Proposed Registration Decision PRD2015-10

Difenoconazole

(publié aussi en français)

28 April 2015

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

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

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

ISSN: 1925-0878 (print)
1925-0886 (online)

Catalogue number: H113-9/2015-10E (print version)
H113-9/2015-10E-PDF (PDF version)

Table of Contents

Overview

Proposed Registration Decision for Difenoconazole

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Difenoconazole Technical, Ascernity Fungicide and Instrata II A Fungicide containing the technical grade active ingredients difenoconazole and benzovindiflupyr to control diseases in turf.

Difenoconazole is currently registered in Canada as a seed treatment (the detailed review for this use can be found in the Proposed Regulatory Decision Document PRDD99-01, *Difenoconazole*) and to control or suppress fungal diseases on a variety of fruit and vegetable crops (the detailed review for this use can be found in the Evaluation Report ERC2011-06, *Difenoconazole*).

Difenoconazole is formulated with benzovindiflupyr in the two end use products being proposed for use in turf.

A full review of benzovindiflupyr can be found in PRD2015-07: *Benzovindiflupyr*.

This consultation document presents the review for the use of difenoconazole on turf.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

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 Difenoconazole Technical, Ascernity Fungicide and Instrata II A Fungicide.

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 (for example, those most sensitive to environmental contaminants). 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 PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on the use of difenoconazole on turf, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on the use of difenoconazole on turf, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA'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 Difenoconazole?

Difenoconazole is a triazole fungicide belonging to the demethylation inhibitor (DMI) group of fungicides (Group 3). Difenoconazole is approved in Canada as a foliar fungicide and a seed treatment on field crops, fruits and vegetables.

---

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."

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*.

Health Considerations

Can Approved Uses of Difenoconazole Affect Human Health?

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

Potential exposure to difenoconazole may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where 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). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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

In laboratory animals, the technical grade active ingredient difenoconazole was of slight acute toxicity by the oral route; consequently, the hazard signal words "CAUTION – POISON" are required on the Difenoconazole Technical Fungicide label. It was of low acute toxicity dermally and through inhalation exposure. Difenoconazole was mildly irritating to the eyes, minimally irritating to the skin and did not cause an allergic skin reaction. The hazard signal words "CAUTION – EYE IRRITANT" are required on the Difenoconazole Technical Fungicide label.

Ascernity Fungicide and Instrata II A Fungicide containing benzovindiflupyr and difenoconazole was slightly acutely toxic via the oral route and of low acute toxicity via the dermal and inhalation routes. It was moderately irritating to the eyes, but non-irritating to the skin and did not cause an allergic skin reaction. Based on these findings, the signal word and hazard statements "POISON" and "WARNING –EYE IRRITANT" are required on the product label.

There was limited evidence that difenoconazole caused damage to the nervous system or immune system. Difenoconazole did not cause birth defects in animals and there were no effects on the ability to reproduce. There was no evidence to suggest that difenoconazole damaged genetic material. Health effects in animals given repeated doses of difenoconazole included effects on the liver, body weight and food consumption. Difenoconazole caused liver tumours in mice, but not in rats. These tumours were observed at very high doses that were considered excessive.

When difenoconazole was given to pregnant animals, effects of a serious nature were observed on the developing fetus at doses that were toxic to the mother. There was an increased incidence of fetal mortality in utero, while the mothers had severely depressed body weight gains. The risk assessment takes these effects into account in determining the allowable level of human exposure to difenoconazole.

The risk assessment protects against the effects of difenoconazole by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

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

Chronic dietary intake estimates (food plus drinking water) revealed that the general population and children between the age of one and two years old, the subpopulation which would ingest the most difenoconazole relative to body weight, are expected to be exposed to less than 61% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from difenoconazole is not of health concern for all population subgroups. There are no lifetime cancer risks of concern from the use of difenoconazole.

The acute dietary (food plus drinking water) intake estimate for the population subgroup of women aged between 13 and 49 years old was less than 14% of the acute reference dose. Estimates for all other subpopulations, including the highest exposed subpopulation of children between the age of one and two years old, were also less than 14%. Hence, none are of health concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

No metabolism or residue data are required by the PMRA to support the registration of the end-use products Ascernity Fungicide and Instrata II A Fungicide (a component of Instrata II Fungicide Tank-Mix), both for use on golf course turfgrass in Canada.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern when Ascernity Fungicide and Instrata IIA Fungicide are used according to the proposed label directions.

Adults and youth may be exposed to difenoconazole while golfing on treated courses. Based on the expected short to intermediate term duration of this activity, risk to golfers is not a concern.

Occupational Risks From Handling Difenoconazole

Occupational risks are not of concern when Ascernity Fungicide and Instrata IIA Fungicide are used according to the proposed label directions, which include protective measures.

Golf course workers, who mix, load or apply Ascernity Fungicide or Instrata IIA Fungicide, as well as field workers re-entering freshly treated turf can come in direct contact with difenoconazole residues on the skin. Therefore, the label specifies that anyone mixing/loading

and applying these products must wear a long-sleeved shirt and long pants, chemical-resistant gloves, and goggles when mixing, loading and applying or during equipment clean-up or repair. Goggles and chemical-resistant gloves are not required during groundboom application. The label also requires that workers and golfers do not enter treated areas until residues have dried. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk from exposure to difenoconazole for these individuals is not a concern.

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

Environmental Considerations

What Happens When Difenoconazole Is Introduced Into the Environment?

When used according to label directions, difenoconazole does not pose an unacceptable risk to the environment.

When difenoconazole is used to control fungal diseases on turf, the environmental fate characteristics are similar to those expected when it is used on agricultural food crops. Any difenoconazole deposited on the ground will remain in soil for a considerable period of time as it is broken down very slowly. With repeated yearly applications, difenoconazole will accumulate in soil and could eventually move to lower soil depths. Difenoconazole is not volatile and is not expected to bioaccumulate.

The turf use of difenoconazole poses potential risks to non-target terrestrial organisms including beneficial arthropods and plants. When used near aquatic habitats, it poses potential risks to amphibians, freshwater and marine/estuarine invertebrates, freshwater and marine/estuarine fish, and freshwater algae. To minimize exposure to non-target organisms, spray buffer zones are required to protect terrestrial, freshwater and marine/estuarine habitats adjacent to areas treated with difenoconazole. Toxicity statements are also required on the product label for terrestrial organisms, beneficial, arthropods, plants, freshwater and marine/estuarine invertebrates and fish and fresh water algae.

Value Considerations

What Is the Value of Instrata II Fungicide and Ascernity Fungicide?

Instrata II and Ascernity Fungicides contain multiple active ingredients that are used in combination to control important diseases on turf.

Instrata II Fungicide is a co-pack product consisting of two components for control of pink and grey snow moulds. Component A contains benzovindiflupyr and difenoconazole fungicides and Component B contains fludioxonil fungicide. Ascernity Fungicide contains benzovindiflupyr and difenoconazole fungicides and controls summer diseases.

Managers of high quality turf found on golf courses and sod farms must preserve the functional and aesthetic characteristics of the crop. Golf courses require high levels of control of turf pests to ensure play areas are maintained according to the expectations of members. Difenoconazole demonstrated a contribution to efficacy against important summer and winter diseases. The activity of multiple active ingredients contributes to overall disease control and the management of resistance. The registration of these turf products provides additional tools to help combat fungicide resistance and enhance control of several key pathogens.

Measures to Minimize Risk

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

The key risk-reduction measures being proposed on the label of Instrata II A Fungicide and Ascernity Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with difenoconazole on the skin or through inhalation of spray mists, anyone mixing/loading and applying Ascernity or Instrata IIA Fungicide must wear a long sleeved-shirt and long pants, chemical-resistant gloves, and goggles when mixing, loading and applying or during equipment clean-up or repair. Goggles and chemical-resistant gloves are not required during groundboom application. The label also requires that workers and golfers do not enter treated areas until residues have dried. In addition, a restriction against use in residential areas was added to the label.

Environment

Include all the environmental label statements that were previously identified as required (ERC-2011-06, *Difenoconazole*), as well as spray buffer zones for terrestrial and aquatic habitats that have been updated to reflect use on turf.

Next Steps

Before making a final registration decision on difenoconazole use on turf, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on difenoconazole use on turf (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 (located in Ottawa).

Science Evaluation

Difenoconazole

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient and Technical Product

Please refer to PRD99-01, *Difenoconazole* and ERC2011-06, *Difenoconazole* for chemistry review of the active ingredient difenoconaziole and Difenoconazole Technical Fungicide.

