS	0.01	PMRA #2962226
	Soil/sediment*	GC-ECD	0.01	PMRA #2962050
	Surface water	HPLC-MS/MS	0.0100 mg/L	PMRA #2961044, 2961920
	Ground water	HPLC-MS/MS	0.0100 mg/L	PMRA #2961044, 2961920
OC 53279	Surface water	HPLC-MS/MS	0.0100 mg/L	PMRA #2961044, 2961920
	Ground water	HPLC-MS/MS	0.0100 mg/L	PMRA #2961044, 2961920
OC 56574	Soil/sediment*	HPLC-MS/MS	0.01	PMRA #2962226
	Soil/sediment*	GC-ECD	0.01	PMRA #2962050
	Surface water	HPLC-MS/MS	0.0100 mg/L	PMRA #2961044, 2961920
	Ground water	HPLC-MS/MS	0.0100 mg/L	PMRA #2961044, 2961920
OC 56635	Soil/sediment*	HPLC-MS/MS	0.01	PMRA #2962226
	Soil/sediment*	GC-ECD	0.01	PMRA #2962050
	Surface water	HPLC-MS/MS	0.0100 mg/L	PMRA# 2961044, 2961920
	Ground water	HPLC-MS/MS	0.0100 mg/L	PMRA# 2961044, 2961920
Flutianil and major metabolites	Plant/animal	Being reviewed by HED residue evaluator.		
* The soil method can be extended to sediment.				

Table 1b Residue analysis

Analytical methods	Matrix	Analyte(s)	Method ID/ Type	LOQ (ppm)	Reference
Plant commodities					
Enforcement Method	Grape, strawberry, cucumber, apple	Flutianil	GC-ECD (CLE 2554/019-01V)	0.01	Study No. 2554/019 PMRA# 2962214
	Grape and processed commodities	Flutianil and metabolite OC 56635	LC-MS/MS (181C-105)	0.01	Study No. 181C-105 PMRA# 2962224
Data-Gathering Method	Apple	Flutianil	GC/MSD (adapted from RM-44C-2)	0.01	Study No. 09634 (PMRA# 2962228) and 09634.06-CAR17 (PMRA# 2962237)
ILV of Enforcement Method	Grape, cucumber	Flutianil	GC-ECD (CLE 2554/019-01V)	0.01	Study No. CEMS-3577 PMRA# 2962218
	Grapes, raisin, juice	Flutianil and metabolite OC 56635	LC-MS/MS (181C-105)	0.01	Study No. 2K15-1403-0114 PMRA# 2962247
	Grape, wheat grain, sunflower seed	Flutianil	QuEChERS (DFG S 19; extended revision): Multi Method L 00.00-34	0.01	Study No. EBJ0005 PMRA# 2962222
Radiovalidation	Cucumber, apple	Flutianil	GC-ECD (CLE 2554/019-01V) GC-MSD (adapted from RM-44C-2)	N/A	Study No. 2554/033 PMRA# 2962216
	Apple	Flutianil	GC-ECD (CLE 2554/019-01V) GC-MSD (adapted from RM-44C-2)	N/A	Study No. 181C-108 PMRA# 2962228

Analytical methods	Matrix	Analyte(s)	Method ID/ Type	LOQ (ppm)	Reference
Multiresidue Method Testing	Cucumber, grape, wheat grain, dry bean seed, sunflower seed	Flutianil	QuEChERS (DFG S 19; extended revision): Multi Method L 00.00-34	0.01	Study No. S10-02916 PMRA# 2962220
		OC 56635		0.01	Study No. ADPEN-2K15-OAT-0501-001 PMRA# 2962230

N/A: not applicable

Table 2 Identification of select transformation products and metabolites of Flutianil

Code	Chemical name	Source
OC 56635	2-fluoro-5-(trifluoromethyl)benzenesulfonic acid	Transformation product, rat metabolite
OC 63421	sodium 2-fluoro-5-(trifluoromethyl) benzenesulfonate	Sodium salt of OC 56635
OC 53276	(Z)-2-[2-fluoro-5-(trifluoromethyl)phenylsulfinyl]-2-[3-(2-methoxyphenyl) thiazolidinylidene]acetonitrile	Transformation product
OC 53429	(z)-2-[(2-fluoro-5-methyl)phenylthio]-2-[3-(2-methoxyphenyl)-2-thiazolidinylidene]acetonitrile	Rat metabolite
OC 53982	(z)-2-[(2-fluoro-5-difluoromethyl)phenylthio]-2-[3-(2-methoxyphenyl)-2-thiazolidinylidene]acetonitrile	Rat metabolite

Table 3 Toxicity profile of Technical Flutianil

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

Study Type/Animal/PMRA#	Study results
Toxicokinetic studies	
Absorption, distribution, toxicokinetics, metabolism and excretion study following single and repeat gavage doses	Absorption, distribution, metabolism and excretion were investigated with [CF_3Ph-U-^{14}C]-flutianil or [MeOPh-U-^{14}C]-flutianil. Single doses were administered by gavage at 10, 250 or 1000 mg/kg bw. Bile duct-cannulated rats were administered a single oral gavage dose of 1 mg/kg bw. In a repeated dose study, animals were administered 10 mg/kg bw/day of flutianil for 14 days

Wistar Rats PMRA# 2961986, 2961989, 2961991, 2961993 and 2961996	followed by a single dose of [CF_3Ph-U-^{14}C]-flutianil or [MeOPh-U-^{14}C]-flutianil at 10 mg/kg bw. **Absorption** Absorption was low and decreased with increasing dose level, ranging from approximately 18% to 2% of the administered dose (AD). The increases in AUC and Cmax of blood from 10 to 1000 mg/kg bw were not proportional to the increase in dose, suggesting saturation of absorption. Comparison of the plasma and blood concentration data suggested that flutianil and/or its radiolabelled metabolites were associated with the cellular fraction of the blood. There were no significant sex-related differences in absorption with either radiolabel. **Distribution** Flutianil was widely distributed throughout the tissues following oral administration. For most tissues, the maximum tissue concentration was detected at 2 hrs and 8 hrs for animals treated with [MeOPh-U-^{14}C]-flutianil and [CF_3Ph-U-^{14}C]-flutianil, respectively. With the exception of the gastrointestinal tract and carcass, liver followed by kidney contained the greatest amount of radioactivity. The increases of radioactivity in tissues were not proportional to the increases in the dose levels. Overall, tissue retention was low with low or no detectable levels of the radioactivity retained in tissues at 120 hrs post-dosing. **Excretion** Most of the radioactivity (>80%) was eliminated in feces within 48 hrs post-dosing. Excretion was mainly via the feces, accounted for up to 97.9% of the AD. Urinary excretion accounted for up to 19% of the AD. Biliary excretion accounted for up to 11% of the AD. The proportion of urinary radioactivity was lower in cannulated rats when compared to that of the intact rats, which suggested enterohepatic circulation of unchanged flutianil and/or metabolites. **Metabolism** There was no significant sex difference in the metabolite profile. The major urinary metabolites were Met 6 and Met 11. Met 6 was identified as a mercapturate conjugate of a hydroxylated methylsulphoxy trifluoromethyl ring structure accounting for up to 5.5% of the AD. Met 11 accounted for up to 3.72% of the AD. Unchanged flutianil was the major component identified in the feces, indicating limited metabolism. Two minor metabolites OC 53429 and OC 53982 were identified in feces, which accounted for up to 3.8% and 1.42% of the AD, respectively. The major biliary metabolites were Met 8 and Met 9, which accounted for 2.03% and 1.21% of the AD, respectively. Numerous uncharacterized metabolites were present in urine, feces and bile. None of the metabolites accounted for more than 10% of the AD. When compared with single-dose administration, repeated-dose administration resulted in slightly lower urinary excretion, but resulted in no major differences in the absorption, distribution, metabolism or excretion of flutianil.

Acute toxicity studies	
Acute oral toxicity (gavage) Sprague-Dawley rats PMRA# 2961735	LD_{50} > 5000 mg/kg bw (♀) No clinical signs of toxicity Low acute toxicity
Acute dermal Toxicity Sprague-Dawley rats PMRA# 2961737	LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity Low acute toxicity
Acute inhalation Toxicity Wistar rats PMRA# 2961739	LC_{50} > 5.17 mg/L (♂/♀) Clinical signs at 5.17 mg/L included unkempt appearance, vocalization, wet fur and staining of the head Low acute toxicity
Primary eye irritation Japanese White rabbits PMRA# 2961741	MAS = 0/110 MIS = 4.7/110 at 1 hour Non-irritating
Primary dermal irritation Japanese White rabbits PMRA# 2961743	MAS = 0/8 MIS = 0/8 Non-irritating
Skin sensitization (Maximization Method) Hartley Guinea pigs PMRA# 2961745	Negative
Short-term toxicity studies	
28-day oral toxicity (dietary) ICR mice PMRA# 2961922	Supplemental NOAEL and LOAEL not established No treatment-related effects Limitations: no histopathology assessment
90-day oral toxicity (dietary) ICR mice PMRA# 2961929	NOAEL = 1387/1555 mg/kg bw/day (♂/♀) LOAEL not identified No treatment-related effects

28-day oral toxicity (dietary) Wistar rats PMRA# 2961924	NOAEL = 159/172 mg/kg bw/day (♂/♀) LOAEL = 1555/1714 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ thyroid wt, ↑ liver wt (♂/♀); ↓ plasma glucose, ↓ plasma triglyceride, ↓ plasma total bilirubin, ↑ kidney wt, ↑ incidence of hyaline droplets in kidney (♂); ↓ heart wt, ↓ spleen wt (♀)
90-day oral toxicity (dietary) Wistar rats PMRA# 2961932	NOAEL = 122/1500 mg/kg bw/day (♂/♀) LOAEL = 1271 mg/kg bw/day/not established (♂/♀) Effects at LOAEL: ↑ liver wt, ↑ PT, ↑ APTT, ↑ incidence of hyaline droplets in kidney
28-day oral toxicity (capsule) Beagle dogs PMRA# 2961934	Supplemental- dose range-finding NOAEL and LOAEL not established No treatment-related effects
90-day oral toxicity (capsule) Beagle dogs PMRA# 2961936	NOAEL = 1000 mg/kg bw/day LOAEL not identified No treatment-related effects
12-month oral toxicity (capsule) Beagle dogs PMRA# 2961956	NOAEL = 1000 mg/kg bw/day LOAEL not identified No treatment-related effects
28-day dermal toxicity Wistar rats PMRA# 2961938	NOAEL = 1000 mg/kg bw/day LOAEL Not identified No treatment-related effects
90-Day dermal toxicity (waiver request) PMRA# 2961702	Request to waive conditional requirement for 90-day dermal toxicity study accepted based on low toxicity of flutianil in the 28-day dermal study and low overall toxicity in oral studies. In addition, this study was not required for this use pattern.
28-Day inhalation toxicity Sprague-Dawley rats PMRA# 2961940	NOAEC = 0.1 mg/L (~26 mg/kg bw /day) (♂/♀) LOAEC = 1 mg/L (~261 mg/kg bw/day) (♂/♀) Effects at LOAEC: ↑ incidence of hepatocellular hypertrophy, atrophy of the olfactory epithelium in the nose, hyperplasia/hypertrophy of the mucous cells in the nose and centriacinar inflammation in the lungs (♂/♀); ↓ bw, ↓ bwg, ↑ incidence of inflammation of nasal turbinates, ↑ incidence of tubular hyaline droplets in kidney (♂); ↑ liver wt (♀)

90-Day inhalation toxicity (waiver request) PMRA# 2961703	Request to waive conditional requirement for 90-day inhalation toxicity study accepted based on the margins of exposure obtained for the inhalation exposure risk assessment when using the point of departure from the 28-day inhalation toxicity study.
Chronic toxicity/Oncogenicity studies	
78-week oncogenicity (dietary) CD-1 mice PMRA# 2961659	NOAEL = 321/316 mg/kg bw/day (♂/♀) LOAEL = 1084/1063 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ incidence of luminal dilatation in urinary bladder, urinary bladder distended with urine, softening/atrophy of the testis (♂); ↓ bw (wks 20-60) (♀) No evidence of tumourigenicity
2-year combined chronic toxicity/oncogenicity with 1-year satellite group (dietary) Wistar rats PMRA# 2961961	NOAEL = 82/376 mg/kg bw/day (♂/♀) LOAEL = 249/1247 mg/kg bw/day (♂/♀) Effects at LOAEL: ↑ incidences of foci of cellular alteration in liver, ↑ incidence of hyaline droplets in kidney (♂); ↑ liver wt, ↑ incidences of bile duct hyperplasia (♀) No evidence of tumourigenicity
Developmental/Reproductive toxicity studies	
1-generation reproductive toxicity (dietary) Wistar rats PMRA# 2961951	Supplemental - dose range-finding NOAEL and LOAEL not established Parental Effect at and above 111/227 mg/kg bw/day (♂/♀): ↑ liver wt Reproductive No treatment-related reproductive effects Offspring No treatment-related offspring effects
2-generation reproductive toxicity (dietary) Wistar rats PMRA# 2961954	Parental NOAEL = 1286/1942 mg/kg bw/day (♂/♀) Parental LOAEL not identified No adverse treatment-related parental effects Offspring NOAEL = 1286/1942 mg/kg bw/day (♂/♀) Offspring LOAEL not identified No treatment-related offspring effects Reproductive NOAEL = 1286/1942 mg/kg bw/day (♂/♀) Reproductive LOAEL not identified No treatment-related reproductive effects

	No evidence of sensitivity of the young
Developmental toxicity (gavage) Wistar rats PMRA# 2961942	Supplemental - dose range-finding NOAEL and LOAEL not established No treatment-related maternal or developmental effects (external examination only) observed up to 1000 mg/kg bw/day
Developmental toxicity (gavage) Wistar rats PMRA# 2961944	Maternal NOAEL = 1000 mg/kg/day Maternal LOAEL not identified Developmental NOAEL = 333 mg/kg bw/day Developmental LOAEL = 1000 mg/kg bw/day Effects at LOAEL: ↑ incidence of incompletely or unossified sternal centra No treatment-related malformations Evidence of sensitivity of the young
Developmental toxicity (gavage) NZW rabbits PMRA# 2961946	Supplemental - dose range-finding NOAEL and LOAEL not established No treatment-related maternal or developmental effects (external examination only) observed up to 1000 mg/kg bw/day
Developmental toxicity (gavage) NZW rabbits PMRA# 2961948	Maternal NOAEL = 1000 mg/kg bw/day Maternal LOAEL not identified Developmental NOAEL = 1000 mg/kg bw/day Developmental LOAEL not identified No treatment-related malformations No evidence of sensitivity of the young
Genotoxicity studies	
Bacterial reverse mutation assay *Salmonella typhimurium* (TA 1535, TA 1537, TA 98, TA 100); *E. coli* (WP2uvrA) PMRA# 2961966	Negative ± metabolic activation Tested up to a limit concentration
In vitro mammalian cell forward gene mutation assay	Negative ± metabolic activation Tested up to a precipitating concentration

L5178Y TK$^{\pm}$ Mouse Lymphoma Cells PMRA# 2961972	
In vitro mammalian cytogenetics [chromosome aberration] Human lymphocyte cells PMRA# 2961978	Negative ± metabolic activation Test up to a cytotoxic concentration
In vivo cytogenetics - micronucleus assay in mouse NMRI mice PMRA# 2961980	Negative No mortality or clinical signs of toxicity Tested up to a limit dose
Special studies (non-guideline)	
28-day immunotoxicity (dietary) Wistar rats PMRA# 2961997	NOAEL = 1251 mg/kg bw/day (♂) LOAEL not identified No treatment-related effects (general systemic effects or on anti-SRBC TDAR response) No evidence of immune system dysregulation
Neurotoxicity studies	
Neurotoxicity (waiver request) PMRA# 2961740	Request to waive the conditional requirement for neurotoxicity testing accepted based on the absence of treatment-related findings in the neurotoxicity functional observation batteries that were assessed in the rat 28-day dermal, 90-day and two-year chronic toxicity/oncogenicity oral studies in rats, as well as consideration of the overall low toxicity of flutianil in the oral toxicity studies.
Metabolite studies	
Metabolite OC 56635	
Acute oral toxicity (Fixed dose) (gavage) Wistar rats PMRA# 2961731	LD_{50} between 500 mg/kg bw and 1000 mg/kg bw (♀) Moderate toxicity The single animal dosed at 2000 mg/kg bw died; no mortality or signs of toxicity in all five animals dosed at 300 mg/kg bw.
Bacterial reverse mutation assay	Negative ± metabolic activation Tested up to a limit concentration