1.2 Physical and Chemical Properties of the End-Use Products

Property	Ascernity	Instrata II A Fungicide
Colour	Light brown	Light brown
Odour	Aromatic	Aromatic
Physical state	Liquid	Liquid
Formulation type	Emulsifiable concentrate	Emulsifiable concentrate
Guarantee	Benzovindiflupyr 24 g/L Difenoconazole 79 g/L	Benzovindiflupyr 24 g/L Difenoconazole 79 g/L
Container material and description	Plastic, jug, tote, 0.5 L to bulk	Plastic, jug, tote, 0.5 L to bulk
Density	1.055 g/mL	1.055 g/mL
pH of 1% dispersion in water	4.2	4.2
Oxidizing or reducing action	Does not contain any oxidising or reducing agents. Incompatible with hypochlorite.	Does not contain any oxidising or reducing agents. Incompatible with hypochlorite.
Storage stability	Stable when stored for one year at ambient temperature in commercial packaging.	Stable when stored for one year at ambient temperature in commercial packaging.
Corrosion characteristics	Not corrosive to the container material	Not corrosive to the container material
Explodability	Not considered to be potentially explosive.	Not considered to be potentially explosive.

1.3 Directions for Use

Instrata II Fungicide: For control of pink and grey snow moulds, Instrata II A Fungicide should be applied at 31.7 ml/100 m^2 in combination with Instrata II B Fungicide should be applied at 34.8 ml/100 m^2 in a spray volume of 4–8 L of water per 100 m^2. Make one application in the late fall before snow cover when conditions are favourable for disease infection and prior to disease symptom expression.

Ascernity Fungicide: To control labelled summer diseases, apply Ascernity Fungicide up to two times at 31 ml/100 m^2 in a spray volume of 4–8 L of water per 100 m^2. Treatment for control of anthracnose, microdochium patch or red thread should be applied on a 14-day interval. Treatment for brown patch or dollar spot should be applied on an interval of 14–21 days. Ascernity Fungicide may be tank mixed with Daconil 2787 or Daconil Ultrex Fungicides.

1.4 Mode of Action

Difenoconazole is a locally systemic fungicide. Difenoconazole is classified as a Group 3 fungicide and belongs to the triazoles chemical group of fungicides. The mode of action of difenoconazole is an inhibitor of demethylation of C-14 during ergosterol biosynthesis leading to accumulation of C-14 methyl sterols. The process slows or stops the growth of the fungus and effectively prevents further infection or invasion of host tissues. Therefore, difenoconazole is considered tobe fungistatic or growth inhibiting rather than fungicidal or lethal.

2.0 Methods of Analysis

Please refer to ERC2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole* for details on the residue analytical methods used for data generation and enforcement purposes.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Please refer to ERC2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole* for details on the toxicology summary.

Incident Reports

Since26 April 2007, registrants have been required by law to report incidents to the PMRA, including adverse effects to Canadian health or the environment. The database was searched for incident reports involving difenoconazole. As of 26 August 2014, the PMRA had received ten human and nine domestic animal incident reports. These incident reports also involved other registered active ingredients.

The symptoms reported in 8 human incidents (mainly minor or moderate in severity) were determined to have some degree of association with the reported exposure scenario. Overall, minor effects like headache, vomiting, dizziness or eye irritation were reported. In most incidents, exposure occurred as a result of application activities associated with treated seeds. Equipment failure was noted in one report.

In 4 domestic animal incidents, the effects experienced by the animal were considered to be related to the reported pesticide exposure. The severity of effects was classified as minor or moderate in 3 cases and major in 1 case. In all 4 cases, a dog accidentally ingested seed treated with difenoconazole and other active ingredients. The symptoms vomiting, diarrhea, tremors, lethargy or dehydration were reported.

Overall, no significant health risks from the use of products containing difenoconazole have been identified from this review of incident reporting data, as most incidents involved minor symptoms or generalized effects that may have been caused by other factors and current label statements address the potential hazards.

3.1.1 Pest Control Products Act Hazard Characterization

Please refer to ERC2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole* for details on the toxicology summary.details on the *Pest Control Products Act* Hazard Characterization.

3.2 Acute Reference Dose (ARfD)

Please refer to ERC2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole* for details on the Acute Reference Dose.

3.3 Acceptable Daily Intake (ADI)

Please refer to ERC2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole* for details on the Acceptable Daily Intake.

Cancer Assessment

Please refer to ERC2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole* for details on the Cancer Assessment.

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Please refer to ERC2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole* for details on the Toxicological Endpoints.

Occupational exposure to difenoconazole is characterized as short- to intermediate-term in duration and is predominantly by the dermal and inhalation routes. Non-occupational exposure to difenoconazole is characterized as acute, short- or intermediate-term and is predominantly by the dermal and oral routes.

3.4.1.1 Dermal Absorption

A dermal absorption estimate of 51% derived from an *in vivo* dermal penetration study in the rat was considered appropriate for risk assessment purposes. Please refer to ERC2011-06, *Difenoconazole* for further details.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to difenoconazole during mixing, loading and application. Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted. Dermal and inhalation exposure estimates for workers mixing/loading and applying were generated from Pesticide Handlers Exposure Database (PHED), and Outdoor Residential Exposure Task Force (ORETF) databases.

Exposure to workers mixing, loading and applying difenoconazole is expected to be short-to intermediate-term in duration and to occur primarily by the dermal and inhalation routes. Exposure estimates were derived for mixers/loaders/applicators applying Ascernity Fungicide and Instrata IIA Fungicide to turf using groundboom, and turf gun application equipment. The exposure estimates are based on mixers/loaders/applicators wearing long-sleeved shirts, long pants and chemical-resistant gloves.

As chemical-specific data for assessing human exposures were not submitted, dermal and inhalation exposures for workers mixing, loading and applying by groundboom, were estimated using the PHED, version 1.1. PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates. In addition, mixing, loading and applying by turf-gun sprayer was estimated using the ORETF data.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day and the dermal absorption 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.

Exposure estimates were compared to the toxicological endpoints (NOAELs; no observed adverse effects levels) to obtain the margin of exposure (MOE); the target MOE is 300. The MOEs for mixers/loaders and applicators were above the target for dermal and inhalation exposure, and therefore, occupational risks associated with mixing/loading and applying Ascernity Fungicide and Instrata IIA Fungicide are not of concern with the personal protective equipment specified on the label. The exposure and risk estimates are presented in Table 3.4.1.

Table 3.4.1 Mixer/loader/applicator risk assessment for chemical handlers wearing a single layer (and gloves when mixing/loading)

Exposure scenario	PHED/ORETF unit exposure (µg/kg a.i. handled)*	ATPD (ha/day)†	Rate (kg ai/ha)	Daily exposure (mg/kg bw/day)‡	MOE¶
Groundboom golf course	45.46	16	0.245	0.00223	11223
Turf gun	404.35	2	0.245	0.00248	10094

* PHED/ORETF total unit exposure based on a dermal absorption factor of 51% from an *in vivo* rat study.
† Default area treated per day
‡ Daily exposure = (unit exposure × ATPD × Rate) / (80 kg bw × 1000 µg/mg)
¶ Based on NOAEL = 25 mg/kg bw/day, target MOE = 300

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure to workers re-entering areas treated with products containing difenoconazole when performing activities such as mowing, cup changing and grooming. The duration of exposure is considered to be short- to intermediate-term. The primary route of exposure for workers re-entering treated areas would be through dermal exposure to treated turf. Inhalation exposure is not considered to be a significant route of exposure for people entering treated areas compared to the dermal route, since active ingredient is relatively non-volatile (Henry's Law Constant = 8.22×10^{-12} atm.m^3/mol) and as such, a risk assessment was not required.

Dermal exposure to workers entering treated areas is estimated by coupling turf transferable residues (TTR) with activity-specific transfer coefficients. Activity transfer coefficients are based on Agricultural Re-entry Task Force (ARTF) data. Chemical-specific TTR data were not submitted. As such, a default TTR of 1% of the application rate was used in the exposure assessment.

Exposure estimates were compared to the toxicological endpoint to obtain the margin of exposure (MOE); the target MOE is 300. The MOEs for workers entering treated golf courses were above the target for dermal exposure; therefore, occupational risk associated with postapplication exposure difenoconazole is not of concern with the restricted entry interval specified on the label. The exposure and risk estimates are presented in Table 3.4.2.

Table 3.4.2 Postapplication exposure and risk estimate for Ascernity Fungicide and Instrata IIA Fungicide on day 0 after the last application

Re-entry activity	Peak DFR/TTR ($\mu g/cm^2$)*	Transfer coefficient (cm^2/hr)†	Dermal exposure (mg/kg bw/day)‡	MOE¶	REI
Transplanting, planting, harvesting	0.0317	6700	0.0108	2309	0
Mowing, watering, cup changing, irrigation repair, miscellaneous grooming	0.0317	3500	0.0057	4421	0
Golfing – adults (16+)	0.0317	5300	0.0043	5839	0
Golfing – youth (11-<16)	0.0317	4400	0.0050	5008	0
Golfing – child (6-<11)	0.0317	2900	0.00586	4266	0

* Calculated using the default 1% turf transferable on the day of application and 10% dissipation per day
† Transfer coefficients obtained from ARTF database
‡ Exposure = (Peak TTR [$\mu g/cm^2$] × TC [cm^2/hr] × Exposure Duration (8 hours for workers, 4 hours for golfers) × 51% dermal absorption) / (80 kg bw for adults, 57 kg bw for youths and 32 kg for children× 1000 µg/mg)
¶ Based on NOAEL = = 25 mg/kg bw/day, target MOE = 300

3.4.3 Residential Exposure and Risk Assessment

3.4.3.1 Handler Exposure and Risk

There is no residential handler exposure expected as Ascernity Fungicide and Instrata IIA Fungicide are not domestic products.

3.4.3.2 Postapplication Exposure and Risk

There is potential for postapplication exposure to the general population entering areas treated with Ascernity Fungicide and Instrata IIA Fungicide. Although these products are not for use on residential turf, they may be used on golf courses where children, youth and adults may enter. The duration of exposure is considered to be short- to intermediate-term for golfing. The primary route of exposure for these individuals would be through the dermal route. Difenoconazole is considered non-volatile and it is not an inhalation concern for postapplication exposure.

A postapplication risk assessment for turf was conducted using default TTR values (1% dislodgeable at Day 0 and 10% dissipation per day) and default transfer coefficients. For the proposed use on turfgrass, there is potential for recreational postapplication exposure to golfers. Exposure was assessed according to equations and parameters stated in the 2012 US EPA Residential SOP. Dermal exposure from golfing was assessed for adults (16 years plus), youth (11-<16 years), and children (6-<11 years). It is noted that the transfer coefficients in the 2012 Residential SOP are from ARTF studies. An exposure duration of 4 hours for golfers was used in the assessment.

Postapplication risk was calculated using a dermal absorption value of 51% from the *in vivo* rat study and toxicological endpoints. Table 3.4.3 presents the calculated MOEs for dermal exposure, which were all above the target MOE on the day of the last application. As such, no risks of concern are expected for postapplication exposure to golf course turf treated with difenoconazole and the proposed REI of "until residues have dried" is adequate to protect golfers.

Table 3.4.3 Postapplication exposure and risk estimate for Ascernity Fungicide and Instrata IIA Fungicide on day 0 after the last application

Re-entry activity	Peak DFR/TTR (µg/cm^2)*	Transfer coefficient (cm^2/hr)†	Dermal exposure (mg/kg bw/day)‡	MOE¶	REI
Golfing – adults (16+)	0.0317	5300	0.0043	5839	0
Golfing – youth (11-<16)	0.0317	4400	0.0050	5008	0
Golfing – child (6-<11)	0.0317	2900	0.00586	4266	0

* Calculated using the default 1% turf transferable on the day of application and 10% dissipation per day
† Transfer coefficients obtained from ARTF Transfer Coefficients
‡ Exposure = (Peak TTR [µg/cm^2] × TC [cm^2/hr] × Exposure Duration (4 hours for golfers) × 51% dermal absorption) / (80 kg bw for adults, 57 kg bw for youths and 32 kg for children × 1000 µg/mg)
¶ Based on NOAEL = = 25 mg/kg bw/day, target MOE = 300

3.4.3.3 Aggregate Exposure

An aggregate (chronic dietary and dermal exposure) risk assessment was not conducted for golfers since the effects from the chronic dietary toxicity and the studies selected to represent short and intermediate dermal exposure differed and could not be combined.

3.4.3.4 Bystander Exposure and Risk

Bystander exposure should be negligible since the potential for drift is expected to be minimal. Application is limited to golf courses 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 inversions, application equipment and sprayer settings.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

Please refer to ERC2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole* for details on the residues in plant and animal foodstuffs.

The information discussed below concerns the changes in dietary exposure due to the update in the drinking water assessments to support the amendment to the registration of difenoconazole by addition of the use on golf course turfgrass in Canada.

3.5.2 Dietary Risk Assessment

Acute and chronic non-cancer dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 3.16), which uses 2003-2008 food consumption data from the US Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America (NHANES/WWEIA).

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the intermediate refined chronic non-cancer analysis for difenoconazole: 100% crop treated; default and experimental processing factors (where available); residues in/on crop commodities based on supervised trial median residue (STMdR) values from available Canadian and American supervised trials; residues in/on animal commodities at MRL levels; established and proposed MRLs; and established American Tolerances or Codex MRLs (where applicable). The intermediate refined chronic dietary exposure from all supported difenoconazole food uses (alone) for the total population, including infants and children, and all representative population subgroups is 24.1% of the acceptable daily intake (ADI). Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that chronic dietary exposure to difenoconazole from food and drinking water is 25.8% (0.002584 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children aged between one and two years old at 60.9% (0.006091 mg/kg bw/day) of the ADI.

3.5.2.2 Acute Dietary Exposure Results and Characterization

The following assumptions were applied in the intermediate refined acute analysis for difenoconazole: 100% crop treated; default and experimental processing factors (where available); residues in/on crop commodities based on maximum residue levels from available Canadian and American supervised trials; established and proposed MRLs; and established American Tolerances or Codex MRLs (where applicable). The intermediate refined acute dietary exposure (food alone) for all supported difenoconazole registered commodities is estimated to be 12.7% (0.010526 mg/kg bw/day) of the ARfD for females 13–49 years old (95th percentile, deterministic) and ranges from 4.1 to 13.4% of the ARfD for other subpopulations. Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that acute dietary exposure to difenoconazole from food and drinking water is 13.3% (0.010672 mg/kg bw/day) of the ARfD for females 13–49 years old and ranges from 4.3 to 13.6% of the ARfD for other subpopulations. The highest exposure and risk estimate is for children aged between one and two years old.

3.5.3 Aggregate Exposure and Risk

The aggregate risk for difenoconazole consists of exposure from food and drinking water sources as well as residential uses (golf). For details concerning golfer exposure, refer to Section 3.4.3.

3.5.4 Maximum Residue Limits

Please refer to the Maximum Residue Limit Database in the Pesticides and Pest Management section of Health Canada's website for the established MRLs for difenoconazole.

The nature of the residues in animal and plant matrices, analytical methodologies and field trial data were assessed under ERC2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole*. The acute and chronic non-cancer dietary risk estimates are summarized in Table 1 of Appendix I.

4.0 Impact on the Environment

An environmental assessment for non-target terrestrial and aquatic organisms was conducted in support of difenoconazole application to turf. Previously published environmental evaluations include foliar treatment products (ERC2011-06, *Difenoconazole*) and seed treatment products (PRDD99-01, *Difenoconazole*) on agricultural food crops.

4.1 Fate and Behaviour in the Environment

The physico-chemical properties of difenoconazole and its environmental behaviour have been reviewed and characterized previously (PRDD99-01, *Difenoconazole* and ERC2011-06, *Difenoconazole*).

In support of the use on turf, an additional terrestrial field dissipation study conducted in an eco-region relevant to Canada was reviewed. Study results demonstrated the persistence of difenoconazole, with a DT_{50} of 359 days and carryover of 25% into the next growing season for turfgrass plots. These estimates fall within the range of previously reported DT_{50}values of 28 – 892 days with carryover up to 68% (ERC-2011-06, *Difenoconazole*).

Three transformation products (all previously known) were identified and quantified: CGA 205375 (maximum of 28% of the applied at Day 60, decreasing to 16% on Day 630); CGA 142856 (maximum of 2.4% of the applied on Day 180) and CGA71019 (maximum of 1% of the applied on Day 120).

Throughout the 22-month study, difenoconazole was found primarily in the uppermost layer of soil (0-5 cm deep), which included the thatch-sod on top of the soil surface. Albeit at lower concentration levels, it was also consistently found in the 5-15 cm and 15-30 cm depths and a single detection occurred in the 30-45 cm depth. This is true of the transformation products as well, with the largest concentrations in the 0-5cm depth and consistent detections up to the 15-30 cm depth. Although there was less downward movement of the parent compound in the current field study compared to that reported in ERC2011-06, *Difenoconazole* (where difenoconazole residue detections occurred down to 60 cm), the current observations show that both the parent and the transformation products are consistently detected up to 30 cm (similar to previous results for the transformation products), further confirming the potential for leaching of this compound through soil.

A summary of the terrestrial environmental fate and behavior of difenoconazole derived from the new study data can be found in Appendix I, Table 2.

4.2 Environmental Risk Characterization

Comprehensive environmental risk assessments for non-target terrestrial and aquatic organisms with respect to the foliar and seed treatment uses of difenoconazole on agricultural food crops have previously been conducted. Estimates of exposure concentrations (EECs) for the current risk assessment were derived from the known environmental behaviour of difenonconazole along with the rates and application methods for the new use pattern on turf. The effects concentrations (*for example,* LD_{50}, EC_{25}, NOEL, *etc.*) were taken from the ecotoxicological data for the identical suite of non-target organisms as in the previous assessments (ERC-2011-06, *Difenoconazole* and PRDD99-01, *Difenoconazole*). Data for non-target terrestrial plants were submitted and evaluated subsequent to these two published reviews, and are included in the current assessment as well.

When conducting the risk assessment, a risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment which takes into consideration of more realistic exposure scenarios (such as drift to non-target habitats) is performed to further characterize the risk.