Salmonella typhimurium (TA 1535, TA 1537, TA 98, TA 100); *E. coli* (WP2uvrA) PMRA# 2961968	
In vitro mammalian cell forward gene mutation assay L5178Y TK$^{\pm}$ Mouse Lymphoma Cells PMRA# 2961974	Negative ± metabolic activation Tested up to a limit concentration
In vivo cytogenetics - micronucleus assay in mice ICR mice PMRA# 2961982	Negative Test up to a maximum tolerated dose
Metabolite OC 63421	
Acute oral toxicity (gavage) Wistar rats PMRA# 2961733	LD_{50} > 2000 mg/kg bw (♀) No clinical signs of toxicity Low acute toxicity
28-day oral (dietary) Wistar rats PMRA# 2961927	NOAEL = 4740/4860 mg/kg bw/day (♂/♀) LOAEL not established No treatment-related effects
Metabolite OC 53276	
Bacterial reverse mutation assay *Salmonella typhimurium* (TA 1535, TA 1537, TA 98, TA 100); *E. coli* (WP2uvrA) PMRA# 2961970	Negative ± metabolic activation Tested up to a limit concentration
In vitro mammalian cell forward gene mutation assay	Negative ± metabolic activation Tested up to a precipitating concentration or a cytotoxic concentration

L5178Y TK$^{\pm}$ Mouse Lymphoma Cells PMRA# 2961976	
In vivo cytogenetics - micronucleus assay in mouse ICR mice PMRA# 2961984	Negative Tested up to a limit dose

Table 4 Toxicity profile of the end-use product GATTEN, containing Flutianil

Study type/Animal/PMRA #	Study results
Acute oral toxicity (gavage) Sprague-Dawley rats PMRA# 2962256	LD_{50} > 5000 mg/kg bw (♀) No clinical signs of toxicity Low acute toxicity
Acute dermal toxicity Sprague-Dawley rats PMRA# 2962258	LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity Low acute toxicity
Acute inhalation toxicity Wistar rats PMRA# 2962260	LC_{50} > 4.82 mg/L (♂/♀) Clinical signs at 4.82 mg/L included wet fur, hunched posture, increased respiratory rate and red/brown staining around eyes Low acute toxicity
Primary eye irritation NZW rabbits PMRA# 2962262	MAS = 20.2/110 MIS = 23.3/110 at 24 hr Moderately irritating
Primary dermal irritation NZW rabbits PMRA# 2962264	MAS = 1.7/8 MIS = 1.7/8 at 24, 48 and 72 hrs Mildly irritating

Study type/Animal/PMRA #	Study results
Skin sensitization (Buehler) Hartley guinea pig PMRA# 2962266	Positive Potential dermal sensitizer

Table 5 Toxicology reference values for use in health risk assessment for Flutianil

Exposure scenario	Study	Point of departure and endpoint	CAF[1] or Target MOE
Acute dietary general population	Not required, as an endpoint of concern attributable to a single exposure was not identified.		
Repeated (chronic) dietary	2-year dietary chronic toxicity/oncogenicity study in rats	NOAEL = 82 mg/kg bw/day Liver toxicity	100
	ADI = 0.8 mg/kg bw/day		
Short and intermediate -term dermal[2]	Developmental toxicity study in rats	Developmental NOAEL = 333 mg/kg bw/day Delayed bone development	300
Short and intermediate -term inhalation	28-day inhalation toxicity study in rats	NOAEC = 0.1 mg/L (~26 mg/kg bw/day) Effects in the liver, nasal cavity and lung as well as decreased body weight	100
Cancer	No treatment-related tumours were observed; therefore, a cancer risk assessment is not required		

[1] CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments; MOE refers to a target MOE for occupational and residential assessments.
[2] Since an oral NOAEL was selected, a dermal absorption factor of 100% (default value) was used in a route-to-route extrapolation.

Table 6 AHETF and PHED Unit exposure estimates for mixers, loaders and applicators handling GATTEN (µg/kg a.i. handled)

Exposure scenario and PPE		Dermal	Inhalation[1]
PPE: Single layer and chemical-resistant gloves			
Mixer/loader AHETF estimates			
A	Open Mix/Load Liquids	58.5	0.63
Applicator AHETF estimates			
B	Open Cab Airblast Liquid Application – Without CR Hat	3769.3	9.08
C	Open Cab Groundboom Liquid Application	25.40	1.68

Exposure scenario and PPE		Dermal	Inhalation[1]
Mixer/loader + applicator AHETF estimates			
A+B	Open Mix/Load Liquids and Open Cab Airblast Liquid Application – Without CR Hat	3827.8	9.71
A+C	Open Mix/Load Liquids and Open Cab Groundboom Liquid Application	83.9	2.31
PHED Mixer/loader/applicator			
E	Liquid/Open Pour/Backpack (M/L/A)	5445.85	62.10
F	Liquid/Open Pour/Manually-Pressurized Handwand	943.37	45.20
G	Liquid/Open Pour/Mechanically-Pressurized Handgun	5585.49	151

[1] Light inhalation rate (moderate for backpack)

Table 7 Mixer/Loader/Applicator exposure and risk estimates for GATTEN

Exposure scenario	Dermal unit exposure (µg/kg a.i. handled)[1]	Inhalation unit exposure (µg/kg a.i. handled)[1]	ATPD (ha/day or L/day)[2]	Rate (kg a.i./ha)	Dermal daily exposure (mg/kg bw/day)[3]	Inhalation daily exposure (mg/kg bw/day)[3]	Dermal MOE[4]	Inhalation MOE[5]
PPE: Single layer and chemical-resistant gloves								
Open Mix/Load Liquids and Open Cab Airblast Application – Without CR Hat	3827.8	9.71	20 ha (cherries / grapes)	0.035	0.03349	8.50E-05	9942	306,017
Open Mix/Load Liquids and Open Cab Groundboom Application	83.9	2.31	26 ha (cucurbits)	0.035	0.00095	1.080E-05	348,924	989,487
Liquid/ Open Pour / Backpack	5445.85	62.10	150 L	0.035	0.00191	2.181E-05	174,241	1,193,037
Liquid/ Open Pour/ Manually-Pressurize Handwand	943.37	45.20	150 L	0.035	0.00033	1.59E-05	1,005,853	1,639,107

Exposure scenario	Dermal unit exposure (µg/kg a.i. handled)[1]	Inhalation unit exposure (µg/kg a.i. handled)[1]	ATPD (ha/day or L/day)[2]	Rate (kg a.i./ha)	Dermal daily exposure (mg/kg bw/day)[3]	Inhalation daily exposure (mg/kg bw/day)[3]	Dermal MOE[4]	Inhalation MOE[5]
Liquid/ Open Pour/ Mechanically-Pressurized Handgun	5585.49	151	3800 L	0.035	0.0496570	0.001342	6706	19,368

PPE: personal protective equipment; CR: chemical-resistant.
[1] Unit exposure based on AHETF or PHED.
[2] Default Area Treated per Day table (updated on 2017-09-20) or lowest dilution (187 L/ha).
[3] Daily exposure = (Unit exposure [µg/kg a.i.] × ATPD [ha/day or L/day] × Rate [kg a.i./ha]) ÷ (80 kg bw × 1000 µg/mg).
[4] Based on the dermal NOAEL of 333 mg/kg bw/day and a dermal target MOE of 300.
[5] Based on the inhalation NOAEL of 26 mg/kg bw/day and an inhalation target MOE of 100.

Table 8 Flutianil dislodgeable foliar residue study results on apples, grapes and cantaloupe using GATTEN

Site	Trend	R^2	Peak DFR (% of application rate after last application)
Apples (New York)	y = -0.0017× - 1.9421	R^2 = 0.8384	19.5% (0.193 µg/cm)
Grapes (California)	y = -0.0029× - 2.9366	R^2 = 0.8119	8.83% (0.083 µg/cm)
Cantaloupe (Texas)	y = -0.0051× - 2.4506	R^2 = 0.9171	29% (0.165 µg/cm)

Table 9 Workers postapplication exposure and risk estimates for Flutianil on day 0 after the last application

Postapplication activity	Peak DFR (µg/cm²)[1]	TC (cm²/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI[5]
Cherries (crop subgroup 12-09A)					
Thinning	0.063 (adjusted actual value)	3000	0.0189	17 619	12 hours
Hand harvesting		1400	0.0088	37 755	
Scouting, training		580	0.0037	91 133	
Transplanting		230	0.0014	229 814	
Hand weeding, bird control, propping		100	0.0006	528 571	

Grapes					
Girdling	0.147 (adjusted actual value)	19,300	0.2837	1174	12 hours
Tying, training, hand harvesting		8500	0.1250	2665	
Hand set irrigation		1750	0.0257	12 945	
Scouting and various other orchard activities		640	0.0094	35 395	
Transplanting		230	0.0034	98 492	
Cucurbits vegetables (crop group 9)					
Irrigation (handset)	0.155 (predicted)	1750	0.0271	12 287	12 hours
Hand harvesting, mechanically assisted harvesting, turning, training		550	0.0085	39 096	
Transplanting		230	0.0036	93 490	
Scouting, hand weeding, hand pruning, hand thinning		90	0.0014	238,919	

DFR = Dislodgeable foliar residue; TC = Transfer Coefficient; MOE = Margin of Exposure; REI = Restricted-Entry Interval
[1] Calculated using the actual highest peak DFR value from the grapes (0.193 µg/cm^2) and apples (0.083 µg/cm^2) after the last application at 45.9 g a.i./ha application rate from the DFR study. The peak DFR was adjusted using the supported rate of 35 g a.i./ha by taking the peak DFR value and multiplying it by the ratio of the supported rate vs the study rate. (Peak DFR × (35 g a.i./ha ÷ 45.9 g a.i./ha)). For cucurbits, the predicted DFR value was calculated using a dissipation rate of 29% per day from the cantaloupe DFR study regression analysis.
[2] Transfer coefficients obtained from PMRA Agricultural TCs Table.
[3] Exposure = (Peak DFR [µg/cm^2] × TC [cm^2/hr] × 8 hours/day) ÷ (80 kg bw × 1000 µg/mg).
[4] Based on the dermal NOAEL of 333 mg/kg bw/day and a dermal target MOE of 300.
[5] Minimum REI is 12 hours to allow residues to dry, suspended particles to settle and vapours to dissipate.

Table 10 Residential Postapplication Exposure and Risk Estimates on Day 0 from Orchard Trees Treated Commercially with Flutianil

Crop (Max rate; # app; RTI)	Life stage	Peak DFR (µg/cm^2)[1]	TC (cm^2/hr)[2]	Exposure duration (hr/day)	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI
Cherries (35 g a.i./ha; 4/season; 7-day RTI)	Adults (≥16 years)	0.063	1700	1	1.34E-03	248,739	Until sprays have dried
	Children (6 < 11 years)		930	0.5	9.15E-04	363,748	Until sprays have dried

DFR = Dislodgeable foliar residue; TC = Transfer Coefficient; MOE = Margin of Exposure.
[1] Calculated using the actual highest peak DFR value for apples (0.083 µg/cm^2) after the last application at 45.9 g a.i./ha application rate from the DFR study. The peak DFR was adjusted using the supported rate of 35 g a.i./ha by taking the peak DFR value and multiplying it by the ratio of the supported rate vs the study rate. (Peak DFR × (35 g a.i./ha ÷ 45.9 g a.i./ha)).
[2] A single TC is representative of all activities in residential fruit trees. TCs were obtained from the PMRA memo entitled

"Review of U.S. EPA Residential SOPs (2012) Section 4: Gardens and Trees" (Sept. 6, 2019) and the 2012 USEPA SOP for Residential Pesticide Exposure Assessment.

[3] Exposure = (Peak DFR [µg/cm^2] × TC [cm^2/hr] × Exposure duration [hours/day]) ÷ (Body weight [80 kg for adults; 32 kg for children] × 1000 µg/mg).

[4] Based on the dermal NOAEL of 333 mg/kg bw/day and a dermal target MOE of 300.

Table 11 Integrated food residue chemistry summary

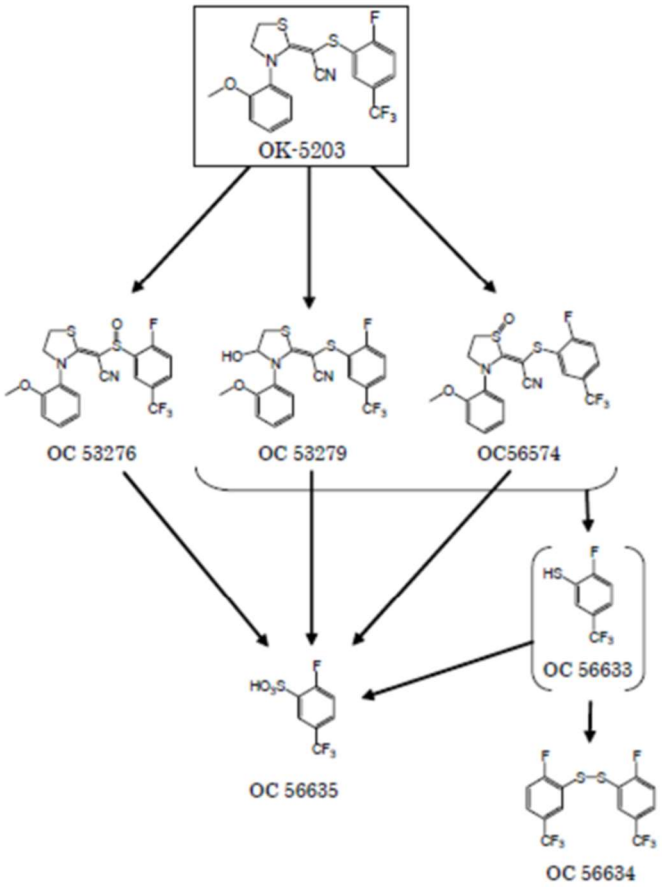
Nature of the residue in grapes			**PMRA# 2961903**
Radiolabel Position	[methoxyphenyl-U-^{14}C]flutianil (MP-label; specific activity 1.25-1.26 MBq/mg) and [trifluoromethylfluorobenzene-U-^{14}C]flutianil (FP-label; specific activity 1.23-1.25 MBq/mg)		
Treatment			
Test Site	In outdoor plots in Porterville, CA		
Treatment	Four foliar broadcast sprays at BBCH 79, BBCH 81, and BBCH 85 (×2)		
Total Rate	Target: 40 g a.i./ha each, for a total rate of 160 g a.i./ha		
Formulation	Suspension concentrate (SC) formulation		
Harvest	Grape bunches and foliage were harvested at PHIs of 1 day (immature), 21 days (early mature), and 45 days (late mature).		
Extraction solvents	Methanol (3×), methanol:water (1:1, v/v, 3×), water (1×), 0.1N hydrochloric acid (1×), 0.1N sodium hydroxide (1×), acetone (1×)		
Matrices	**PHI (days)**	**MP-label TRR (ppm)**	**FP-label TRR (ppm)**
Grape	1 (Immature)	0.302	0.355
	21 (Early mature)	0.149	0.222
	45 (Mature)	0.170	0.228
Foliage	1 (Immature)	3.974	2.693
	21 (Early mature)	5.186	5.409
	45 (Mature)	5.337	3.872
NATURE OF THE RESIDUE IN APPLE			**PMRA# 2961905**
Radiolabel Position	[methoxyphenyl-U-^{14}C]flutianil (MP-label; specific activity 3.782 MBq/mg) and [trifluoromethylfluorobenzene-U-^{14}C]flutianil (FP-label; specific activity 3.735 MBq/mg)		
Treatment			
Test Site	In outdoor plots in Porterville, CA		
Treatment	Three foliar broadcast applications at BBCH 79 (2×) and BBCH 81		
Total Rate	Target: 75 g a.i./ha each, for a total rate of 225 g a.i./ha		