There are two difenoconazole containing end use products being proposed for ground application (i.e. field sprayer use) on turf: Ascernity Fungicide (with a maximum use rate of 245 g a.i./ha × 4 applications for a total of 980 g a.i./ha per season) and Instrata II A Fungicide (with a maximum use rate of 1 application of 250 g a.i./ha per season). The current risk assessment incorporates these seasonal maximum use rates for difenoconazole.

Each of these two end use products, Ascernity Fungicide and Instrata II A Fungicide, is formulated with the active ingredient benzovindiflupyr. For details on the environmental risk assessment of benzovindiflupyr, please refer to PRD2015- 07; *Benzovindiflupyr*. Instrata II A Fungicide will be sold as a tankmix with Instrata II B Fungicide (containing fludioxonil) in the Instarta II Tank-Mix. For the environmental risk assessment summary of fludioxonil (Instrata IIB Fungicide) for this specific use, see Cat B. Evaluation Report 2012-5379.

4.2.1 Risks to Terrestrial Organisms

Terrestrial organisms such as earthworms, honeybees, beneficial arthropods, birds, small wild mammals and terrestrial vascular plants may be exposed to difenoconazole-containing end use products in the environment through direct contact with treated material, contact with spray drift, or from ingestion of contaminated food.

The most sensitive ecotoxicity endpoints for these non-target terrestrial organisms (Table 9 in ERC2011-06, *Difenoconazole*) along with the EECs derived from the seasonal maximum use rate on turf were used in the current risk assessment. Whereas the screening level assessment assumes direct overspray onto a terrestrial habitat, or in the case of dietary exposure – a completely contaminated food source; the refined assessment identifies the risk from difenoconazole spray drift onto adjacent habitats and a wider range of dietary exposure scenarios. At the screening level, the EEC for direct on-field application was considered for all terrestrial organisms. During refined risk assessment, EECs for off-field were considered for beneficial arthropods, birds and mammals. Off-field EECs are calculated using the percent deposition expected at a point one metre downwind from the application site. The percent off-field drift expected is 6% for medium droplet size of field sprayer equipment. See Appendix I, Tables 3–8 for a summary of RQ calculations.

Earthworms and Honeybees: The proposed use of difenoconazole on turf at the maximum use rates for both Ascernity Fungicide (980 g a.i./ha per season) and Instrata II A Fungicide (250 g a.i./ha per season) poses a negligible risk to terrestrial invertebrates including earthworms and honeybees.

Beneficial Arthropods: Difenoconazole may pose a potential risk to beneficial arthropods that are exposed to direct application as the screening level LOC of 2 is exceeded on a reproductive basis for on-field exposure of the predatory mite. However, once spray drift is taken into account, the reproductive LOC is no longer exceeded for off-field exposure. This result applies to the maximum use rate for both of the proposed difenoconazole end use products (Ascernity Fungicide and Instrata II A Fungicide). This means that beneficial arthropods dwelling in terrestrial habitats adjacent to treatment areas, and subject to indirect exposure of spray drift, are at negligible risk from the proposed use of difenoconazole on turf.

This risk to beneficial arthropods dwelling on-field can be further refined to take into account the foliar deposition factor since difenoconazole will likely be applied to turf rather than bare soil plots. Once this refinement is taken into account, the LOC is no longer exceeded. Due to the exceedance of the LOC at the screening level, a precautionary label statement is required.

Terrestrial Vascular Plants: The plant ecotoxicity studies that were identified as an outstanding data requirement in ERC2011-06, *Difenoconazole* have subsequently been submitted and reviewed. The new data satisfy the environmental assessment requirements for difenoconazole on both turf and agricultural crops (Appendix I, Table 3).

In the vegetative vigour study, no adverse effects from the test substance were observed on the biomass, height and survival of the ten species tested up to the highest test concentration of 140 g. The $EC_{25}$was therefore estimated to be > 140 g a.i./ha. In the seedling emergence study, signs of phytotoxicity were infrequent, and effects on emergence, survival, height and biomass were considerably less than 25% for 9/10 plant species tested. In the case of lettuce, 10% plant mortality and 27% reduction in seedling biomass was observed at the highest test concentration of 140 g a.i./ha. The EC_{25} was determined to be 140 g a.i./ha based on observed effects in lettuce.

The risk to vegetative terrestrial habitats was determined on the basis of an EC_{25} of 140 kg a.i./ha for biomass reduction in seedling emergence and the maximum cumulative application rate of difenoconazole. The LOC is exceeded at the screening level for both Ascernity Fungicide and Instrata II A Fungicide. When drift is taken into account, the LOC is no longer exceeded for field sprayer (i.e. ground) application. Due to the exceedance of the LOC at the screening level, a precautionary label statement and terrestrial buffer zones are required.

Birds and Mammals: The proposed turf use of difenoconazole poses a negligible risk to birds. The LOC is not exceeded on both an acute oral and short-term dietary basis for all size classes and for all feeding guilds. This result is true for both end use products: Ascernity Fungicide (seasonal maximum of 980 g a.i./ha) and Instrata II A Fungicide (seasonal maximum of 250 g a.i./ha). The LOC for birds is exceeded on a reproductive basis, however, only by a small margin. For Instrata II A Fungicide, the reproductive RQ values at the screening level are 2.0, 1.6, and 1.1 for small, medium and large sized birds, respectively. The corresponding RQ values for Ascernity Fungicide are 3.2, 2.5 and 1.6. The reproductive risks were further examined for Ascernity Fungicide as this has the highest seasonal maximum use rate of all the newly proposed difenoconazole containing end use products.

When one further examines the reproductive risks, it can be seen that for large sized birds, the LOC is exceeded only for herbivores foraging on short grass and broadleaf plants. However, this risk occurs only when considering maximum nomogram residues. Furthermore, the LOC is exceeded only for on-field exposure; there is negligible risk for those birds feeding adjacent to the treated field.

For small and medium sized birds, the reproductive LOC is exceeded for insectivores residing on-field using both maximum and medium nonogram residues. The off-field risk is not exceeded. Although these types of birds may be found foraging for insects in and around turf plots, birds would need a large amount of highly contaminated food items to elicit adverse effects on reproduction. Under actual conditions, a variety of contaminated and uncontaminated food items is likely to be consumed.

The proposed turf use of difenoconazole is expected to pose a negligible risk to small wild mammals. The LOC is not exceeded on an acute oral basis for all size classes and for all feeding guilds. This result is true for both end use products. The LOC for mammals is exceeded on a reproductive basis, however, by an even smaller margin than that for birds. For Instrata II A Fungicide, reproductive LOC is exceeded only for medium-sized herbivores (RQ = 1.3) and it is not exceeded for both small and large size groupings of mammals. For Ascernity Fungicide, the reproductive RQ values at the screening level are 1.0, 2.0, and 1.1 for small, medium and large sized mammals, respectively.

While the LOC for mammals is exceeded on a reproductive basis, this is only the case for on-field values and only for maximum nomogram residues, and only for two types of feeding guilds: herbivores and insectivores. When one looks at mean (rather than maximum) nomogram residues; which are more representative of an actual diet in the wild; the LOC is no longer exceeded, both on-field and off-field. This suggests a low probability of adverse reproductive effects under actual field conditions.

In summary, it was concluded that there is not a concern for risk to birds and mammals from the use of difenoconazole on turf.

4.2.2 Risks to Aquatic Organisms

Although the use of difenoconazole on turf does not include direct application to water, the possibility that aquatic systems will be exposed cannot be ruled out. Difenoconazole may enter the aquatic environment through spray drift and/or runoff. Also, pesticides that are bound to soil particles may enter aquatic environments through soil erosion. Since difenoconazole has a tendency to adsorb to soil, this latter route of exposure may potentially be a source of contamination of aquatic environments. The most sensitive ecotoxicity endpoints for the representative non-target aquatic organisms (Table 10 in ERC2011-06, *Difenoconazole*) along with the proposed turf use pattern were used in the screening level risk assessment (Appendix I, Tables 9 and 10). In those cases where the screening level assessments resulted in the LOC being exceeded, a refined assessment was conducted to further characterize the risk (Appendix I, Tables 11-14). Whereas the screening level assessment assumes a direct overspray to a water body, the refined assessment identifies the risk from drift and runoff exposure into aquatic habitats.

Freshwater Invertebrates: The LOC for daphnids exposed to difenoconazole is not exceeded on an acute basis; however, it is exceeded on a chronic basis for both Ascernity Fungicide and Instrata II A Fungicide. The chronic risk from drift and the chronic risk from run-off are both exceeded for Ascernity Fungicide with respective RQ values of 1.3 and 3.8 (seasonal maximum use rate of 980 g a.i./ha). The chronic risk from drift and run-off are not exceeded for Instrata II Component A Fungicide due to the lower overall use rate (seasonal maximum of 250 g a.i./ha).

Freshwater Fish: The LOC for freshwater fish exposed to difenoconazole is exceeded on an acute basis, depending on the application rate, as the screening level RQ is higher than the LOC for acute exposure of Ascernity Fungicide, but not for acute exposure of Instrata II A Fungicide. When one further examines the risk from drift and run-off of Ascernity fungicide, the LOC is not exceeded for these two types of exposure routes on an acute basis.