Formulation	Emulsifiable concentrate (EC) formulation		
Harvest	Mature apples were harvested at PHIs of 1, 14, 21, and 35 days. Foliage was harvested at PHIs of 14, 30, and 35 days.		
Extraction solvents	Methanol (3×), methanol:water (1:1, v/v; 3×), water (1×), 0.1N hydrochloric acid (1×), 0.1N sodium hydroxide (1×), and acetone (1×).		
Matrices	**PHI (days)**	**MP-label**	**FP-label**
		TRR (ppm)	**TRR (ppm)**
Apple	1	0.151	0.188
	14	0.078	0.077
	21	0.075	0.046
	35	0.093	0.027
Foliage	14	8.499	4.873
	30	8.209	5.055
	35	6.726	4.530
NATURE OF THE RESIDUE IN CUCUMBER			**PMRA# 2961907**
Radiolabel Position	[methoxyphenyl-U-^{14}C]flutianil (MP-label; specific activity 3.782 MBq/mg) and [trifluoromethylfluorobenzene-U-^{14}C]flutianil (FP-label; specific activity 3.735 MBq/mg)		
Treatment			
Test Site	In individual containers in a greenhouse in North Yorkshire, UK.		
Treatment	Four foliar broadcast applications at 50, 64, 78, and 91 days after planting.		
Total Rate	Actual: 52–60 g a.i./ha each, for a total rate of 221 g a.i/ha (MP-label) and 56–58 g a.i./ha each for a total rate of 228 g a.i./ha (FP-label). Applications were made 13 and 14 days apart.		
Formulation	Emulsifiable concentrate (EC) formulation		
Harvest	Mature cucumbers were harvested at BBCH 8, at PHIs of 1, 3, and 15 days. Cucumber foliage was harvested at PHIs of 3 and 15 days.		
Extraction solvents	Methanol (3×), methanol:water (1:1, v/v; 3×), 0.1N hydrochloric acid (3×), and 0.1N sodium hydroxide (3×).		
Matrices	**PHI (days)**	**MP-label**	**FP-label**
		TRR (ppm)	**TRR (ppm)**
Cucumber	1	0.012	0.026
	3	0.008	0.006
	15	0.004	0.001
Foliage	3	2.108	3.238
	15	1.136	1.333
NATURE OF THE RESIDUE IN LETTUCE			**PMRA # 2961909**
Radiolabel Position	[methoxyphenyl-U-^{14}C]flutianil (MP-label; specific activity 3.782 MBq/mg) and [trifluoromethylfluorobenzene-U-^{14}C]flutianil (FP-label; specific activity 3.735 MBq/mg)		

Treatment			
Test Site	In containers in a greenhouse in North Yorkshire, UK.		
Treatment	Five foliar broadcast applications at 57, 64, 71, 78, and 85 days after planting.		
Total Rate	Actual: 42–46 g a.i./ha each, for a total rate of 223 g a.i/ha (MP-label) and 45 g a.i./ha each for a total rate of 225 g a.i./ha (FP-label). Applications were made 7 days apart.		
Formulation	Emulsifiable concentrate (EC) formulation		
Harvest	Mature lettuce was harvested 92 days after planting (7-day PHI)		
Extraction solvents	Methanol (3×), methanol:water (1:1, v/v; 3×), water (3×), 0.1N hydrochloric acid (3×), 0.1N sodium hydroxide (3×), and acetone.		
Matrices	**PHI (days)**	**MP-label**	**FP-label**
		TRR (ppm)	**TRR (ppm)**
Lettuce heads	7	0.050	0.026
Lettuce wrapper leaves	7	2.112	1.937

Summary of major identified metabolites in plant matrices		
Radiolabel position	**MP-label**	**FP-label**
Metabolites identified	**Major metabolites**	
Grapes	Flutianil	Flutianil
Grape foliage	Flutianil	Flutianil
Apples	Flutianil	Flutianil
Apple foliage	Flutianil	Flutianil OC 56635 (35-day PHI only)
Cucumbers	Flutianil Unknown 5(A) (15-day PHI only)	Flutianil
Cucumber foliage	Flutianil	Flutianil
Lettuce head	Flutianil	Flutianil
Lettuce wrapper leaves	Flutianil	Flutianil

Proposed Metabolic Scheme in Plants



FREEZER STORAGE STABILITY IN PLANT MATRICES

Tested matrices	Analyte(s)	Tested intervals (months)	Temperature (°C)	Demonstrated stability (months)
Apple	Flutianil	0, 1, 3, 6, 9, 12[1] and 18[2]	-20	18
Grapes	Flutianil	0, 1, 3, 6, 9, and 12[1]		12
Grapes, grape juice, raisins	Flutianil	0, 3, 6, and 14.6[1]		14.6
	OC 56635	0, 3, and ~6[1]		~6
Summer squash	Flutianil	~13[2]		~13
Cucumber	Flutianil	~15[2]		~15
Cantaloupe	Flutianil	~11[2]		~11
Cherries	Flutianil	~12[2]		~12
Strawberries	Flutianil	~12[2]		~12
Radish	Flutianil + OC 56635	0, 1 and 7.3[2]		7.3
Spinach	Flutianil + OC 56635	0, 1 and 7.3[2]		7.3

Wheat	Flutianil + OC 56635	0, 1, 7, and 8.2[2] (forage) 0, 1, 6, and 8.9[2] (hay) 0, 1, and 4.4[2] (straw and grain)		8.2 (forage) 8.9 (hay) 4.4 (straw and grain)

[1] Stand-alone freezer storage stability study
[2] Concurrent freezer storage stability data

Crop field trials and residue decline on cucurbit vegetables	**PMRA# 2962239 (summer squash), 2962241 (cucumber), 2962243 (cantaloupe)**

Crop field trials were conducted in 2006–2007. Cantaloupe trials were conducted in North American growing regions 2 (2 trials), 5 (1 trial), 6 (1 trial), and 10 (3 trials) for a total of 7 trials; cucumber trials were conducted in North American growing regions 2 (2 trials), 3 (1 trial), 5 (2 trials) and 6 (1 trial) for a total of 6 trials; summer squash trials were conducted in North American growing regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (1 trial), 10 (1 trial), and 11 (1 trial) for a total of 6 trials. V-10118, an emulsifiable concentrate formulation of flutianil, was applied five times as foliar broadcast sprays at a rate of 45 g a.i./ha for a seasonal application rate of 225 g a.i./ha. The applications were made at 7-day intervals with the last application occurring approximately 0 days before harvest. No adjuvant was used. Independence of trials was assessed for each representative crop from the various crop groups. Residue decline data show that residues of flutianil decreased in cantaloupe with increasing PHIs. Adequate concurrent storage stability data are available to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total Application Rate (g a.i./ha)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Summer squash	223–229	0	Flutianil	6	<0.01	0.020	0.01	0.012	0.004
Cucumber	221–231			6	<0.01	0.012	0.01	0.010	<0.001
Cantaloupe	224–226			7	<0.01	0.042	0.014	0.018	0.011

n = number of independent trials. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SDEV = Standard Deviation
For computation, values <LOQ are assumed to be at the LOQ.

Crop field trials and residue decline on cherries	**PMRA# 2962269**

Crop field trials were conducted in 2007–2008 in North American growing regions 1 (1 trial), 5 (2 trials), 9 (1 trial), 10 (2 trials), 11 (1 trial), and 12 (3 trials) for a total of 10 trials; however, independence of trials was assessed and, after accounting for replicate trials, there are a total of 8 independent trials. V-10118, an emulsifiable concentrate formulation of flutianil, was applied four times as foliar broadcast sprays at a rate of 45 g a.i./ha for a seasonal application rate of 180 g a.i./ha. The applications were made at 6- to 8-day intervals with the last application occurring approximately 2-4 days before harvest. No adjuvant was used. Foliar applications were made using ground equipment with concentrated and/or dilute spray volumes; residues from dilute and concentrate spray volumes were similar. Residue decline data show that residues of flutianil decreased in cherries with increasing PHIs. Adequate concurrent storage stability data are available to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total Application Rate (g a.i./ha)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Cherries	157–235	2–4	Flutianil	8	0.07	0.24	0.11	0.13	0.06

n = number of independent trials. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SDEV = Standard Deviation

Crop field trials and residue decline on grapes **PMRA# 2962271**

Crop field trials were conducted in 2012 in North American growing regions 1 (2 trials), 10 (8 trials), and 11 (2 trials) for a total of 12 trials; however, independence of trials was assessed and, after accounting for replicate trials, there are a total of 7 independent trials. GATTEN was applied five times as foliar broadcast sprays at a rate of 45 g a.i./ha for a seasonal application rate of 224 g a.i./ha. The applications were made at 7-day intervals with the last application occurring approximately 13–15 days before harvest. A non-ionic surfactant was used in/on grapes at all field trial sites. Foliar applications were made using ground equipment with concentrated and/or dilute spray volumes; residues from dilute and concentrate spray volumes were similar. Residue decline data of flutianil in grapes are too variable to assess decline with increasing PHIs. Adequate storage stability data are available to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total Application Rate (g a.i./ha)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Grapes	211–231	13–15	Flutianil	7	0.0189	0.3826	0.056	0.101	0.127

n = number of independent trials. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SDEV = Standard Deviation
For computation, values <LOQ are assumed to be at the LOQ.

Crop field trials and residue decline on apples **PMRA# 2962237**

Crop field trials were conducted in 2006 in North American growing regions 1 (3 trials), 2 (1 trial), 5 (2 trials), 9 (1 trial), 10 (1 trial), and 11 (4 trials) for a total of 12 trials; however, independence of trials was assessed and, after accounting for replicate trials, there are a total of 9 independent trials. V-10118, an emulsifiable concentrate formulation of flutianil, was applied four times as foliar broadcast sprays at a rate of 45 g a.i./ha for a seasonal application rate of 180 g a.i./ha. The applications were made at 7-day intervals with the last application occurring approximately 14 days before harvest. No adjuvant was used. Foliar applications were made using ground equipment with concentrated and/or dilute spray volumes; residues from dilute and concentrate spray volumes were similar. Residue decline data show that residues of flutianil generally decreased in apples with increasing PHIs. Adequate storage stability data are available to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total Application Rate (g a.i./ha)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Apples	157–191	13–15	Flutianil	9	<0.0185	0.062	0.031	0.036	0.014

n = number of independent trials. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SDEV = Standard Deviation
For computation, values <LOQ are assumed to be at the LOQ.

Crop field trials and residue decline on strawberries	**PMRA# 2962245**

Crop field trials were conducted in 2006-2007 in North American growing regions 2 (2 trials), 3 (1 trial), 5 (1 trial), 10 (3 trials), and 12 (1 trial) for a total of 8 trials. V-10118, an emulsifiable concentrate formulation of flutianil, was applied five times as foliar broadcast sprays at a rate of 45 g a.i./ha for a seasonal application rate of 225 g a.i./ha. The applications were made at 7-day intervals with the last application occurring approximately 0 days before harvest. No adjuvant was used. Independence of trials was assessed. Residue decline data show that residues of flutianil decreased in strawberries with increasing PHIs. Adequate concurrent storage stability data are available to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	Total Application Rate (g a.i./ha)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	LAFT	HAFT	Median	Mean	SDEV
Strawberries	221–232	0	Flutianil	8	0.025	0.17	0.055	0.067	0.047

n = number of independent trials. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SDEV = Standard Deviation

Processed food and feed – Grapes and apples	**PMRA# 2962271 (grapes) PMRA# 2962237 (apples)**

For grapes, processing studies were conducted using GATTEN at 1125 g a.i./ha (8-fold of maximum seasonal rate). For apples, processing studies were conducted using Flutianil 0.4EC at 898–911 g a.i./ha (fivefold of maximum seasonal rate). Adequate storage stability data are available on diverse crop types to support the storage intervals of the processed food and feed. Samples were analyzed using a validated analytical method.

RAC	Processed Fractions	$HAFT_{[RAC]}$ (ppm)	Median Processing Factor of Flutianil	Anticipated Residues of Flutianil (ppm)
Grapes	Juice	0.383	0.7	0.27
	Raisins		1.2	0.46
Apples	Juice	0.062	0.1	0.01
	Wet Pomace		3.3	0.20

Confined accumulation in rotational crops – Radish, sorghum and spinach	**PMRA# 2962212**
Radiolabel Position	MP-label (specific activity: 2.92 Bq/mg) and FP-label (specific activity: 2.87 MBq/mg)
Treatment	
Test Site	In a greenhouse or on concrete pads with plastic rain shields
Soil Type	Sandy loam
Treatment	Bare soil was treated at 224 g a.i./ha, and aged for 30, 120 and 365 days.
Formulation	Emulsifiable concentrate (EC) formulation

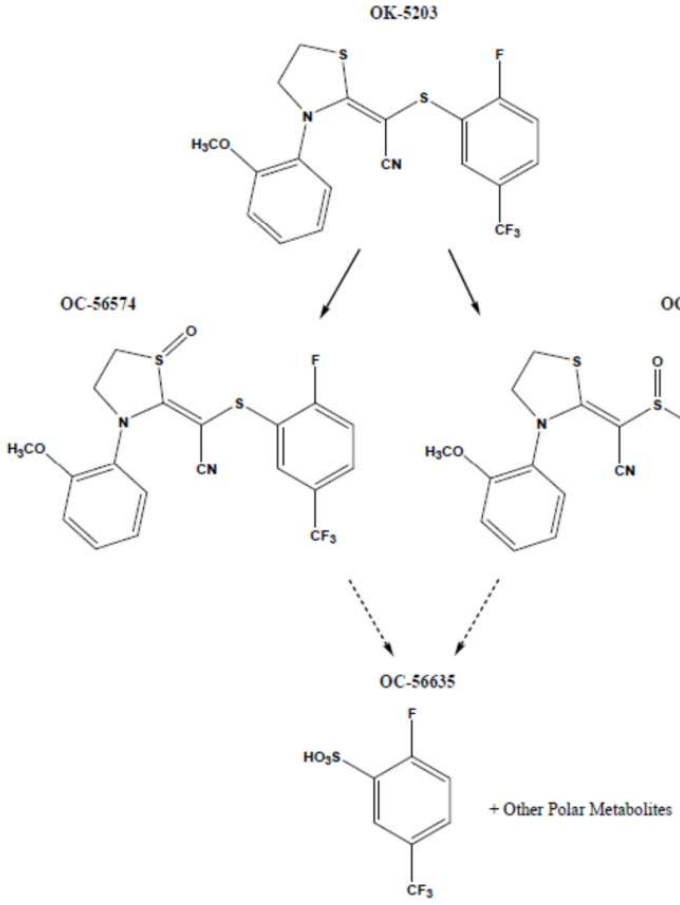
Extraction solvent(s)	ACN:water (50:50, v/v; 2×) and ACN (1×). Non-extractable residues in some samples were subjected to sequential acid and base hydrolysis with 0.1N HCl, 0.1N NaOH, 6N HCl, and 6N NaOH for 2 hours under ambient conditions, and with 6N HCl and 6N NaOH for 2 hours under reflux.