On a chronic basis, the LOC is exceeded at the screening level for both proposed end use products. When one considers the chronic exposure route of drift, the LOC from Ascernity Fungicide is not exceeded; however, the chronic LOC from exposure to run-off is still exceeded (RQ = 2.4) for Ascernity Fungicide (seasonal maximum use rate of 980 g a.i./ha). The chronic LOC from drift and run-off are not exceeded for Instrata II A Fungicide due to the lower overall use rate (seasonal maximum of 250 g a.i./ha).

Amphibians: This group of organisms may have higher exposure to difenoconazole due to their habitats in shallow water bodies. On both an acute chronic basis, the LOC is exceeded at the screening level for both end use products. When one considers the acute risk from drift, the LOC is not exceeded for both end use products. When one considers the chronic risk from drift, the LOC is exceeded for Ascernity Fungicide (RQ = 4.4), but not for Instrata II A Fungicide, due to its relatively lower seasonal use rate. The same pattern may be observed for acute and chronic risk from run-off, i.e. the acute LOC from run-off is not exceeded for both end use products, while the chronic LOC from drift is exceeded for Ascernity Fungicide (RQ = 2.6), but not for Instrata II A Fungicide.

Freshwater Algae: The acute LOC for freshwater algae exposed to difenoconazole is exceeded for Ascernity Fungicide, but not for Instrata II A Fungicide. When one further examines the acute risk from drift and run-off of Ascernity Fungicide, the LOC is not exceeded for these two types of exposure routes.

Freshwater Vascular Plants: Difenoconazole is expected to pose a negligible risk to freshwater vascular plants since the LOC is not exceeded at the screening level for both end-use products.

Marine Algae: Difenoconazole is expected to pose a negligible risk to marine algae since the LOC is not exceeded at the screening level for both end-use products.

Marine Invertebrates: The acute LOC for marine invertebrates exposed to difenoconazole is exceeded for Ascernity Fungicide, but not for Instrata II A Fungicide. When one further examines the risk from drift and run-off of Ascernity fungicide, the LOC is not exceeded for these two types of exposure routes on an acute basis.

On a chronic basis, the LOC is exceeded at the screening level for both proposed end use products. While the chronic risks from both drift and run-off of Ascernity Fungicide are exceeded with respective RQ values of 1.5 and 4.6, the chronic risks from these two exposure routes (drift and run-off) are not exceeded for Instrata II A Fungicide due to the lower overall use rate (seasonal maximum of 250 g a.i./ha).

Marine Fish: The acute LOC for marine fish exposed to difenoconazole is exceeded for Ascernity Fungicide, but not for Instrata II A Fungicide. When one further examines the risk from drift and run-off of Ascernity fungicide, the LOC is not exceeded for these two types of exposure routes on an acute basis.

On a chronic basis, the LOC is exceeded at the screening level for both proposed end use products. While the chronic risk from drift of Ascernity Fungicide is not exceeded, the chronic risk from run-off is exceeded (RQ = 2.4). The chronic risks from both these exposure scenarios (drift and run-off) are not exceeded for Instrata II A Fungicide.

Due to the exceedance of the LOC for several representative species identified above precautionary label statements and aquatic buffer zones are required to protect aquatic organisms.

4.2.3 Incident Reports

Samples collected during the PMRA investigation of honey bee mortality incidents that occurred in Canada in 2013 were analyzed using an analytical method that included difenoconazole. This active ingredient was detected at low levels in one soil sample and in comb pollen from one affected hive. Difenonconazole is non-toxic to bees and no link to the honey bee mortality reports was established.

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Instrata II Fungicide

A full review of Instrata II Fungicide tankmix (containing both Instrata II A Fungicide and Instrata II B Fungicide) can be found in PRD2015-07, *Benzovindiflupyr*.

The following information is a summary of the review of Instrata II A Fungicide, containing benzovindiflupyr and difenoconazole.

Pink snow mould: The level of control expressed by the various Instrata II A Fungicide components was variable in the trials, ranging from partial suppression to control. Under moderate to high disease pressure, benzovindiflupyr reduced snow mould symptoms by 71–89% and difenoconazole by 78–83%. In the low disease pressure trial, these treatments reduced snow mould to very low levels that could potentially be managed culturally. Mixing fludioxonil with difenoconazole improved efficacy over difenoconazole applied alone in all trials.

Grey snow mould: Benzovindiflupyr provided good control of grey snow mould under very high disease pressure and reduced symptoms to a manageable level in a low disease pressure trial. Difenoconazole suppressed symptoms under high disease pressure when applied alone or in a mixture with fludioxonil. This active ingredient did not perform well in the low disease pressure trial as an alone treatment. The addition of fludioxonil improved efficacy over difenoconazole alone in both trials.

The active ingredients in Instrata II Fungicide demonstrated various levels of efficacy against pink and grey snow moulds. Variable control of snow mould diseases is not uncommon as product efficacy must last through the duration of snow cover. Grey snow mould is also caused by two pathogens with varying virulence. The combination of active ingredients with differing modes of action is a benefit in overcoming environmental influences and multiple pathogens. In addition, multiple active ingredients acting against the pathogens may eliminate the perceived need to apply multiple products in the fall, thereby reducing chemical applications to turf.

5.1.3 Ascernity Fungicide

A full review of the value of Ascernity Fungicide can be found in PRD2015-07. The following is a summary of the value review for the difenoconazole component against summer turf diseases.

Dollar spot: Difenoconazole demonstrated good control of dollar spot on turf under moderate to high disease pressure when applied on 14-, 21- or 28-day intervals. The performance of difenoconazole was comparable to the registered commercial standard. The combination of this fungicide with benzovindiflupyr is expected to provide good control of dollar spot and contribute to resistance management.

Anthracnose: The results from the submitted value information demonstrate control of anthracnose by both difenoconazole applied alone and in combination with benzovindiflupyr at a level statistically comparable to the registered commercial standards.

Microdochium patch: The results from all treatments against microdochium patch were statistically comparable to the commercial standards. The efficacy of the mixture of difenoconazole and benzovindiflupyr consistently resulted in numerically higher levels of control compared to difenoconazole applied alone.

Red thread: Under moderate to high disease pressure, Ascernity Fungicide significantly controlled red thread on susceptible turf. The disease assessments were statistically comparable or significantly lower than the commercial standards. It could not be determined from the data whether only one or both of the active ingredients are effective against the pest.

Brown patch: The contribution of difenoconazole against brown patch was not demonstrated.

5.2 Non-Safety Adverse Effects

No phytotoxicity was observed in any trial conducted with Instrata II Fungicide, Ascernity Fungicide or any of their individual components.

5.3 Consideration of Benefits

5.3.1 Social and Economic Impact

The quality of play areas on golf courses is very important and turf aesthetics contribute to the overall golf experience. In order to attract new members, turf managers have very high standards with respect to the level of control expected from pesticide treatments. Difenoconazole did not always provide a level of control that would meet the expectations of managers of high value turf; however, this active ingredient is intended to be applied in combination with other active ingredients. The activity of multiple active ingredients contributes to overall disease control and the management of pathogen resistance. The registration of these turf products provides Canadian golf superintendents with additional tools to help combat fungicide resistance and enhance control of several key pathogens.

5.3.2 Survey of Alternatives

A number of fungicides are registered on turf to control or suppress diseases on the Instrata II Fungicide and Ascernity Fungicide product labels. Refer to Appendix I, Table 15 for further information on alternative products.

5.3.3 Compatibility with Current Management Practices Including Integrated Pest Management

Products containing difenoconazole can be easily integrated into a disease management plan for turf. Multiple fungicides with different modes of action are registered for each disease, which

will facilitate resistance management. Cultural methods are applied as regular practice by turf managers and will aid in reducing disease incidence and severity.

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

As mentioned previously, multiple alternative products with different modes of action are registered for all of the turf diseases on the Instrata II Fungicide and Ascernity Fungicide labels. In addition, both products contain multiple active ingredients acting against the pathogens. As such, turf managers will be able to develop a disease management plan with product rotation that will best accommodate resistance management.

5.4 Supported Uses

The following diseases on turf are controlled by Instrata II Fungicide or Ascernity Fungicide when applied according to the use directions:

- pink snow mould (*Microdochium nivale*)
- grey snow mould (*Typhula incarnata, T. ishikariensis*)
- dollar spot (*Sclerotinia homeocarpa*)
- anthracnose (*Colletotrichum cereale*)
- microdochium patch (*Microdochium nivale*)
- red thread (*Laetisaria fuciformis*)
- brown patch (*Rhizoctonia solani*)

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, i.e. 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*].

During the formal review processes (PRD99-01, *Difenoconazole* and ERC2011-06, *Difenoconazole*), difenoconazole and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria (See Table 11 in ERC2011-06, *Difenoconazole* for more details). The previously published TSMP conclusions apply to the current review:

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

- Difenoconazole does not meet all the Track 1 criteria

- Difenoconazole does meet the Track 1 criterion for persistence because the half-life values in soil (103-1600 days) and water (307-494 days), do exceed the Track 1 criterion for soil and water.