Matrices	**Matrix**	**MP-label**			**FP-label**		
		TRR (ppm)			**TRR (ppm)**		
		30-day PBI	**120-day PBI**	**365-day PBI**	**30-day PBI**	**120-day PBI**	**365-day PBI**
Radish	Immature root	0.041	0.034	0.004	0.196	0.184	0.024
	Immature tops	0.015	0.016	0.003	0.425	0.779	0.586
	Mature root	0.005	0.003	0.008	0.040	0.030	0.053
	Mature tops	0.007	0.004	0.004	0.293	0.221	0.335
Spinach	Immature leaves	0.007	0.015	0.003	0.160	0.363	0.112
	Mature leaves	0.010	0.006	0.001	0.452	0.138	0.179
Sorghum	Forage	0.007	0.005	0.04	0.572	0.463	0.221
	Grain	0.012	0.006	0.002	0.069	0.046	0.041
	Stover	0.020	0.015	0.010	0.817	0.990	0.545

Summary of Major Identified Metabolites in Rotated Crops

Plant-Back Intervals (PBI)	**30 days**		**120 days**		**365 days**	
Radiolabel Position	**MP-label**	**FP-label**	**MP-label**	**FP-label**	**MP-label**	**FP-label**
Metabolites Identified	**Major Metabolites**					
Immature radish roots	None	None	Flutianil; OC 52376	OC 56635	None	OC 56635
Immature radish tops	None	OC 56635	None	OC 56635	None	OC 56635
Mature radish roots	None	OC 56635	None	OC 56635	None	OC 56635
Mature radish tops	None	OC 56635	None	OC 56635	None	OC 56635
Immature spinach	None	OC 56635	None	OC 56635	None	OC 56635
Mature spinach	None	OC 56635	None	OC 56635	None	OC 56635
Sorghum forage	None	OC 56635	None	OC 56635	None	OC 56635
Sorghum grain	None	OC 56635	None	OC 56635	None	OC 56635
Sorghum stover	None	OC 56635	None	OC 56635	None	OC 56635

Proposed metabolic scheme in rotational crops



Residue data in rotational crops | **PMRA# 3151576**

Two trials were conducted during the 2014-2016 growing seasons in North American growing regions 2 and 10. Flutianil was applied 5 times to a primary crop (cucumbers) at a rate of 44.8 g a.i./ha, for a total seasonal application of 224 g a.i./ha. Cucumbers were removed from the plots at 11–30, 93–121, and 338–368 days after treatment, and any leftover cucumber plant material was worked into the soil before secondary crops were planted. No adjuvants were used. Adequate concurrent storage stability data were submitted to support the storage intervals of the rotational crop field trials. Samples were analyzed using a validated analytical method.

Commodity	Total Application Rate (g a.i./ha)	PBI (days)	Residue Levels (ppm)			
			n	LAFT	HAFT	Mean
OC 56635						
Radish (top)	224	11-30	2	0.034	0.387	0.211
		93-121		0.047	0.482	0.265
		338-367		0.024	0.125	0.075
Radish (root)		11-30	2	<0.017	0.129	0.073
		93-121		<0.017	0.088	0.053
		338-367		<0.017	<0.017	<0.017

Lettuce (leaf)	11	1	<0.017	<0.017	<0.017
	93		<0.017	<0.017	<0.017
	338		<0.017	<0.017	<0.017
Spinach (leaf)	30	1	<0.017	<0.017	<0.017
	121		0.018	0.019	0.019
	367		0.018	0.018	0.018
Wheat (forage)	11–30	2	0.073	0.131	0.102
	93–120[1]		<0.017	0.103	0.060
	338–368		0.042	0.054	0.048
Wheat (hay)	11–30	2	0.142	0.773	0.458
	93–120[1]		0.137	1.677	0.907
	33–368		0.073	0.373	0.223
Wheat (straw)	11–30	2	0.088	0.652	0.370
	93–120[1]		0.066	0.854	0.460
	338–368		0.024	0.783	0.404
Wheat (grain)	11–30	2	<0.017	<0.017	<0.017
	93–120[1]		<0.017	<0.017	<0.017
	338–368		<0.017	0.021	0.019

Values based on per-trial averages. For computation, values <LOQ are assumed to be at the LOQ.
n = number of independent field trials.
[1] The planting date of wheat in the 120-day PBI plot was not stated; therefore, the nominal PBI of 120 is reported.

Based on the results of the field accumulation study, a plant-back interval of 365 days (12 months) is required for all non-labelled crops.

Table 12 Food residue chemistry overview of metabolism studies and risk assessment

Plant studies	
Residue definition for enforcement Primary crops (fruits and cucurbits)	Flutianil
Residue definition for risk assessment Primary crops (fruits and cucurbits)	Flutianil (cucurbit vegetables) Flutianil + OC 56635 (fruits – cherries, grape, apples, and strawberries)
Metabolic profile in diverse crops	The profile in diverse crops cannot be determined, because only fruit (apple, grape, and cucumber) and leafy (lettuce) crops were investigated. Metabolism was similar in fruit and leafy crops.

	Population	Estimated risk % of acceptable daily intake (ADI)	
		Food Alone	Food and drinking water
Basic chronic dietary exposure analysis **ADI = 0.8 mg/kg bw/day** **Estimated chronic drinking water concentration = 0.244 ppm**	All infants <1 year	0.2	2.5
	Children 1–2 years	0.6	1.5
	Children 3–5 years	0.4	1.1
	Children 6–12 years	0.1	0.7
	Youth 13–19 years	0.1	0.5
	Adults 20–49 years	0.1	0.7
	Adults 50+ years	0.1	0.7
	Females 13-49 years	0.1	0.7
	Total population	0.1	0.7

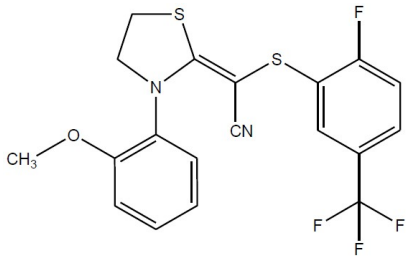
Table 13 Fate and behaviour in the environment

Property	Test substance	Parameter	Value	Transformation products (max. % AR)	Classification	PMRA#*
Abiotic transformation						
Hydrolysis	Flutianil	DT_{50} at pH 4, 7, and 9	>365 days	None identified	Persistant	2961747
Phototransformation on soil	Flutianil	DT_{50}	110 days	OC 56635 (10.7) OC 56574 (1.8) OC 53276 (3.3)	Persistent	2961753
Phototransformation in water	Flutianil	DT_{50} natural water pH 7	1.1 days 1.0 days	OC 56635 (71.2) OC 53279 (2.8) Unk AP5A (29.5) Unk AP1B (25.7)	Non-persistent	2961749
	Unk AP5A	DT_{50} natural water pH 7	3.8 days 4.4 days	N/A	Non-persistent	
	Unk AP1B	DT_{50} natural water pH 7	3.8 days 6.0 days	N/A	Non-persistent	
	OC 56635	DT_{50} natural water pH 7	61.9 days 71.3 days	N/A	Moderately persistent	
Reaction with hydroxyl radicals in air	Flutianil	Half-life	0.285 days	N/A	Non-persistent in air	2961751
Biotransformation						
Biotransformation in aerobic soil	Flutianil	DT_{50} 90% upper	1114–2855 days 2410 days	OC 56635 (3.9) OC 56574 (3.4) OC 53276 (2.5) OC 53279 (1.2)	Persistent	2961755

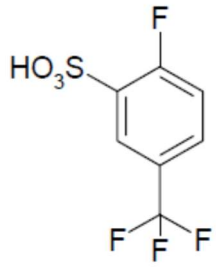
Property	Test substance	Parameter	Value	Transformation products (max. % AR)	Classification	PMRA#*
		confidence bound on the mean		CO_2 (1.2)		
Biotransformation in anaerobic soil	Flutianil	DT_{50} 90^{th} percentile of mean	1460–13 191 days 9512 days	OC 56635 (2.6) OC 56574 (2.2) OC 53276 (1.2) OC 53279 (1.2) CO_2 (0.9)	Persistent	2961757
Biotransformation in aerobic water systems	Flutianil	Whole system DT_{50} 80^{th} percentile	236–699 days 579 days	OC 56574 (13.7) OC 53276 (7.4) OC 53279 (3.7) CO_2 (9.2)	Persistent	2961759; 2962008
Biotransformation in anaerobic water systems	Flutianil	Whole system DT_{50}	766–2280 days	OC 56574 (6.8) CO_2 (0.8)	Persistent	2961761
Mobility						
Adsorption / desorption in soil	Flutianil	K_d K_{oc}	384–814 L/kg 11779–47320 L/kg	N/A	Immobile in soil	2961763
	OC 56635	K_d K_{oc}	No adsorption – 0.0024 L/kg No adsorption – 1.853 L/kg	N/A	Very highly mobile	2961769
	OC 56574	K_d K_{oc}	26.7–75.4 L/kg 1278–2090 L/kg	N/A	Slight to low mobility in soil	2961767
	OC 53276	K_d K_{oc}	10.48–43.30 L/kg 821–919 L/kg	N/A	Low mobility in soil	2961765
Field studies						
Field dissipation	Flutianil	DT_{50} Iowa New York	 312 days 398 days	OC 56635 (29.8) OC 56574 (11.4) OC 53276 (14.4)	Persistent Max. depth detected: Iowa: 15–30 cm New York: 8–15 cm Max. carry-over (% after ~365 d): Iowa – <LOQ (359 and 451 d) New York - 20.6% after 370 d (34.6% after 460 d)	2961901

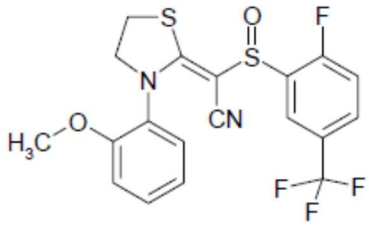
Property	Test substance	Parameter	Value	Transformation products (max. % AR)	Classification	PMRA#*
	OC 56635	DT_{50} Iowa	42.2 days	N/A	Moderately persistent Max. depth detected: Iowa: 8–15 cm New York: 8–15 cm	
	OC 53276	DT_{50} Iowa	259 days	N/A	Persistent Max. depth detected: Iowa: 0–8 cm New York: 0–8 cm	
Bioconcentration						
Bioconcentration	Flutianil	BCF_k (whole body) Depuration DT_{50}	345 L/kg (high dose), 380 L/kg (low dose) 1.87–2.03 days	N/A	Not expected to bioaccumulate	2961827

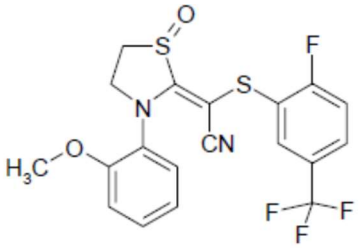
Table 13 Record of transformation products

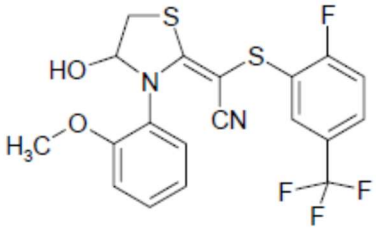
Chemical name, code, and structure	Study (PMRA#)	Max %AR (d)	%AR at Study end (study length, d)
PARENT			
Parent – **flutianil** (OK-5203)  **CAS Name:** (2Z)-2-[[2-fluoro-5-(trifluoromethyl)phenyl]thio]-2-[3- (2-methoxyphenyl)-2-thiazolidinylidene]acetonitrile **IUPAC Name:** (Z)-[3-(2-methoxyphenyl)-1,3-thiazolidin-2-ylidene](α, α, α, 4-tetrafluoro-*m*-tolylthio)acetonitrile	Hydrolysis (2961747)	**pH 4** 101.3 (0) **pH 7** 99.0 (0) **pH 9** 97.0 (0)	98.1 (5) 96.7 (5) 96.7 (5)
	Soil Phototransformation (2961753)	**[MeOPh-U-^{14}C]-flutianil** 91.8 (0) **[CF_3Ph-U-^{14}C]-flutianil** 97.4 (0)	69.1 (45) 68.3 (37)
	Aqueous Phototransformation (2961749)	**Natural Water** **[MeOPh-U-^{14}C]-flutianil** 99.8 (0) **[CF_3Ph-U-^{14}C]-flutianil** 94.2 (0) **pH 7 Buffer** **[MeOPh-U-^{14}C]-flutianil** 95.4 (0) **[CF_3Ph-U-^{14}C]-flutianil** 95.6 (0)	 ND (0) ND (0) ND (0) ND (0)
	Aerobic soil (2961755)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 94.2 (0) **[CF_3Ph-U-^{14}C]-flutianil** 93.7 (0) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** 92.7 (0) **New York loam** **[MeOPh-U-^{14}C]-flutianil** 94.4 (0)	 74.5 (365) 75.6 (365) 83.1 (365) 85.5 (365) 79.1 (365)

Chemical name, code, and structure	Study (PMRA#)	Max %AR (d)	%AR at Study end (study length, d)
		Georgia sand **[MeOPh-U-^{14}C]-flutianil** 95.4 (0)	
	Anaerobic soil (2961757)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 94.0 (0) **[CF$_3$Ph-U-^{14}C]-flutianil** 92.4 (0) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** 95.2 (0) **New York loam** **[MeOPh-U-^{14}C]-flutianil** 96.2 (0) **Georgia sand** **[MeOPh-U-^{14}C]-flutianil** 97.1 (0)	85.5 (365) 86.5 (365) 78.8 (365) 91.4 (365) 85.6 (365)
	Aerobic aquatic (2961759) (2962008)	**Florida sand** **[MeOPh-U-^{14}C]-flutianil** 100.6 (0) **[CF$_3$Ph-U-^{14}C]-flutianil** 99.1 (0) **California loam** **[MeOPh-U-^{14}C]-flutianil** 98.2 (0) **[CF$_3$Ph-U-^{14}C]-flutianil** 98.5 (0) **Abbey Lake silt loam** **[MeOPh-U-^{14}C]-flutianil** 93.0 (0) **[CF$_3$Ph-U-^{14}C]-flutianil** 94.9 (7) **Swiss Lake sand** **[MeOPh-U-^{14}C]-flutianil** 93.0 (0) **[CF$_3$Ph-U-^{14}C]-flutianil** 95.0 (14)	59.2 (370) 49.1 (370) 53.5 (370) 45.3 (370) 79.6 (100) 84.9 (100) 89.0 (100) 88.1 (100)
	Anaerobic aquatic (2961761)	**Florida sand** **[MeOPh-U-^{14}C]-flutianil** 96.1 (0) **[CF$_3$Ph-U-^{14}C]-flutianil** 98.4 (0) **California loam** **[MeOPh-U-^{14}C]-flutianil** 99.2 (3) **[CF$_3$Ph-U-^{14}C]-flutianil** 96.0 (3, 14)	74.8 (368) 72.1 (368) 69.7 (368) 66.9 (368)
	Field studies (2961901)	**New York** 29.0 (0.17) **Iowa** 55.2 (0.17)	5.2 (460) < LOQ (451)
	K_{oc} (2961763)	**Derbyshire loam** **Nottinghamshire loamy sand**	11779 47320

Chemical name, code, and structure	Study (PMRA#)	Max %AR (d)	%AR at Study end (study length, d)
		Alaska silt loam 22733 **North Dakota silt loam** 34229 **Ushiku loam** 18083	
MAJOR (> 10%) TRANSFORMATION PRODUCTS			
OC 56635  **IUPAC Name:** 2-fluoro-5--(trifluoromethyl)benzenesulfonic acid	Soil Phototransformation (2961753)	**[MeOPh-U-^{14}C]-flutianil** N/A **[CF$_3$Ph-U-^{14}C]-flutianil** 10.7 (37)	N/A 10.7 (37)
	Aqueous Phototransformation (2961749)	**Natural Water** **[MeOPh-U-^{14}C]-flutianil** N/A **[CF$_3$Ph-U-^{14}C]-flutianil** 71.2 (7) **pH 7 Buffer** **[MeOPh-U-^{14}C]-flutianil** N/A **[CF$_3$Ph-U-^{14}C]-flutianil** 64.6 (18)	N/A 59.5 (30) N/A 59.1 (30)
	Aerobic soil (2961755)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 0.3 (365) **[CF$_3$Ph-U-^{14}C]-flutianil** 3.9 (365) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** N/A **New York loam** **[MeOPh-U-^{14}C]-flutianil** N/A **Georgia sand** **[MeOPh-U-^{14}C]-flutianil** 0.2 (120)	0.3 (365) 3.9 (365) N/A N/A 0 (365)
	Anaerobic soil (2961757)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 0.6 (246) **[CF$_3$Ph-U-^{14}C]-flutianil** 2.6 (365) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** 0.9 (365) **New York loam** **[MeOPh-U-^{14}C]-flutianil** N/A **Georgia sand** **[MeOPh-U-^{14}C]-flutianil** 1.0 (365)	0.5 (365) 2.6 (365) 0.9 (365) N/A 1.0 (365)
	Field studies (2961901)	**New York** 29.8 (61) **Iowa** 29.3 (10)	<10 (LOQ, 460) <10 (LOQ, 451)
	K_{oc} (2961769)	No adsorption observed.	

Chemical name, code, and structure	Study (PMRA#)	Max %AR (d)	%AR at Study end (study length, d)
OC 53276  **IUPAC Name:** (Z)-2-[2-fluoro-5-(trifluoromethyl)phenylsulfinyl]-2-[3-(2-methoxyphenyl)thiazolidinylidene]acetonitrile	Soil Phototransformation (2961753)	**[MeOPh-U-^{14}C]-flutianil** 2.8 (45) **[CF$_3$Ph-U-^{14}C]-flutianil** 3.3 (37)	2.8 (45) 3.3 (37)
	Aerobic soil (2961755)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 2.5 (365) **[CF$_3$Ph-U-^{14}C]-flutianil** 2.2 (365) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** 1.1 (246) **New York loam** **[MeOPh-U-^{14}C]-flutianil** 1.6 (365) **Georgia sand** **[MeOPh-U-^{14}C]-flutianil** 1.3 (246)	2.5 (365) 2.2 (365) 0.9 (365) 1.6 (365) 1.2 (365)
	Anaerobic soil (2961757)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 0.6 (246) **[CF$_3$Ph-U-^{14}C]-flutianil** 1.0 (246) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** 0.4 (246) **New York loam** **[MeOPh-U-^{14}C]-flutianil** 0.9 (120) **Georgia sand** **[MeOPh-U-^{14}C]-flutianil** 0.7 (246, 365)	0.5 (365) 0.5 (365) 0 (365) 0 (365) 0.7 (365)
	Aerobic aquatic (2961759) (2962008)	**Florida sand** **[MeOPh-U-^{14}C]-flutianil** N/A **[CF$_3$Ph-U-^{14}C]-flutianil** 1.9 (370) **California loam** **[MeOPh-U-^{14}C]-flutianil** N/A **[CF$_3$Ph-U-^{14}C]-flutianil** 4.2 (370) **Abbey Lake silt loam** **[MeOPh-U-^{14}C]-flutianil** 7.4 (7) **[CF$_3$Ph-U-^{14}C]-flutianil** 4.7 (100) **Swiss Lake sand** **[MeOPh-U-^{14}C]-flutianil** 6.7 (100) **[CF$_3$Ph-U-^{14}C]-flutianil** 5.1 (61)	N/A 1.9 (370) N/A 4.2 (370) 1.3 (100) 4.7 (100) 6.7 (100) 2.3 (100)

Chemical name, code, and structure	Study (PMRA#)	Max %AR (d)	%AR at Study end (study length, d)
	Field studies (2961901)	**New York** 8.2 (61) **Iowa** 14.4 (0.17)	5.1 (460) 3.3 (451)
	K_{oc} (2961765)	**Derbyshire loam** **Nottinghamshire loam** **Germany silt loam**	443.3 919.4 205.3
OC 56574  **IUPAC Name:** (Z)-2-[2-fluoro-5-(trifluoromethyl)phenylthio]-2-[3-(2-methoxyphenyl)-1-oxo-1,3-thiaolidin-2-ylidene]acetonitrile	Soil Phototransformation (2961753)	**[MeOPh-U-^{14}C]-flutianil** 1.6 (30) **[CF$_3$Ph-U-^{14}C]-flutianil** 1.8 (30)	1.5 (45) 1.7 (37)
	Aerobic soil (2961755)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 3.0 (365) **[CF$_3$Ph-U-^{14}C]-flutianil** 3.4 (365) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** 1.6 (365) **New York loam** **[MeOPh-U-^{14}C]-flutianil** 2.3 (365) **Georgia sand** **[MeOPh-U-^{14}C]-flutianil** 2.2 (365)	3.0 (365) 3.4 (365) 1.6 (365) 2.3 (365) 2.2 (365)
	Anaerobic soil (2961757)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 0.7 (120, 246, 365) **[CF$_3$Ph-U-^{14}C]-flutianil** 1.4 (120, 246) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** 0.8 (30, 246) **New York loam** **[MeOPh-U-^{14}C]-flutianil** 1.1 (120) **Georgia sand** **[MeOPh-U-^{14}C]-flutianil** 2.2 (246)	0.7 (365) 1.1 (365) 0 (365) 0 (365) 0.9 (365)
	Aerobic aquatic (2961759) (2962008)	**Florida sand** **[MeOPh-U-^{14}C]-flutianil** 9.1 (370) **[CF$_3$Ph-U-^{14}C]-flutianil** 8.7 (272, 370) **California loam** **[MeOPh-U-^{14}C]-flutianil** 10.7 (370) **[CF$_3$Ph-U-^{14}C]-flutianil** 13.7	9.1 (370) 8.7 (370) 10.7 (370) 10.9 (370)

Chemical name, code, and structure	Study (PMRA#)	Max %AR (d)	%AR at Study end (study length, d)
		(272) **Abbey Lake silt loam** **[MeOPh-U-^{14}C]-flutianil** 2.0 (61) **[CF$_3$Ph-U-^{14}C]-flutianil** 2.2 (30) **Swiss Lake sand** **[MeOPh-U-^{14}C]-flutianil** 2.9 (7) **[CF$_3$Ph-U-^{14}C]-flutianil** 2.4 (100)	0.9 (100) 0.6 (100) 2.1 (100) 2.4 (100)
	Anaerobic aquatic (2961761)	**Florida sand** **[MeOPh-U-^{14}C]-flutianil** 3.2 (101) **[CF$_3$Ph-U-^{14}C]-flutianil** 1.3 (368) **California loam** **[MeOPh-U-^{14}C]-flutianil** 5.4 (271) **[CF$_3$Ph-U-^{14}C]-flutianil** 6.8 (271)	0.9 (368) 1.3 (368) 4.3 (368) 5.9 (368)
	Field studies (2961901)	**New York** 5.1 (0.17, 0.33) **Iowa** 11.4 (1)	< LOQ (460) < LOQ (451)
	K_{oc} (2961767)	**Derbyshire loam** **Nottinghamshire loam** **Germany silt loam**	1566 1278 2090
OC 53279  IUPAC Name: (2Z)-{[2-fluoro-5-(trifluoromethyl)phenyl]sulfanyl}[4-hydroxy-3-(2-methoxyphenyl)-1,3-thiazolidin-2-ylidene]acetonitrile	Aqueous Phototransformation (2961749)	**Natural Water** **[MeOPh-U-^{14}C]-flutianil** N/A **[CF$_3$Ph-U-^{14}C]-flutianil** 2.2 (1) **pH 7 Buffer** **[MeOPh-U-^{14}C]-flutianil** 2.8 (7) **[CF$_3$Ph-U-^{14}C]-flutianil** 2.3 (2)	N/A ND (30) ND (30) ND (30)
	Aerobic soil (2961755)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 0.9 (246) **[CF$_3$Ph-U-^{14}C]-flutianil** 1.2 (246) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** 0.5 (365) **New York loam** **[MeOPh-U-^{14}C]-flutianil** 0.7 (365) **Georgia sand** **[MeOPh-U-^{14}C]-flutianil** 0.5 (246, 365)	0 (365) 0.9 (365) 0.5 (365) 0.7 (365) 0.5 (365)

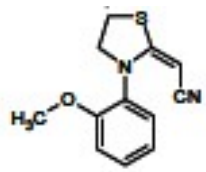
Chemical name, code, and structure	Study (PMRA#)	Max %AR (d)	%AR at Study end (study length, d)
	Anaerobic soil (2961757)	**California sandy loam** **[MeOPh-U-^{14}C]-flutianil** 0.9 (246) **[CF$_3$Ph-U-^{14}C]-flutianil** 1.2 (246) **Iowa loam** **[MeOPh-U-^{14}C]-flutianil** 0.4 (246) **New York loam** **[MeOPh-U-^{14}C]-flutianil** 0.7 (246) **Georgia sand** **[MeOPh-U-^{14}C]-flutianil** 0.8 (246)	0.8 (365) 0.8 (365) 0 (365) 0 (365) 0.4 (365)
	Aerobic aquatic (2962008)	**Abbey Lake silt loam** **[MeOPh-U-^{14}C]-flutianil** 0.1 (61) **[CF$_3$Ph-U-^{14}C]-flutianil** 17.0 (61) **Swiss Lake sand** **[MeOPh-U-^{14}C]-flutianil** 2.8 (100) **[CF$_3$Ph-U-^{14}C]-flutianil** 3.7 (61)	ND (100) 0.3 (100) 2.8 (100) 1.9 (100)
Unk AP5A 	Aqueous Phototransformation (2961749)	**Natural Water** **[MeOPh-U-^{14}C]-flutianil** 24.4 (2) **[CF$_3$Ph-U-^{14}C]-flutianil** N/A **pH 7 Buffer** **[MeOPh-U-^{14}C]-flutianil** 29.5 (1) **[CF$_3$Ph-U-^{14}C]-flutianil** N/A	ND (30) N/A ND (30) N/A
Unk AP1B	Aqueous Phototransformation (2961749)	**Natural Water** **[MeOPh-U-^{14}C]-flutianil** N/A **[CF$_3$Ph-U-^{14}C]-flutianil** 10.3 (1) **pH 7 Buffer** **[MeOPh-U-^{14}C]-flutianil** N/A **[CF$_3$Ph-U-^{14}C]-flutianil** 25.7 (2)	N/A ND (30) N/A ND (30)
MINOR (< 10%) TRANSFORMATION PRODUCTS			
Unk AP6A	Aqueous Phototransformation (2961749)	**Natural Water** **[MeOPh-U-^{14}C]-flutianil** 4.2 (7) **[CF$_3$Ph-U-^{14}C]-flutianil** N/A **pH 7 Buffer** **[MeOPh-U-^{14}C]-flutianil** N/A **[CF$_3$Ph-U-^{14}C]-flutianil** N/A	ND (30) N/A N/A N/A

Table 15 Effects on terrestrial organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Invertebrates					
Earthworm, *Eisenia fetida*	14d-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LC_{50} > 1000 mg a.i./kg dw soil*	N/A	2962012
		OC 56635 (TP; Purity: 99.9% w/w)	LC_{50} > 1000 mg/kg dw soil*	N/A	2962014
		OC 56574 (TP; Purity: 99.76% w/w)	LC_{50} > 1000 mg/kg dw soil*	N/A	2962020
		OC 53276 (TP; Purity: 99.16% w/w)	LC_{50} > 1000 mg/kg dw soil*	N/A	2962022
	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.3% w/w)	**$NOAEC_{reproduction}$ = 12.5 mg a.i./kg dw soil**	N/A	2962024
	56d-Chronic	OC 53276 (TP; Purity: 99.16% w/w)	**NOAEC = 100 mg/kg dw soil***	N/A	2962026
Honey bee, *Apis mellifera* - Adult	48h-Oral	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	**LD_{50} > 100 µg a.i./bee***	Practically non-toxic	2961850
		GATTEN (end-use product; Purity: 4.99% w/w)	**LD_{50} > 21.7 µg a.i./bee***	Practically non-toxic	2962048
	10d-Oral	GATTEN (end-use product; Purity: 4.71% w/w)	**LD_{50} > 22.1 µg a.i./bee***	Practically non-toxic	2961857
	48h-Contact	Flutianil (technical grade active ingredient; Purity:	**LD_{50} > 100 µg a.i./bee***	Practically non-toxic	2961850

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
		99.22% w/w)			
		GATTEN (end-use product; Purity: 4.99% w/w)	**LD_{50} > 50 µg a.i./bee***	Practically non-toxic	2962048
Honey bee, *Apis mellifera* - Larvae	72h-Oral – single exposure	GATTEN (end-use product; Purity: 4.71% w/w)	**LD_{50} = 8.19 µg a.i./larvae**	Moderately toxic	2961852
	120h-Oral – repeated exposure	GATTEN (end-use product; Purity: 4.71% w/w)	LD_{50} = 10.4 µg a.i./larvae	Moderately toxic	2961854
	22d-Brood / hive	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	**NOED = 44 µg a.i./larvae***	N/A	2962018
Predatory mite, *Typhlodromus pyri*	14d-Contact glass plate	GATTEN (end-use product; Purity: 4.77% w/w)	**ER_{50} = 950.5 g a.i./ha**	N/A	2962030
Aphid parasitoid, *Aphidius rhopalosiphi*	48h-Contact glass plate	GATTEN (end-use product; Purity: 4.77% w/w)	**LR_{50} = 236.1 g a.i./ha**	N/A	2962028
Springtail, *Folsomia candida*	28d-Chronic	OC 53276 (TP; Purity: 4.99% w/w)	**$NOEC_{reproduction}$ = 8.00 mg/kg dw soil**	N/A	2962032
Birds					
Mallard duck, *Anas platyrhynchos*	8d-Dietary	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LD_{50} > 2718 mg a.i./kg bw/d*	Practically non-toxic	2961839
	20w-Reproduction	Flutianil (technical grade active ingredient; Purity: 98.77% w/w)	NOAEL = 259.9 mg a.i./kg bw/d*	N/A	2961848

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Bobwhite quail, *Colinus virginianus*	Acute-Oral	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LD_{50} > 2250 mg a.i./kg*	Practically non-toxic	2961834
	8d-Dietary	Flutianil (technical grade active ingredient; Purity: 98.7% w/w)	**LD_{50} > 1485 mg a.i./kg bw/d***	Practically non-toxic	2961842
	20w-Reproduction	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	**NOAEL = 184.6 mg a.i./kg bw/d***	N/A	2961846
Zebra finch, *Taeniopygia guttata*	Acute-Oral	Flutianil (technical grade active ingredient; Purity: 99.54% w/w)	**LD_{50} > 2000 mg a.i./kg***	Practically non-toxic	2961837
Mammals					
Norway rat, *Rattus norvegicus*	Acute-Oral	Flutianil (technical grade active ingredient; Purity: 99% w/w)	**LD_{50} > 5000 mg a.i./kg bw***	Practically non-toxic	2961735
	Reproduction	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	**NOAEL = 1286 mg a.i./kg bw/d***	N/A	2961954
Vascular plants					
Vascular plants, 10 species	21d-Seedling emergence	GATTEN (end-use product; Purity: 4.97% w/w)	**ER_{25} > 42.59 g a.i./ha**	N/A	2961860
	21d-Vegetative vigour	GATTEN (end-use product; Purity: 4.97% w/w)	**ER_{25} > 42.59 g a.i./ha**	N/A	2961862

[a]Atkins et al. (1981) for bees and USEPA classification for others, where applicable; *no significant toxic effects in any treatment. Bolded values were carried forward to the risk assessment.