- Difenoconazole does not meet the Track 1 criterion for bioaccumulation, as its octanol-water partition coefficient (log K_{ow} = 4.4) is just below the Track 1 criterion and the highest BCF in fish was 570.

6.2.1 Formulants and Contaminants of Health or Environmental Concern

During the current review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02,[8] 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 following conclusions:

- Technical grade difenoconazole and the end-use products Ascernity Fungicide and Instrata II A Fungicide do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

Additionally it should be noted that in ERC2011-06, *Difenoconozole*, it was reported that:

- Technical grade difenoconazole is expected to contain traces of TSMP Track 1 polychlorinated dibenzodioxins and furans generated during the manufacturing process;

This original text should be revised to:

- Technical grade difenoconazole does not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

---

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

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

8 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 Summary

7.1 Human Health and Safety

Mixers, loaders and applicators handling Ascernity and Instrata IIA and workers re-entering treated golf courses are not expected to be exposed to levels of difenoconazole that will result in health risks of concern when the these products are used according to label directions. The personal protective equipment and REIs on the product labels are adequate to protect workers.

Residential exposure to golfers entering treated golf courses is not expected to result in risks of concern when Ascernity Fungicide and Instrata IIA Fungicide are used according to label directions.

The proposed use expansion of difenoconazole by addition of golf course turfgrass does not constitute a health risk of concern for chronic (cancer + non-cancer) or acute dietary exposure (food + drinking water) for any segment of the population, including infants, children, adults and seniors. For a summary of all other uses, please refer to ERC2011-06, *Difenoconozole*, and PRDD99-01, *Difenoconozole*.

7.2 Environmental Risk

Current environmental risk assessment methodology was used to conduct the screening level and refined risk assessment for difenoconazole fungicide use on turf, including an evaluation of risk from spray drift and runoff. Using the previously evaluated information in PRD99-01, *Difenoconazole* and ERC2011-06, *Difenoconazole*, as well as the additional environmental fate and ecotoxicological studies provided, it has been determined that there are potential risks to beneficial arthropods, non-target terrestrial plants and aquatic organisms. It has been determined that terrestrial spray buffer zones of 1m or less are adequate to mitigate risk to non-target organisms resulting from difenoconazole spray drift resulting from use on turf by ground application equipment. Spray buffer zones will not mitigate run-off. To reduce the potential for run-off of difenoconazole to adjacent aquatic habitats, precautionary statements for sites with characteristics that may be conducive to run-off and when heavy rain is forecasted are required. In addition, a vegetative strip between the area and the edge of a water body is recommended to reduce run-off of difenoconazole to aquatic areas.

7.3 Value

The value information reviewed in support of the registration of Instrata II Fungicide and Ascernity Fungicide demonstrated the value of difenoconazole in the mixtures of active ingredients. The information supports registration of these two products to control winter and summer diseases of high value turf.

8.0 Proposed Regulatory Decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Difenoconazole Technical, Ascernity Fungicide and Instrata II A Fungicide containing the technical grade active ingredients difenoconazole and benzovindiflupyr to control diseases in turf.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

Human Health

Because there is a concern with users coming into direct contact with difenoconazole on the skin or through inhalation of spray mists, anyone mixing/loading and applying Ascernity Fungicide or Instrata IIA Fungicide must wear a long sleeved-shirt and long pants, chemical-resistant gloves, and goggles when mixing, loading and applying or during equipment clean-up or repair. Goggles and chemical-resistant gloves are not required during groundboom application. The label also requires that workers and golfers do not enter treated areas until residues have dried. In addition, a restriction against use in residential areas was added to the label.

Environment

To reduce environmental impacts resulting from use of difenoconazole fungicide, mitigation in the form of precautionary label statements and spray buffer zones are required on all difenoconazole-containing products.

List of Abbreviations

µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
atm	atmosphere
ATPD	area treated per day
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetres
DF	dry flowable
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{75}	dissipation time 75% (the dose required to observe a 75% decline in concentration)
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
ED	exposure duration
EPA	Environmental Protection Agency
ER_{25}	effective rate for 25% of the population
g	gram
ha	hectare(s)
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
mg	milligram
mL	millilitre
MAS	maximum average score

MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
NOAEL	no observable adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
ORETF	Outdoor Residential Exposure Task Force
PBI	plantback interval
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
REI	restricted entry interval
RSD	relative standard deviation
SC	soluble concentrate
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TC	transfer coefficient
TDE	total dermal exposure
TSMP	Toxic Substances Management Policy
TTR	transferable turf residue
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 1 Food Residue Chemistry Overview and Risk Assessment

DIETARY RISK FROM FOOD AND WATER			
Intermediate refined chronic non-cancer dietary exposure analysis **ADI (all populations) = 0.01 mg/kg bw/day** **Estimated chronic drinking water concentration = 8.4 µg a.i./L**	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Alone	**Food and Water**
	All infants < 1 year	26.7	31.2
	Children 1–2 years	58.4	60.9
	Children 3–5 years	46.3	48.5
	Children 6–12 years	29.2	30.8
	Youth 13–19 years	18.8	20.1
	Adults 20–49 years	20.7	22.5
	Adults 50–99 years	22.6	24.3
	Females 13-49 years	20.6	22.3
	Total population	24.1	25.8
Intermediate refined acute dietary exposure analysis, 95th percentile **ARfD (females 13-49 yrs) = 0.083 mg/kg bw** **ARfD (all other subpopulations) = 0.25 mg/kg bw** **Estimated acute drinking water concentration = 16 µg a.i./L**	**POPULATION**	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**	
		Food Alone	**Food and Water**
	All infants < 1 year	8.8	9.0
	Children 1–2 years	13.4	13.6
	Children 3–5 years	9.6	9.7
	Children 6–12 years	6.4	6.5
	Males 13–49 years	4.1	4.3
	Adults 50–99 years	4.8	4.9
	Females 13-49 years	12.7	13.3

Table 2 Fate and behaviour of difenoconazole in the terrestrial environment –New Study Data (Additional to PRDD99-01, *Difenoconazole* and ERC2011-06, *Difenoconozole*)

Property	Value and Description	Transformation products (TPs)	Comments	PMRA#
Terrestrial Field Dissipation Study				
EcoRegion 8.1: New York State - Turfgrass plots	- DT_{50} = 359 days - Persistent in soil - 25% carryover into the next growing season - difenoconazole (parent compound) detected down to 45 cm depth - TPs down to 30 cm depth	Major TP: CGA205375 Minor TPs: CGA 142856, CGA 71019	Classification of persistence in soil based on Goring et al, 1979. Downward movement through soil	2334695

Property	Value and Description	Transformation products (TPs)	Comments	PMRA#
			indicates potential for leaching	

Table 3 Toxicity of difenoconazole to non-target terrestrial species – New Study Data (Additional to PRDD99-01, *Difenoconozole* and ERC2011-06 *Difenoconozole*)

Organism	Exposure	Test Substance	Endpoint Value	PMRA#
Vascular Plants (10 species)	Seedling Emergence	Difenoconazole formulation	EC_{25} = 140 g a.i./ha	2142303
	Vegetative Vigour	Difenoconazole formulation	EC_{25} > 140 g a.i./ha	2142300

Table 4 Risk Assessment for Ascernity Fungicide For Non-target Terrestrial Invertebrates, Beneficial Arthropods and Plants

Organism	Exposure Scenario	Endpoint Value [a]	Exposure Type	Exposure Value	Units	RQ	LOC Exceeded
TERRESTRIAL INVERTEBRATES							
Screening Level - Exposure to treated soil (for earthworms) and contact exposure to treated surfaces or ingestion of a treated sucrose solution (for bees)							
Earthworm	Acute	> 250	on-field	0.43	mg a.i./kg soil	< 0.002	No
Bee	Contact	> 100	on-field	0.59	µg a.i./bee	< 0.006	No
Bee	Oral	> 64	on-field	7.11	µg a.i./bee	< 0.1	No
BENEFICIAL ARTHROPODS							
Screening Level - Glass Plates (contact exposure)							
Predatory mite (*Typhlodromus pyri*)	Glass plate 7-day LR50	115.4	on-field	386.23	g a.i./ha	**3.4**	**Yes**
			off-field (6% drift)	23.17	g a.i./ha	0.2	No
Parasitic wasp *(Aphidius rhopalosiphi)*	Glass plate 48-hr LR50	197.9	on-field	386.23	g a.i./ha	2.0	No
			off-field (6% drift)	23.17	g a.i./ha	0.1	No
Predatory mite (*Typhlodromus pyri*)	Glass plate 7-day LR50	> 126.5	on-field	386.23	g a.i./ha	**< 3.0**	**Yes**
			off-field (6% drift)	23.17	g a.i./ha	<0.2	No
Screening Level - Extended Laboratory Studies (contact exposure)							
Predatory mite (*Typhlodromus pyri*)	Contact LR50 (mortality)	206.9	on-field	386.23	g a.i./ha	**1.9**	**Yes**
			off-field (6% drift)	23.17	g a.i./ha	0.1	No
	Contact NOEC (reproduction)	151.8	on-field	386.23	g a.i./ha	**2.5**	**Yes**
			off-field (6% drift)	23.17	g a.i./ha	0.2	No

Organism	Exposure Scenario	Endpoint Value [a]	Exposure Type	Exposure Value	Units	RQ	LOC Exceeded
Refinement – Extended Laboratory Studies (contact exposure)							
Predatory mite (*Typhlodromus pyri*)	Contact LR50 (mortality)	206.9	on-field (grass foliar deposition factor: 0.40)	154.49	g a.i./ha	0.8	No
	Contact NOEC (reproduction)	151.8	on-field (grass foliar deposition factor: 0.40)	154.49	g a.i./ha	1.0	No
TERRESTRIAL PLANTS							
Screening Level - Exposure to treated soil (emergence), and from direct overspray (vigour)							
Vascular Plants	Seedling Emergence[b] (EC25)	0.0622	on-field	0.43	mg a.i./kg soil	**6.9**	**Yes**
Vascular Plants	Vegetative Vigour (EC25)	> 140	on-field	386.23	g a.i./ha	**< 2.8**	**Yes**
Refinement - Drift Deposition Factor							
Vascular Plants	Seedling Emergence[b] (EC25)	0.0622	off-field (6% drift)	0.03	mg a.i./kg soil	0.4	No
Vascular Plants	Vegetative Vigour (EC25)	> 140	off-field (6% drift)	23.17	g a.i./ha	< 0.2	No

[a] Source of Ecotoxicity Endpoint Values:
Table 9 in ERC 2011-06 (Earthworm, Bee – Acute Contact, and Predatory Mite – Extended Laboratory Study, Contact);
PMRA #s 1757747, 1757748, 1757750 (Additional Beneficial Arthopod data); PMRA # (Bee – Acute Oral);
PMRA # 2142303 (Vascular Plants – Seedling Emergence), PMRA # 2142300 (Vascular Plants – Vegetative Vigour).

[b] Ecotox Endpoint for seedling emergence Reported as 140 g ai/ha converted to a soil concentration of 0.0622 mg a.i./kg soil.

Table 5 Risk Assessment for Instrata II A Fungicide For Non-target Terrestrial Invertebrates, Beneficial Arthropods and Plants

Organism	Exposure Scenario	Endpoint Value	Exposure Type	Exposure Value	Units	RQ	LOC Exceeded
TERRESTRIAL INVERTEBRATES							
Screening Level - Exposure to treated soil (for earthworms) and contact exposure to treated surfaces or ingestion of a treated sucrose solution (for bees)							
Earthworm	Acute	> 250	on-field	0.11	mg a.i./kg soil	< 0.0004	No
Bee	Contact	> 100	on-field	0.60	µg a.i./bee	< 0.006	No
Bee	Oral	> 64	on-field	7.25	µg a.i./bee	< 0.1	No
BENEFICIAL ARTHROPODS							
Screening Level - Glass Plates (contact exposure)							
Predatory mite (*Typhlodromus pyri*)	Glass plate 7-day LR50	115.4	on-field	250.43	g a.i./ha	**2.2**	**Yes**
			off-field (6% drift)	15.03	g a.i./ha	0.1	No
Pasrasitic wasp *(Aphidius rhopalosiphi)*	Glass plate 48-hr LR50	197.9	on-field	250.43	g a.i./ha	1.3	No
			off-field (6% drift)	15.03	g a.i./ha	0.08	No
Predatory mite (*Typhlodromus pyri*)	Glass plate 7-day LR50	> 126.5	on-field	250.43	g a.i./ha	< 2.0	No
			off-field (6% drift)	15.03	g a.i./ha	< 0.1	No
Screening Level - Extended Laboratory Studies (contact exposure)							
Predatory mite (*Typhlodromus pyri*)	Contact LR50 (mortality)	206.9	on-field	250.43	g a.i./ha	**1.2**	**Yes**
			off-field (6% drift)	15.03	g a.i./ha	0.073	No
	Contact NOEC	151.8	on-field	250.43	g a.i./ha	**1.6**	**Yes**

Organism	Exposure Scenario	Endpoint Value	Exposure Type	Exposure Value	Units	RQ	LOC Exceeded
	(reproduction)		off-field (6% drift)	15.03	g a.i./ha	0.1	No
Refinement - Extended Laboratory Studies (contact exposure)							
Predatory mite (*Typhlodromus pyri*)	Contact LR50 (mortality)	206.9	on-field (grass foliar deposition factor: 0.40)	100.17	g a.i./ha	0.5	No
	Contact NOEC (reproduction)	151.8	on-field (grass foliar deposition factor: 0.40)	100.17	g a.i./ha	0.7	No
TERRESTRIAL PLANTS							
Screening Level - Exposure to treated soil (emergence), and from direct overspray (vigour)							
Vascular Plants	Seedling Emergence[a] (EC25)	0.0622	on-field	0.11	mg a.i./kg soil	**1.8**	**Yes**
	Vegetative Vigour (EC25)	> 140	on-field	250.43	g a.i./ha	**< 1.8**	**Yes**
Refinement - Drift Deposition Factor							
Vascular Plants	Seedling Emergence [b] (EC25)	0.0622	off-field (6% drift)	0.01	mg a.i./kg soil	0.1	No
	Vegetative Vigour (EC25)	> 140	off-field (6% drift)	15.03	g a.i./ha	< 0.1	No

[a] Source of Ecotoxicity Endpoint Values:
Table 9 in ERC 2011-06 (Earthworm, Bee – Acute Contact, and Predatory Mite – Extended Laboratory Study, Contact); PMRA #s 1757747, 1757748, 1757750 (Additional Beneficial Arthopod data); PMRA # (Bee – Acute Oral); PMRA # 2142303 (Vascular Plants – Seedling Emergence), PMRA # 2142300 (Vascular Plants – Vegetative Vigour).

[b] Ecotox Endpoint for seedling emergence Reported as 140 g ai/ha converted to a soil concentration of 0.0622 mg a.i./kg soil.

Table 6 a Screening Level - Ascernity Fungicide – Birds

	Ecotoxicity Endpoint[a] (mg ai/kg bw/d)	**Feeding Guild (food item)**	**EDE (mg ai/kg bw)**	**RQ**
Small Bird (0.02 kg)				
Acute	215.00	Insectivore	31.44	0.2
Reproduction	9.70	Insectivore	31.44	**3.2**
Medium Sized Bird (0.1 kg)				
Acute	215.00	Insectivore	24.53	0.1
Reproduction	9.70	Insectivore	24.53	**2.5**
Large Sized Bird (1 kg)				
Acute	215.00	Herbivore (short grass)	15.85	0.07
Reproduction	9.70	Herbivore (short grass)	15.85	**1.6**

[a] Source of Ecotoxicity Endpoint Values:
Table 9 in ERC 2011-06

Table 6 b Screening Level Ascernity Fungicide – Mammals

	Ecotoxicity Endpoint[a] (mg ai/kg bw/d)	Feeding Guild (food item)	EDE (mg ai/kg bw)	RQ
Small Mammal (0.015 kg)				
Acute	145.30	Insectivore	18.08	0.1
Reproduction	17.70	Insectivore	18.08	**1.0**
Medium Sized Mammal (0.035 kg)		Insectivore		
Acute	145.30	Herbivore (short grass)	35.07	0.2
Reproduction	17.70	Herbivore (short grass)	35.07	**2.0**
Large Sized Mammal (1 kg)				
Acute	145.30	Herbivore (short grass)	18.74	0.1
Reproduction	17.70	Herbivore (short grass)	18.74	**1.1**

[a] Source of Ecotoxicity Endpoint Values:
Table 9 in ERC 2011-06

Table 7 a Screening Level Instrata II Fungicide – Birds

	Ecotoxicity Endpoint [a] (mg ai/kg bw/d)	Feeding Guild (food item)	EDE (mg ai/kg bw)	RQ
Small Bird (0.02 kg)				
Acute	215.00	Insectivore	20.35	0.09
Reproduction	9.70	Insectivore	20.35	**2.1**
Medium Sized Bird (0.1 kg)				
Acute	215.00	Insectivore	15.88	0.07
Reproduction	9.70	Insectivore	15.88	**1.6**
Large Sized Bird (1 kg)				
Acute	215.00	Herbivore (short grass)	10.26	0.05
Reproduction	9.70	Herbivore (short grass)	10.26	**1.1**