Table 16 Effects on aquatic organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Freshwater species					
Daphnia magna	48h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	**EC_{50} > 0.0065 mg a.i./L***	Non-toxic up to limit of solubility	2961771
		Flutianil (technical grade active ingredient; Purity: 99.38% w/w)	EC_{50} > 0.95 mg a.i./L*	Non-toxic up to limit of solubility	2961773
		GATTEN (end-use product; Purity: 4.99 w/w)	**EC_{50} = 0.044 mg a.i./L**	Very highly toxic	2961781
		OC 56635 (TP; Purity: 99.9% w/w)	**EC_{50} > 96.8 mg/L***	Practically non-toxic	2961775
		OC56574 (TP; Purity: 99.76% w/w)	**EC_{50} > 4.59 mg/L***	Non-toxic up to limit of solubility	2961777
		OC 53276 (TP; Purity: 99.16% w/w)	**EC_{50} > 3.35 mg/L***	Non-toxic up to limit of solubility	2961779

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
	21d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	**NOAEC = 0.00711 mg a.i./L***	N/A	2961817
		OC 56635 (TP; Purity: 99.9% w/w)	**NOAEC ≥ 101 mg/L***	N/A	2961819
Non-biting midge, *Chironomus riparius*	28d-Chronic – spiked sediment: sediment	Flutianil (technical grade active ingredient; Purity: 98.77% w/w)	$NOAEC_{emergence}$ = 114 mg a.i./kg	N/A	2961829
Amphipod, *Hyalella azteca*	42d-Chronic – spiked sediment: sediment	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	**$NOAEC_{reproduction}$ = 13 mg a.i./kg**	N/A	2961831
	42d-Chronic – spiked sediment: pore water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	**$NOAEC_{reproduction}$ = 0.021 mg a.i./L**	N/A	2961831
	42d-Chronic – spiked sediment: overlying water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	**$NOAEC_{reproduction}$ = 0.0056 mg a.i./L**	N/A	2961831

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Rainbow trout, *Oncorhynchus mykiss*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LC_{50} > 0.014 mg a.i./L*	Non-toxic up to limit of solubility	2961791
			LC_{50} > 0.90 mg a.i./L*	Non-toxic up to limit of solubility	2961793
		GATTEN (end-use product; Purity: 4.99% w/w)	**LC_{50} = 0.0522 mg a.i./L**	Very highly toxic	2961809
		OC 56635 (TP; Purity: 99.9% w/w)	**LC_{50} > 102 mg/L***	Practically non-toxic	2961799
		OC56574 (TP; Purity: 99.76% w/w)	**LC_{50} > 3.33 mg/L***	Non-toxic up to limit of solubility	2961803
		OC 53276 (TP; Purity: 99.16% w/w)	**LC_{50} > 4.14 mg/L***	Non-toxic up to limit of solubility	2961805
	28d-Chronic	OC 56635 (TP; Purity: 99.9% w/w)	**NOEC = 99.2 mg/L***	N/A	2962010
Fathead minnow, *Pimephales promelas*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	**LC_{50} > 0.00522 mg a.i./L***	Non-toxic up to limit of solubility	2961795

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
		Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	LC_{50} > 0.79 mg a.i./L*	Non-toxic up to limit of solubility	2961815
		OC 56635 (TP; Purity: 99.9% w/w)	LC_{50} > 102 mg/L*	Practically non-toxic	2961801
	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 98.77% w/w)	**$NOEC_{growth}$ = 0.00224 mg a.i./L**	N/A	2961823
Common carp, *Cyprinus carpio*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.38% w/w)	LC_{50} > 0.87 mg a.i./L*	Non-toxic up to limit of solubility	2961797
		GATTEN (end-use product; Purity: 4.99% w/w)	LC_{50} = 0.158 mg a.i./L	Highly toxic	2961811
Freshwater alga, *Pseudokirchneriella subcapitata*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	EC_{50} > 0.330 mg a.i./L*	Non-toxic up to limit of solubility	2961867
			EC_{50} > 0.0137 mg a.i./L $NOAEC_{biomass}$ = 0.0008 mg a.i./L	Non-toxic up to limit of solubility	2961870

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
		GATTEN (end-use product; Purity: 4.97% w/w)	EC_{50} > 0.240 mg a.i./L $NOEC_{growth\ rate,\ yield}$ = 0.00663 mg a.i./L	Non-toxic up to limit of solubility	2961890
		OC 56635 (TP; Purity: 99.9% w/w)	**EC_{50} > 994 mg/L**	Practically non-toxic	2961874
	72h-Acute	OC56574 (TP; Purity: 99.76% w/w)	**EC_{50} = 2.109 mg/L**	Moderately toxic	2961878
		OC 53276 (TP; Purity: 99.76% w/w)	**EC_{50} > 4.28 mg/L**	Non-toxic up to limit of solubility	2961882
Freshwater cyanobacteria, *Anabaena flos-aquae*	96h-Acute	GATTEN (end-use product; Purity: 4.97% w/w)	EC_{50} > 0.217 mg a.i./L*	Non-toxic up to limit of solubility	2961899
Freshwater diatom, *Navicula pelliculosa*	96h-Acute	GATTEN (end-use product; Purity: 4.97% w/w)	EC_{50} > 0.240 mg a.i./L $NOEC_{growth\ rate,\ yield}$ = 0.0724 mg a.i./L	Non-toxic up to limit of solubility	2961897
Duckweed, *Lemna gibba*	7d-Dissolved	GATTEN (end-use product; Purity: 4.97% w/w)	**EC_{50} > 0.214 mg a.i./L***	Non-toxic up to limit of solubility	2961864

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Marine species					
Saltwater mysid, *Americamysis bahia*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.0% w/w)	EC_{50} > 0.62 mg a.i./L*	Non-toxic up to limit of solubility	2961787
		GATTEN (end-use product; Purity: 4.97% w/w)	EC_{50} > 0.057 mg a.i./L*	Non-toxic up to limit of solubility	2961789
	21d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	**$NOEC_{growth}$ = 0.0456 mg a.i./L**	N/A	2961821
Eastern oyster, *Crassostrea virginica*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	**EC_{50} > 0.019 mg a.i./L***	Non-toxic up to limit of solubility	2961783
		GATTEN (end-use product; Purity: 4.97% w/w)	**EC_{50} > 0.036 mg a.i./L** $NOEC_{growth}$ = 0.014 mg a.i./L	Non-toxic up to limit of solubility	2961785

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Amphipod, *Leptocheirus plumulosus*	28d-Chronic – spiked sediment: sediment	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	**$NOAEC_{reproduction}$ = 11 mg a.i./kg**	N/A	2962016
Sheepshead minnow, *Cyprinodon variegatus*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.0% w/w)	**LC_{50} > 0.85 mg a.i./L***	Non-toxic up to limit of solubility	2961807
		GATTEN (end-use product; Purity: 4.97% w/w)	**LC_{50} > 0.077 mg a.i./L***	Non-toxic up to limit of solubility	2961813
	34d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	**$NOEC_{growth}$ = 0.070 mg a.i./L**	N/A	2961825
Marine diatom, *Skeletonema costatum*	96h-Acute	GATTEN (end-use product; Purity: 4.97% w/w)	**E_bC_{50} = 0.132 mg a.i./L**	Highly toxic	2961894

[a] USEPA classification, where applicable; *no toxic effects in any treatment. Bolded values were carried forward to the risk assessment.

Table 17 Endpoints and uncertainty factors used to establish effects metrics for the risk assessment

Organism	Exposure	Test substance	Endpoint value	UF applied[1]	Effect metric	LOC[2]
Terrestrial organisms						
Invertebrates						
Earthworm, *Eisenia fetida*	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.3% w/w)	$NOAEC_{reproduction}$ = 12.5 mg a.i./kg dw soil	1	12.5 mg a.i./kg dw soil	1.0
	56d-Chronic	OC 53276 (TP; Purity: 99.16% w/w)	NOEC = 100 mg/kg dw soil	1	100 mg/kg dw soil	1.0
Honey bee, *Apis mellifera*	48h-Oral	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	48h-LD_{50} > 100 µg a.i./bee	1	>100 µg a.i./bee	0.4
		GATTEN (EP; Purity: 4.99% w/w)	48h-LD_{50} > 21.7 µg a.i./bee	1	>21.7 µg a.i./bee	0.4
	48h-Contact	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	48h-LC_{50} > 100 µg a.i./bee	1	>100 µg a.i./bee	0.4
		GATTEN (end-use product; Purity: 4.99% w/w)	48h-LC_{50} > 50 µg a.i./bee	1	>50 µg a.i./bee	0.4
	10d-Oral	GATTEN (end-use product; Purity: 4.71% w/w)	LD_{50} > 22.1 µg a.i./bee	1	>22.1 µg a.i./bee	1.0

Organism	Exposure	Test substance	Endpoint value	UF applied[1]	Effect metric	LOC[2]
	72h-Oral – larva single exposure	GATTEN (end-use product; Purity: 4.71% w/w)	LD_{50} = 8.19 µg a.i./larvae	1	8.19 µg a.i./larvae	0.4
	22d-Brood / hive	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	NOED = 44 µg a.i./larvae	1	44 µg a.i./larvae	1.0
Predatory mite, *Typhlodromus pyri*	14d-Contact	GATTEN (end-use product; Purity: 4.77% w/w)	ER_{50} = 950.5 g a.i./ha	1	950.5 g a.i./ha	2.0
Aphid parasitoid, *Aphidius rhopalosiphi*	48h-Contact	GATTEN (end-use product; Purity: 4.77% w/w)	LR_{50} = 236.1 g a.i./ha	1	236.1 g a.i./ha	2.0
Springtail, *Folsomia candida*	28d-Chronic	OC 53276 (TP; Purity: 4.99% w/w)	$NOEC_{reproduction}$ = 8.00 mg/kg dw soil	1	8.00 mg/kg dw soil	2.0
Birds						
Bobwhite quail, *Colinus virginianus*	8d-Dietary	Flutianil (technical grade active ingredient; Purity: 98.7% w/w)	LD_{50} > 1485 mg a.i./kg bw/d	10	> 148.5 mg a.i./kg bw/d	1.0
	20w-Reproduction	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	NOAEL = 184.6 mg a.i./kg bw/d	1	184.6 mg a.i./kg bw/d	1.0

Organism	Exposure	Test substance	Endpoint value	UF applied[1]	Effect metric	LOC[2]
Zebra finch, *Taeniopygia guttata*	Acute-Oral	Flutianil (technical grade active ingredient; Purity: 99.54% w/w)	LD_{50} > 2000 mg a.i./kg	10	> 200 mg a.i./kg	1.0
Mammals						
Norway rat, *Rattus norvegicus*	Acute-Oral	Flutianil (technical grade active ingredient; Purity: 99% w/w)	LD_{50} > 5000 mg a.i./kg bw	10	> 500 mg a.i./kg bw	1.0
	Reproduction	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	NOAEL = 1286 mg a.i./kg bw/d	1	131 mg a.i./kg bw/d	1.0
Vascular plants						
Vascular plants, 10 species	21d-Seedling emergence	GATTEN (end-use product; Purity: 4.97% w/w)	ER_{25} > 42.59 g a.i./ha	1	>42.59 g a.i./ha	1.0
	21d-Vegetative vigour	GATTEN (end-use product; Purity: 4.97% w/w)	ER_{25} > 42.59 g a.i./ha	1	>42.59 g a.i./ha	1.0
Freshwater organisms						
Invertebrates						
Daphnia magna	48h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	EC_{50} > 0.0065 mg a.i./L	2*	>0.00325 mg a.i./L	1.0

Organism	Exposure	Test substance	Endpoint value	UF applied[1]	Effect metric	LOC[2]
		GATTEN (end-use product; Purity: 4.99 w/w)	EC_{50} = 0.044 mg a.i./L	2	0.022 mg a.i./L	1.0
		OC 56635 (TP; Purity: 99.9% w/w)	EC_{50} > 96.8 mg/L	2	>48.4 mg/L	1.0
		OC56574 (TP; Purity: 99.76% w/w)	EC_{50} > 4.59 mg/L	2	>2.295 mg/L	1.0
		OC 53276 (TP; Purity: 99.16% w/w)	EC_{50} > 3.35 mg/L	2	>1.675 mg/L	1.0
	21d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	NOEC = 0.00711 mg a.i./L	1	0.00711 mg a.i./L	1.0
		OC 56635 (TP; Purity: 99.9% w/w)	NOAEC = 101 mg/L	1	101 mg/L	1.0
Amphipod, *Hyalella azteca*	42d-Chronic – spiked sediment: sediment	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	$NOAEC_{reproduction}$ = 13 mg a.i./kg	1	13 mg a.i./kg	1.0
	42d-Chronic – spiked sediment: pore water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	$NOAEC_{reproduction}$ = 0.021 mg a.i./L	1	0.021 mg a.i./L	1.0

Organism	Exposure	Test substance	Endpoint value	UF applied[1]	Effect metric	LOC[2]
	42d-Chronic – spiked sediment: overlying water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	$NOAEC_{reproduction}$ = 0.0056 mg a.i./L	1	0.0056 mg a.i./L	1.0
Fish						
Rainbow trout, *Oncorhynchus mykiss*	96h-Acute	GATTEN (end-use product; Purity: 4.99% w/w)	LC_{50} = 0.0522 mg a.i./L	10	0.00522 mg a.i./L	1.0
		OC 56635 (TP; Purity: 99.9% w/w)	LC_{50} > 102 mg/L	10	>10.2 mg/L	1.0
		OC56574 (TP; Purity: 99.76% w/w)	LC_{50} > 3.33 mg/L	10	>0.333 mg/L	1.0
		OC 53276 (TP; Purity: 99.16% w/w)	LC_{50} > 4.14 mg/L	10	>0.414 mg/L	1.0
	28d-Chronic	OC 56635 (TP; Purity: 99.9% w/w)	NOEC = 99.2 mg/L	1	99.2 mg/L	1.0
Fathead minnow, *Pimephales promelas*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LC_{50} > 0.00522 mg a.i./L	10*	>0.000522 mg a.i./L	1.0
	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 98.77% w/w)	$NOEC_{growth}$ = 0.00224 mg a.i./L	1	0.00224 mg a.i./L	1.0

Organism	Exposure	Test substance	Endpoint value	UF applied[1]	Effect metric	LOC[2]
Amphibians						
Rainbow trout, *Oncorhynchus mykiss*[3]	96h-Acute	GATTEN (end-use product; Purity: 4.99% w/w)	LC_{50} = 0.0522 mg a.i./L	10	0.00522 mg a.i./L	1.0
		OC 56635 (TP; Purity: 99.9% w/w)	LC_{50} > 102 mg/L	10	>10.2 mg/L	1.0
		OC56574 (TP; Purity: 99.76% w/w)	LC_{50} > 3.33 mg/L	10	>0.333 mg/L	1.0
		OC 53276 (TP; Purity: 99.16% w/w)	LC_{50} > 4.14 mg/L	10	>0.414 mg/L	1.0
	28d-Chronic	OC 56635 (TP; Purity: 99.9% w/w)	NOEC = 99.2 mg/L	1	99.2 mg/L	1.0
Fathead minnow, *Pimephales promelas*[3]	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LC_{50} > 0.00522 mg a.i./L	10*	>0.000522 mg a.i./L	1.0
	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 98.77% w/w)	$NOEC_{growth}$ = 0.00224 mg a.i./L	1	0.00224 mg a.i./L	1.0

Organism	Exposure	Test substance	Endpoint value	UF applied[1]	Effect metric	LOC[2]
Plants						
Freshwater alga, *Pseudokirchneriella subcapitata*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	EC_{50} > 0.0137 mg a.i./L	2	>0.00685 mg a.i./L	1.0
		OC 56635 (TP; Purity: 99.9% w/w)	EC_{50} > 994 mg/L	2	>497 mg/L	1.0
	72h-Acute	OC56574 (TP; Purity: 99.76% w/w)	EC_{50} = 2.109 mg/L	2	1.0545 mg/L	1.0
		OC 53276 (TP; Purity: 99.76% w/w)	EC_{50} > 4.28 mg/L	2	>2.14 mg/L	1.0
Duckweed, *Lemna gibba*	7d-Dissolved	GATTEN (end-use product; Purity: 4.97% w/w)	EC_{50} > 0.214 mg a.i./L	2	>0.107 mg a.i./L	1.0
Marine organisms						
Invertebrates						
Saltwater mysid, *Americamysis bahia*	21d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	$NOEC_{growth}$ = 0.0456 mg a.i./L	1	0.0456 mg a.i./L	1.0
Eastern oyster, *Crassostrea virginica*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	EC_{50} > 0.019 mg a.i./L	2*	>0.0095 mg a.i./L	1.0

Organism	Exposure	Test substance	Endpoint value	UF applied[1]	Effect metric	LOC[2]
		GATTEN (end-use product; Purity: 4.97% w/w)	EC_{50} > 0.036 mg a.i./L	2	>0.018 mg a.i./L	1.0
Amphipods, *Leptocheirus plumulosus*	28d-Chronic – spiked sediment: sediment	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	$NOAEC_{reproduction}$ = 11 mg a.i./kg	1	11 mg a.i./kg	1.0
Fish						
Sheepshead minnow, *Cyprinodon variegatus*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.0% w/w)	LC_{50} > 0.85 mg a.i./L	10	>0.085 mg a.i./L	1.0
		GATTEN (end-use product; Purity: 4.97% w/w)	LC_{50} > 0.077 mg a.i./L	10*	>0.0077 mg a.i./L	1.0
	34d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	$NOEC_{growth}$ = 0.070 mg a.i./L	1	0.07 mg a.i./L	1.0
Plants						
Marine diatom, *Skeletonema costatum*	96h-Acute	GATTEN (end-use product; Purity: 4.97% w/w)	E_bC_{50} = 0.132 mg a.i./L	2	0.066 mg a.i./L	1.0

[1] UF = uncertainty factor; [2]LOC = Level of Concern; [3]used as a surrogate for amphibians; *UF removed for further characterization.

Table 18 Screening level risk to terrestrial organisms other than birds and mammals

Organism	Exposure	Test substance	Effect metric	EEC[1]	RQ[2]	Risk
Invertebrates						
Earthworm, *Eisenia fetida*	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.3% w/w)	$NOAEC_{reproduction}$ = 12.5 mg a.i./kg dw soil	0.077 mg a.i./kg dw soil	0.01	No
	56d-Chronic	OC 53276 (TP; Purity: 99.16% w/w)	NOEC = 100 mg/kg dw soil	0.080 mg/kg dw soil	0.01	No
Honey bee, *Apis mellifera*	48h-Oral	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LD_{50} > 100 µg a.i./bee	1.002 µg a.i./bee	<0.01	No
		GATTEN (end-use product; Purity: 4.99% w/w)	LD_{50} > 21.7 µg a.i./bee	1.002 µg a.i./bee	<0.05	No
	48h-Contact	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LC_{50} > 100 µg a.i./bee	0.084 µg a.i./bee	<0.01	No
		GATTEN (end-use product; Purity: 4.99% w/w)	LC_{50} > 50 µg a.i./bee	0.084 µg a.i./bee	<0.01	No

Organism	Exposure	Test substance	Effect metric	EEC[1]	RQ[2]	Risk
	10d-Oral	GATTEN (end-use product; Purity: 4.71% w/w)	LD_{50} > 22.1 µg a.i./bee	1.002 µg a.i./bee	<0.05	No
	72h-Oral – larva single exposure	GATTEN (end-use product; Purity: 4.71% w/w)	LD_{50} = 8.19 µg a.i./larvae	0.425 µg a.i./larvae	0.05	No
	22d-Brood / hive	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	NOED = 44 µg a.i./larvae	0.425 µg a.i./larvae	0.01	No
Predatory mite, *Typhlodromus pyri*	14d-Contact	GATTEN (end-use product; Purity: 4.77% w/w)	ER_{50} = 950.5 g a.i./ha	83.01 g a.i./ha	0.09	No
Aphid parasitoid, *Aphidius rhopalosiphi*	48h-Contact	GATTEN (end-use product; Purity: 4.77% w/w)	LR_{50} = 236.1 g a.i./ha	83.01 g a.i./ha	0.35	No
Springtail, *Folsomia candida*	28d-Chronic	OC 53276 (TP; Purity: 4.99% w/w)	$NOEC_{reproduction}$ = 8.00 mg/kg dw soil	0.080 mg/kg dw soil	0.01	No

Organism	Exposure	Test substance	Effect metric	EEC[1]	RQ[2]	Risk
Vascular plants						
Vascular plants, 10 species	21d-Seedling emergence	GATTEN (end-use product; Purity: 4.97% w/w)	ER_{25} > 42.59 g a.i./ha	Cucurbits – in field: 174.3 g a.i./ha	**<4.09**	Yes
				Cucurbits – off-field (groundboom): 19.17 g a.i./ha	<0.45	No
				Cherries and Grape – in field: 139.6 g a.i./ha	**<3.28**	Yes
				Cherries and Grape – off-field (early season airblast): 103.3 g a.i./ha	**<2.43**	Yes
				Cherries and Grape – off-field (late season airblast): 82.35 g a.i./ha	**<1.93**	Yes
	21d-Vegetative vigour	GATTEN (end-use product; Purity: 4.97% w/w)	ER_{25} > 42.59 g a.i./ha	Cucurbits – in field: 83.01 g a.i./ha	**<1.95**	Yes
				Cucurbits – off-field (groundboom): 9.13 g a.i./ha	<0.21	No
				Cherries and Grape – in field: 78.00 g a.i./ha	**<1.83**	Yes
				Cherries and Grape – off-field (early season airblast): 57.70 g a.i./ha	**<1.35**	Yes

Organism	Exposure	Test substance	Effect metric	EEC[1]	RQ[2]	Risk
				Cherries and Grape – off-field (late season airblast): 46.01 g a.i./ha	**<1.08**	Yes

[1]EEC = Estimated Environmental concentration. The soil EEC of 0.077 mg a.i./kg was calculated based on the maximum proposed foliar rate of five applications of 35 g a.i./ha with a 7-day re-treatment interval, accounting for soil degradation using the 90th upper percentile on the mean of aerobic soil representative half-lives of 2410 days and was used for soil dwelling organisms and seedling emergence effects metrics. This concentration was calculated assuming that the product is evenly distributed in the top 0 to 15 cm depth of soil with a bulk density of 1.5 g/cm^3.

The foliar EEC of 83.01 g a.i./ha was calculated based on the cumulative maximum application rate accounting for dissipation between applications using the default foliar dissipation half-life of 10 days and was used for foliar dwelling organisms and vegetative vigour effects metrics.

The pollinator EECs were calculated using the single maximum application rate of 35 g a.i./ha as follows:

Estimated contact exposure = 2.4 µg a.i./bee × 0.0035 g a.i./ha;
Estimated dietary exposure = 98 µg a.i./g × 0.292 g/day × 0.0035 g a.i./ha; and
Estimated brood exposure = 98 µg a.i./g × 0.124 g/day × 0.0035 g a.i./ha.

The further characterized EECs for off-field exposure to non-target terrestrial plants accounted for a 11% drift factor for applications to cucurbits via groundboom using an ASAE fine spray quality, and a 74 and 59% spray drift factor for applications to cherries and grape via airblast. For the further risk characterization, the application rate for cherries and grape (four × 35 g a.i./ha with a 7-day re-treatment interval) was modelled.

EECs for transformation products were calculated conservatively assuming 100% of the applied flutianil was instantly transformed into the transformation product on a molecular weight/weight basis.

[2]RQ = Risk Quotient. The RQ is calculated by dividing the EEC by the effect metric (RQ = EEC/effect metric). The RQ is then compared to the level of concern (LOC = 2.0 for beneficial arthropods, 0.4 for acute exposures to bees, and 1.0 for everything else). If the screening level RQ is below the LOC, the risk is considered acceptable and no further risk characterization is necessary. For groups where the LOC is exceeded (RQ > 1), further characterization of the risk is conducted.

Table 19 Screening level risk to birds and mammals

Organism	Toxicity (mg a.i./kg bw/d)	Feeding guild (food item)	EDE (mg a.i./kg bw) [a]	RQ	LOC	LOC Exceeded?
Small bird (0.02 kg)						
Acute	>200.0	Insectivore	6.76	<0.03	1	No
Reproduction	186.2	Insectivore	6.76	0.04	1	No
Medium sized bird (0.1 kg)						
Acute	>200.0	Insectivore	5.27	<0.03	1	No
Reproduction	186.2	Insectivore	5.27	0.03	1	No
Large sized bird (1 kg)						
Acute	>200.0	Herbivore (short grass)	3.41	<0.02	1	No
Reproduction	186.2	Herbivore (short grass)	3.41	0.02	1	No
Small mammal (0.015 kg)						
Acute	>5000	Insectivore	3.89	<0.01	1	No
Reproduction	131	Insectivore	3.89	<0.01	1	No

Organism	Toxicity (mg a.i./kg bw/d)	Feeding guild (food item)	EDE (mg a.i./kg bw) [a]	RQ	LOC	LOC Exceeded?
Medium sized mammal (0.035 kg)						
Acute	>5000	Herbivore (short grass)	7.54	<0.02	1	No
Reproduction	131	Herbivore (short grass)	7.54	0.01	1	No
Large sized mammal (1 kg)						
Acute	>5000	Herbivore (short grass)	4.03	<0.01	1	No
Reproduction	131	Herbivore (short grass)	4.03	<0.01	1	No

(1) EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/bw) × EEC, where:
FIR: Food Ingestion Rate (Nagy, 1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; 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(bw in g) $^{0.850}$.
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(bw in g) $^{0.651}$.
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235(bw 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.

Table 20 Screening level risk to aquatic organisms

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	LOC exceeded
Freshwater organisms						
Invertebrates						
Daphnia magna	48h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	½ EC_{50} > 0.00325 mg a.i./L	0.022	**<6.62**	Yes
		GATTEN (end-use product; Purity: 4.99 w/w)	½ EC_{50} = 0.022 mg a.i./L	0.022	0.98	No
		OC 56635 (TP; Purity: 99.9% w/w)	½ EC_{50} > 48.4 mg/L	0.012	<0.01	No
		OC56574 (TP; Purity: 99.76% w/w)	½ EC_{50} > 2.295 mg/L	0.022	<0.01	No
		OC 53276 (TP; Purity: 99.16% w/w)	½ EC_{50} > 1.675 mg/L	0.022	<0.01	No

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	LOC exceeded
	21d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	NOEC = 0.00711 mg a.i./L	0.022	**3.03**	Yes
		OC 56635 (TP; Purity: 99.9% w/w)	NOAEC = 101 mg/L	0.012	0.01	No
Amphipod, *Hyalella azteca*	42d-Chronic – spiked sediment: sediment	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	$NOAEC_{reproduction}$ = 13 mg a.i./kg	0.077	0.01	No
	42d-Chronic – spiked sediment: pore water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	$NOAEC_{reproduction}$ = 0.021 mg a.i./L	0.022	**1.02**	Yes
	42d-Chronic – spiked sediment: overlying water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	$NOAEC_{reproduction}$ = 0.0056 mg a.i./L	0.022	**3.84**	Yes
Fish						
Rainbow trout, *Oncorhynchus mykiss*	96h-Acute	GATTEN (end-use product; Purity: 4.99% w/w)	1/10 LC_{50} = 0.00522 mg a.i./L	0.022	**4.12**	Yes
		OC 56635 (TP; Purity: 99.9% w/w)	1/10 LC_{50} > 10.2 mg/L	0.012	<0.01	No
		OC56574 (TP; Purity: 99.76% w/w)	1/10 LC_{50} > 0.333 mg/L	0.022	<0.07	No
		OC 53276 (TP; Purity: 99.16% w/w)	1/10 LC_{50} > 0.414 mg/L	0.022	<0.05	No

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	LOC exceeded
	28d-Chronic	OC 56635 (TP; Purity: 99.9% w/w)	NOEC = 99.2 mg/L	0.012	0.01	No
Fathead minnow, *Pimephales promelas*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	1/10 LC_{50} > 0.000522 mg a.i./L	0.022	**<41.2**	Yes
	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 98.77% w/w)	$NOEC_{growth}$ = 0.00224 mg a.i./L	0.022	**8.96**	Yes
Amphibians						
Rainbow trout, *Oncorhynchus mykiss*[3]	96h-Acute	GATTEN (end-use product; Purity: 4.99% w/w)	1/10 LC_{50} = 0.00522 mg a.i./L	0.115	**21.98**	Yes
		OC 56635 (TP; Purity: 99.9% w/w)	1/10 LC_{50} > 10.2 mg/L	0.066	<0.01	No
		OC56574 (TP; Purity: 99.76% w/w)	1/10 LC_{50} > 0.333 mg/L	0.119	<0.34	No
		OC 53276 (TP; Purity: 99.16% w/w)	LC_{50} > 4.14 mg/L	0.119	<0.29	No
	28d-Chronic	OC 56635 (TP; Purity: 99.9% w/w)	NOEC = 99.2 mg/L	0.066	0.01	No

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	LOC exceeded
Fathead minnow, *Pimephales promelas*[3]	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	1/10 LC_{50} > 0.00522 mg a.i./L	0.115	**<220**	Yes
	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 98.77% w/w)	$NOEC_{growth}$ = 0.00224 mg a.i./L	0.115	**47.8**	Yes
Plants						
Freshwater alga, *Pseudokirchneriella subcapitata*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	½ EC_{50} > 0.00685 mg a.i./L	0.022	**<3.14**	Yes
		OC 56635 (TP; Purity: 99.9% w/w)	½ EC_{50} > 497 mg/L	0.012	<0.01	No
	72h-Acute	OC56574 (TP; Purity: 99.76% w/w)	½ EC_{50} = 1.0545 mg/L	0.022	0.02	No
		OC 53276 (TP; Purity: 99.76% w/w)	½ EC_{50} > 2.14 mg/L	0.022	<0.01	No
Duckweed, *Lemna gibba*	7d-Dissolved	GATTEN (end-use product; Purity: 4.97% w/w)	½ EC_{50} > 0.107 mg a.i./L	0.022	<0.20	No
Marine organisms						
Invertebrates						
Saltwater mysid, *Americamysis bahia*	21d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	$NOEC_{growth}$ = 0.0456 mg a.i./L	0.022	0.47	No

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	LOC exceeded
Eastern oyster, *Crassostrea virginica*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	½ EC_{50} > 0.0095 mg a.i./L	0.022	**<2.26**	Yes
		GATTEN (end-use product; Purity: 4.97% w/w)	½ EC_{50} > 0.018 mg a.i./L	0.022	**<1.20**	Yes
Amphipods, *Leptocheirus plumulosus*	28d-Chronic – spiked sediment: sediment	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	$NOAEC_{reproduction}$ = 11 mg a.i./kg	0.077	0.01	No
Fish						
Sheepshead minnow, *Cyprinodon variegatus*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.0% w/w)	1/10 LC_{50} > 0.085 mg a.i./L	0.022	<0.25	No
		GATTEN (end-use product; Purity: 4.97% w/w)	1/10 LC_{50} > 0.0077 mg a.i./L	0.022	**<2.79**	Yes
	34d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.43% w/w)	$NOEC_{growth}$ = 0.070 mg a.i./L	0.022	0.31	No
Plants						
Marine diatom, *Skeletonema costatum*	96h-Acute	GATTEN (end-use product; Purity: 4.97% w/w)	½ E_bC_{50} = 0.066 mg a.i./L	0.022	0.33	No

[1]EEC = Estimated Environmental concentration. An EEC of 0.022 mg a.i./L for a waterbody at a depth of 80 cm was used to evaluate risks to all organisms except amphibians, where an EEC of 0.115 mg a.i./L for a waterbody at a depth of 15 cm was used. The sediment and pore water concentrations were conservatively assumed to be equal to the soil and 80 cm water EECs of

0.077 mg a.i./kg and 0.022 mg a.i./L, respectively. EECs for transformation products were calculated conservatively assuming 100% of the applied flutianil was instantly transformed into the transformation product on a molecular weight/weight basis.
[2]RQ = Risk Quotient. The RQ is calculated by dividing the EEC by the effect metric (RQ = EEC/effect metric). The RQ is then compared to the level of concern (LOC = 1.0 for all aquatic organisms). If the screening level RQ is below the LOC, the risk is considered acceptable and no further risk characterization is necessary. For groups where the LOC is exceeded (RQ > 1), further characterization of the risk is conducted.
[3]used as a surrogate for amphibians.

Table 21 Refined risk to aquatic organisms from spray drift

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	Risk
Freshwater organisms						
Invertebrates						
Daphnia magna	48h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	EC_{50} > 0.0065 mg a.i./L	Cucurbits – off-field (groundboom): 0.002	<0.36	No
				Cherries and Grape – off-field (early season airblast): 0.013	**<1.97**	Yes
				Cherries and Grape – off-field (late season airblast): 0.010	**<1.57**	Yes
	21d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	NOEC = 0.00711 mg a.i./L	Cucurbits – off-field (groundboom): 0.002	0.33	No
				Cherries and Grape – off-field (early season airblast): 0.013	**1.80**	Yes
				Cherries and Grape – off-field (late season airblast): 0.010	**1.43**	Yes
Amphipod, *Hyalella azteca*	42d-Chronic – spiked sediment: pore water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	$NOAEC_{reproduction}$ = 0.021 mg a.i./L	Cucurbits – off-field (groundboom): 0.002	0.11	No
				Cherries and Grape – off-field (early season airblast): 0.013	0.61	No

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	Risk
				Cherries and Grape – off-field (late season airblast): 0.010	0.49	No
	42d-Chronic – spiked sediment: overlying water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	$NOAEC_{reproduction}$ = 0.0056 mg a.i./L	Cucurbits – off-field (groundboom): 0.002	0.42	No
				Cherries and Grape – off-field (early season airblast): 0.013	**2.28**	Yes
				Cherries and Grape – off-field (late season airblast): 0.010	**1.82**	Yes
Fish						
Rainbow trout, *Oncorhynchus mykiss*	96h-Acute	GATTEN (end-use product; Purity: 4.99% w/w)	1/10 LC_{50} = 0.00522 mg a.i./L	Cucurbits – off-field (groundboom): 0.002	0.45	No
				Cherries and Grape – off-field (early season airblast): 0.013	**2.45**	Yes
				Cherries and Grape – off-field (late season airblast): 0.010	**1.95**	Yes
Fathead minnow, *Pimephales promelas*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LC_{50} > 0.00522 mg a.i./L	Cucurbits – off-field (groundboom): 0.002	<0.45	No
				Cherries and Grape – off-field (early season airblast): 0.013	**<2.45**	Yes
				Cherries and Grape – off-field (late season airblast): 0.010	**<1.95**	Yes

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	Risk
	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 98.77% w/w)	$NOEC_{growth}$ = 0.00224 mg a.i./L	Cucurbits – off-field (groundboom): 0.002	0.99	No
				Cherries and Grape – off-field (early season airblast): 0.013	**5.33**	Yes
				Cherries and Grape – off-field (late season airblast): 0.010	**4.25**	Yes
Amphibians						
Rainbow trout, *Oncorhynchus mykiss*[3]	96h-Acute	GATTEN (end-use product; Purity: 4.99% w/w)	1/10 LC_{50} = 0.00522 mg a.i./L	Cucurbits – off-field (groundboom): 0.013	**2.42**	Yes
				Cherries and Grape – off-field (early season airblast): 0.068	**13.1**	Yes
				Cherries and Grape – off-field (late season airblast): 0.054	**10.4**	Yes
Fathead minnow, *Pimephales promelas*[3]	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	LC_{50} > 0.00522 mg a.i./L	Cucurbits – off-field (groundboom): 0.013	**<2.42**	Yes
				Cherries and Grape – off-field (early season airblast): 0.068	**<13.1**	Yes
				Cherries and Grape – off-field (late season airblast): 0.054	**<10.4**	Yes
	28d-Chronic		$NOEC_{growth}$ = 0.00224 mg a.i./L	Cucurbits – off-field (groundboom): 0.013	**5.26**	Yes

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	Risk
		Flutianil (technical grade active ingredient; Purity: 98.77% w/w)		Cherries and Grape – off-field (early season airblast): 0.068	**28.4**	Yes
				Cherries and Grape – off-field (late season airblast): 0.054	**22.7**	Yes
Plants						
Freshwater alga, *Pseudokirchneriella subcapitata*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	½ EC_{50} > 0.00685 mg a.i./L	Cucurbits – off-field (groundboom): 0.002	<0.35	No
				Cherries and Grape – off-field (early season airblast): 0.013	**<1.87**	Yes
				Cherries and Grape – off-field (late season airblast): 0.010	**<1.49**	Yes
Marine organisms (based on the single highest application rate)						
Invertebrates						
Eastern oyster, *Crassostrea virginica*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	EC_{50} > 0.019 mg a.i./L	Cucurbits – off-field (groundboom): 0.0005	<0.03	No
				Cherries and Grape – off-field (early season airblast): 0.003	<0.17	No
				Cherries and Grape – off-field (late season airblast): 0.003	<0.14	No
			½ EC_{50} > 0.018 mg a.i./L	Cucurbits – off-field (groundboom): 0.0005	<0.03	No

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	Risk
		GATTEN (end-use product; Purity: 4.97% w/w)		Cherries and Grape – off-field (early season airblast): 0.003	<0.18	No
				Cherries and Grape – off-field (late season airblast): 0.003	<0.14	No
Fish						
Sheepshead minnow, *Cyprinodon variegatus*	96h-Acute	GATTEN (end-use product; Purity: 4.97% w/w)	LC_{50} > 0.077 mg a.i./L	Cucurbits – off-field (groundboom): 0.0005	<0.01	No
				Cherries and Grape – off-field (early season airblast): 0.003	<0.04	No
				Cherries and Grape – off-field (late season airblast): 0.003	<0.03	No

[1]EEC = Estimated Environmental concentration. An EEC of 0.022 mg a.i./L for a waterbody at a depth of 80 cm was used to evaluate risks to all organisms except amphibians, where an EEC of 0.115 mg a.i./L for a waterbody at a depth of 15 cm was used. The pore water concentration was conservatively assumed to be equal to the 80 cm water EEC of 0.022 mg a.i./L. The further characterized EECs for off-field exposure to non-target terrestrial plants accounted for a 11% drift factor for applications to cucurbits via groundboom using an ASAE fine spray quality, and a 74 and 59% spray drift factor for applications to cherries and grape via airblast. For the further risk characterization, the application rate for cherries and grape (four × 35 g a.i./ha with a 7-day re-treatment interval) was modelled.

[2]RQ = Risk Quotient. The RQ is calculated by dividing the EEC by the effect metric (RQ = EEC/effect metric). The RQ is then compared to the level of concern (LOC = 1.0 for all aquatic organisms). If the screening level RQ is below the LOC, the risk is considered acceptable and no further risk characterization is necessary. For groups where the LOC is exceeded (RQ > 1), further characterization of the risk is conducted.

[3]used as a surrogate for amphibians.

Table 22 Environmental fate parameters used for the ecological water modelling

Parameter	Flutianil	Unit
K_d	451	L/kg
Aerobic aquatic half-life at 20ºC	579	d
Anaerobic aquatic half-life at 20ºC	1980	d
Aqueous photolysis half-life	1.03	d
Hydrolysis half-life at pH 7	stable	-
Aerobic soil half-life at 20ºC	2410	d

Table 23 EECs (in µg a.i./L) for the ecological risk assessment of Flutianil

Use	Water depth (cm)	Water column				Pore water	
		Peak	24-hour	96-hour	21-day	Peak	21-day
Grapes/Cherry 4 × 35 g a.i./ha	80	2.3	1.9	1.3	0.90	0.79	0.78
	15	9.2	3.1	1.4	0.93	-	-
Cucumbers/Pumpkins 5 × 35 g a.i./ha	80	3.4	2.9	2.3	1.9	1.8	1.8
	15	11.5	4.3	2.4	1.9	-	-

Table 24 Refined risk to aquatic organisms from runoff

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	Risk
Freshwater organisms						
Invertebrates						
Daphnia magna	48h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	EC_{50} > 0.0065 mg a.i./L	Cucurbits: 0.0029	<0.45	No
				Cherries and Grape: 0.0019	<0.29	No
	21d-Chronic	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	NOEC = 0.00711 mg a.i./L	Cucurbits: 0.0019	0.27	No
				Cherries and Grape: 0.0009	0.13	No
Amphipod, *Hyalella azteca*	42d-Chronic – spiked sediment: pore water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	$NOAEC_{reproduction}$ = 0.021 mg a.i./L	Cucurbits: 0.0018	0.09	No
				Cherries and Grape: 0.00078	0.04	No
			$NOAEC_{reproduction}$ = 0.0056 mg a.i./L	Cucurbits: 0.0029	0.52	No

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	Risk
	42d-Chronic – spiked sediment: overlying water	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)		Cherries and Grape: 0.0019	0.34	No
Fish						
Rainbow trout, *Oncorhynchus mykiss*	96h-Acute	GATTEN (end-use product: 4.99% w/w)	1/10 LC_{50} > 0.00522 mg a.i./L	Cucurbits: 0.0029	<0.56	No
				Cherries and Grape: 0.0019	<0.36	No
Fathead minnow, *Pimephales promelas*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	1/10 LC_{50} > 0.000522 mg a.i./L	Cucurbits: 0.0029	<0.56	No
				Cherries and Grape: 0.0019	<0.36	No
	28d-Chronic	Flutianil (technical grade active ingredient; Purity: 98.77% w/w)	$NOEC_{growth}$ = 0.00224 mg a.i./L	Cucurbits: 0.0019	0.85	No
				Cherries and Grape: 0.0009	0.40	No
Amphibians						
Fathead minnow, *Pimephales promelas*[3]	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	1/10 LC_{50} > 0.000522 mg a.i./L	Cucurbits: 0.0043	<0.82	No
				Cherries and Grape: 0.0031	<0.59	No
	28d-Chronic	Flutianil (technical grade active	$NOEC_{growth}$ = 0.00224 mg a.i./L	Cucurbits: 0.0019	0.85	No

Organism	Exposure	Test substance	Effect metric	EEC[1] (mg a.i./L)	RQ[2]	Risk
		ingredient; Purity: 98.77% w/w)		Cherries and Grape: 0.00093	0.42	No
Plants						
Freshwater alga, *Pseudokirchneriella subcapitata*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.22% w/w)	½ EC_{50} > 0.00685 mg a.i./L	Cucurbits: 0.0029	<0.42	No
				Cherries and Grape: 0.0019	<0.28	No
Marine organisms						
Invertebrates						
Eastern oyster, *Crassostrea virginica*	96h-Acute	Flutianil (technical grade active ingredient; Purity: 99.19% w/w)	EC_{50} > 0.019 mg a.i./L	Cucurbits: 0.0029	<0.15	No
				Cherries and Grape: 0.0019	<0.10	No

[1] EEC = Estimated Environmental concentration. EECs were estimated via the Pesticide in Water Calculator (PWC) by modelling a 10 ha field adjacent to 1 ha waterbodies of 80 and 15 cm in depth. See Tables 22 and 23 for EECs.
[2]RQ = Risk Quotient. The RQ is calculated by dividing the EEC by the effect metric (RQ = EEC/effect metric). The RQ is then compared to the level of concern (LOC = 1.0 for all aquatic organisms). If the screening level RQ is below the LOC, the risk is considered acceptable and no further risk characterization is necessary. For groups where the LOC is exceeded (RQ > 1), further characterization of the risk is conducted.
[3]used as a surrogate for amphibians.

Table 25 Toxic substances management policy considerations-comparison to TSMP Track 1 criteria

TSMP Track 1 criteria	TSMP Track 1 criterion value		Flutianil (Active ingredient) endpoints	OC 56574 (Transformation product) endpoints	OC 56635 (Transformation product) endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes	Yes	Yes
Predominantly anthropogenic[2]	Yes		Yes	Yes	Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	Yes	No	No

TSMP Track 1 criteria	TSMP Track 1 criterion value		Flutianil (Active ingredient) endpoints	OC 56574 (Transformation product) endpoints	OC 56635 (Transformation product) endpoints
			Laboratory studies: DT_{50} of 1114 to 2855 days in aerobic soil and 1460 to 13191 d days in anaerobic soil. Field studies: DT_{50} of 312 to 398 days.	Laboratory studies: not enough data to calculate a DT_{50}. Field studies: not enough data to calculate a DT_{50}. However, it was not detected after 91 days.	Laboratory studies: not enough data to calculate a DT_{50}. Field studies: DT_{50} of 42.2 days.
	Whole system (water + sediment)	Half-life ≥ 365 days	Yes Laboratory studies: DT_{50} of 236 to 699 days in aerobic systems and 766 to 2280 days in anaerobic systems.	N/A Laboratory studies: not enough data to calculate a DT_{50}.	N/A Laboratory studies: not enough data to calculate a DT_{50}.
	Air	Half-life ≥ 2 days, or evidence of long-range atmospheric transport	No Estimated half-life of < 0.3 hours for reaction with hydroxyl radicals (AOPWIN). Flutianil is unlikely to enter the atmosphere	N/A	N/A

TSMP Track 1 criteria	TSMP Track 1 criterion value	Flutianil (Active ingredient) endpoints	OC 56574 (Transformation product) endpoints	OC 56635 (Transformation product) endpoints
		based on the vapour pressure (1.530×10^{-7} Pa at 20°C) and Henry's Law Constant (8.259×10^{-3} Pa m^3/mol).		
Bioaccumulation[4]	Log $K_{ow} \geq 5$	No 3.1	Yes 5248	No -0.0016
	BCF ≥ 5000	No Whole body BCF of 380 L/kg	N/A	N/A
	BAF ≥ 5000	Not available	N/A	N/A
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?		**No, does not meet all TSMP Track 1 criteria.**	**No, does not meet all TSMP Track 1 criteria.**	**No, does not meet all TSMP Track 1 criteria.**

[1]All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (in other words, all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3]If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4]Bioaccumulation Factors (BAF) are preferred over Bioconcentration Factors (BCF); in the absence of BAF or BCF data, the octanol-water partition coefficient (log K_{ow}) may be used.).

Table 26 List of supported uses

Supported use claims for GATTEN
1. Control of powdery mildew (*Podosphaera clandestina*) on cherries (Crop Subgroup 12-09A) at a rate of 400–690 mL/ha (20.0–35.0 g a.i./ha) when applied to foliage during the fruiting stage using airblast ground equipment. Repeat applications at 7- to 14-day intervals. Within the stated ranges, use a higher rate and shorter interval under conditions that are conducive to high disease pressure. Do not exceed a maximum of 4 applications per year and a maximum of 140 g a.i./ha per year.
2. Control of powdery mildew (*Erysiphe necator*) on grape at a rate of 400–690 mL/ha (20.0–35.0 g a.i./ha) when applied to foliage during the fruiting stage using airblast ground equipment. Repeat applications at 7- to 14-day intervals. Within the stated ranges, use a higher rate and shorter interval under conditions that are conducive to high disease pressure. Do not exceed a maximum of 4 applications per year and a maximum of 140 g a.i./ha per year.
3. Control of powdery mildew (*Sphaerotheca fuliginea* syn. *Podosphaera xanthii*) on cucurbit vegetables (Crop Group 9) at a rate of 400–690 mL/ha (20.0–35.0 g a.i./ha) when applied to foliage during the seedling to the fruiting stage using broadcast ground equipment. Repeat applications at 7- to 14-day intervals. Within the stated ranges, use a higher rate and shorter interval under conditions that are conducive to high disease pressure. Do not exceed a maximum of 5 applications per year and a maximum of 175 g a.i./ha per year.

Appendix II Supplemental maximum residue limit information—International situation and trade implications

Flutianil is an active ingredient that is being registered in Canada for use on cucurbit vegetables (CG 9), cherries (CSG 12-09A), and grape (representative crop of the small fruit vine climbing, except fuzzy kiwifruit (CSG 13-07F)), as well as on imported strawberries (representative crop of the low growing berries (CSG 13-07G)), and apples. The MRLs proposed for flutianil in Canada are the same as corresponding tolerances in the United States.

The American tolerances for flutianil are listed in the Electronic Code of Federal Regulations, 40 CFR Part 180, by pesticide.

Currently, there are no Codex MRLs[10] listed for flutianil in or on any commodity on the Codex Alimentarius Pesticide Index website.

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

References

A. List of studies/Information submitted by registrant

PMRA document number	References
1.0	**Chemistry**
2961707	2004, Determination of Appearance of OK-5203, DACO: 2.14.1,2.14.2,2.14.3
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4.0 Value

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B. Additional information considered

i) Published information

1.0 Human and animal health

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