[a] Source of Ecotoxicity Endpoint Values:
Table 9 in ERC 2011-06

Table 7 b Screening Level Instrata II Fungicide – Mammals

	Ecotoxicity Endpoint [a] (mg ai/kg bw/d)	Feeding Guild (food item)	EDE (mg ai/kg bw)	RQ
Small Mammal (0.015 kg)				
Acute	145.30	Insectivore	11.70	0.08
Reproduction	17.70	Insectivore	11.70	0.7
Medium Sized Mammal (0.035 kg)		Insectivore		
Acute	145.30	Herbivore (short grass)	22.70	0.2
Reproduction	17.70	Herbivore (short grass)	22.70	**1.3**
Large Sized Mammal (1 kg)				
Acute	145.30	Herbivore (short grass)	12.13	0.08
Reproduction	17.70	Herbivore (short grass)	12.13	0.7

[a] Source of Ecotoxicity Endpoint Values:
Table 9 in ERC 2011-06

Table 8 a Refined Assessment – Ascernity Funigicide – Birds

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Ecotoxicity ($mg_{ai}/kg_{bw}/d$)	Food Guild (food item)	EDE (mg_{ai}/kg_{bw})	RQ	EDE (mg_{ai}/kg_{bw})	RQ	EDE (mg_{ai}/kg_{bw})	RQ	EDE (mg_{ai}/kg_{bw})	RQ
Small Bird (0.02 kg)										
Acute	215.00	Insectivore	31.44	0.2	1.89	0.01	21.71	0.1	1.30	0.01
	215.00	Granivore (grain and seeds)	4.87	0.02	0.29	< 0.01	2.32	0.01	0.14	< 0.01
	215.00	Frugivore (fruit)	9.73	0.05	0.58	< 0.01	4.64	0.02	0.28	< 0.01

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Ecotoxicity ($mg_{ai}/kg_{bw}/d$)	**Food Guild (food item)**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**
Dietary	50.50	Insectivore	31.44	0.6	1.89	0.04	21.71	0.4	1.30	0.03
	50.50	Granivore (grain and seeds)	4.87	0.1	0.29	0.01	2.32	0.05	0.14	< 0.01
	50.50	Frugivore (fruit)	9.73	0.2	0.58	0.01	4.64	0.09	0.28	0.01
Reproduction	9.70	Insectivore	31.44	3.2	1.89	0.19	21.71	2.2	1.30	0.1
	9.70	Granivore (grain and seeds)	4.87	0.5	0.29	0.03	2.32	0.2	0.14	0.01
	9.70	Frugivore (fruit)	9.73	1.0	0.58	0.06	4.64	0.5	0.28	0.03
Medium Sized Bird (0.1 kg)										
Acute	215.00	Insectivore	24.53	0.1	1.47	0.01	16.94	0.08	1.02	< 0.01
	215.00	Granivore (grain and seeds)	3.80	0.02	0.23	< 0.01	1.81	0.01	0.11	< 0.01
	215.00	Frugivore (fruit)	7.59	0.04	0.46	< 0.01	3.62	0.02	0.22	< 0.01
Dietary	50.50	Insectivore	24.53	0.5	1.47	0.03	16.94	0.3	1.02	0.02
	50.50	Granivore (grain and seeds)	3.80	0.08	0.23	< 0.01	1.81	0.04	0.11	< 0.01
	50.50	Frugivore (fruit)	7.59	0.2	0.46	0.01	3.62	0.07	0.22	< 0.01
Reproduction	9.70	Insectivore	24.53	2.5	1.47	0.2	16.94	1.8	1.02	0.1
	9.70	Granivore (grain and seeds)	3.80	0.4	0.23	0.02	1.81	0.2	0.11	0.01
	9.70	Frugivore (fruit)	7.59	0.8	0.46	0.05	3.62	0.4	0.22	0.02
Large Sized Bird (1 kg)										
Acute	215.00	Insectivore	7.16	0.03	0.43	< 0.01	4.95	0.02	0.30	< 0.01
	215.00	Granivore (grain and seeds)	1.11	0.01	0.07	< 0.01	4.95	0.02	0.03	< 0.01
	215.00	Frugivore (fruit)	2.22	0.01	0.13	< 0.01	1.06	< 0.01	0.06	< 0.01
	215.00	Herbivore (short grass)	15.85	0.07	0.95	< 0.01	5.63	0.03	0.34	< 0.01
	215.00	Herbivore (long grass)	9.68	0.05	0.58	< 0.01	3.16	0.01	0.19	< 0.01
	215.00	Herbivore (Broadleaf plants)	14.66	0.07	0.88	< 0.01	4.85	0.02	0.29	< 0.01
Dietary	50.50	Insectivore	7.16	0.1	0.43	0.01	4.95	0.1	0.30	0.01
	50.50	Granivore (grain and seeds)	1.11	0.02	0.07	< 0.01	4.95	0.1	0.03	< 0.01
	50.50	Frugivore (fruit)	2.22	0.04	0.13	< 0.01	1.06	0.02	0.06	< 0.01
	50.50	Herbivore (short grass)	15.85	0.3	0.95	0.02	5.63	0.1	0.34	0.01

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Ecotoxicity ($mg_{ai}/kg_{bw}/d$)	**Food Guild (food item)**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**
	50.50	Herbivore (long grass)	9.68	0.2	0.58	0.01	3.16	0.06	0.19	< 0.01
	50.50	Herbivore (Broadleaf plants)	14.66	0.3	0.88	0.02	4.85	0.1	0.29	0.01
Reproduction	9.70	Insectivore	7.16	0.7	0.43	0.04	4.95	0.5	0.30	0.03
	9.70	Granivore (grain and seeds)	1.11	0.1	0.07	0.01	4.95	0.5	0.03	< 0.01
	9.70	Frugivore (fruit)	2.22	0.2	0.13	0.01	1.06	0.1	0.06	0.01
	9.70	Herbivore (short grass)	15.85	1.6	0.95	0.1	5.63	0.6	0.34	0.03
	9.70	Herbivore (long grass)	9.68	1.0	0.58	0.06	3.16	0.3	0.19	0.02
	9.70	Herbivore (Broadleaf plants)	14.66	1.5	0.88	0.09	4.85	0.5	0.29	0.03

Table 8 b Refined Assessment Ascernity Fungicide – Mammals

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Ecotoxicity ($mg_{ai}/kg_{bw}/d$)	**Food Guild (food item)**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**
Small Mammal (0.015 kg)										
Acute	145.30	Insectivore	18.08	0.1	1.08	0.008	12.49	0.09	0.75	0.005
	145.30	Granivore (grain and seeds)	2.80	0.02	0.17	0.001	1.33	0.009	0.08	0.0006
	145.30	Frugivore (fruit)	5.60	0.04	0.34	0.002	2.67	0.02	0.16	0.001
Reproduction	17.70	Insectivore	18.08	**1.0**	1.08	0.06	12.49	0.7	0.75	0.04
	17.70	Granivore (grain and seeds)	2.80	0.2	0.17	0.01	1.33	0.08	0.08	0.004
	17.70	Frugivore (fruit)	5.60	0.3	0.34	0.02	2.67	0.2	0.16	0.009
Medium Sized Mammal (0.035 kg)										
Acute	145.30	Insectivore	15.85	0.1	0.95	0.006	10.94	0.08	0.66	0.004
	145.30	Granivore (grain and seeds)	2.45	0.02	0.15	0.001	1.17	0.008	0.07	0.0005

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Ecotoxicity ($mg_{ai}/kg_{bw}/d$)	**Food Guild (food item)**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**	**EDE (mg_{ai}/kg_{bw})**	**RQ**
	145.30	Frugivore (fruit)	4.91	0.03	0.29	0.002	2.34	0.02	0.14	0.001
	145.30	Herbivore (short grass)	35.07	0.2	2.10	0.01	12.45	0.09	0.75	0.005
	145.30	Herbivore (long grass)	21.41	0.1	1.28	0.009	6.99	0.05	0.42	0.003
	145.30	Herbivore (forage crops)	32.45	0.2	1.95	0.01	10.73	0.07	0.64	0.004
Reproduction	17.70	Insectivore	15.85	0.9	0.95	0.05	10.94	0.6	0.66	0.04
	17.70	Granivore (grain and seeds)	2.45	0.1	0.15	0.008	1.17	0.07	0.07	0.004
	17.70	Frugivore (fruit)	4.91	0.3	0.29	0.02	2.34	0.1	0.14	0.008
	17.70	Herbivore (short grass)	35.07	**2.0**	2.10	0.1	12.45	0.7	0.75	0.04
	17.70	Herbivore (long grass)	21.41	**1.2**	1.28	0.07	6.99	0.4	0.42	0.02
	17.70	Herbivore (Broadleaf plants)	32.45	**1.8**	1.95	0.1	10.73	0.6	0.64	0.04
Large Sized Mammal (1 kg)										
Acute	145.30	Insectivore	8.47	0.06	0.51	0.004	5.85	0.04	0.35	0.002
	145.30	Granivore (grain and seeds)	1.31	0.009	0.08	0.0005	0.63	0.004	0.04	0.0003
	145.30	Frugivore (fruit)	2.62	0.02	0.16	0.001	1.25	0.009	0.08	0.0005
	145.30	Herbivore (short grass)	18.74	0.1	1.12	0.008	6.65	0.05	0.40	0.003
	145.30	Herbivore (long grass)	11.44	0.08	0.69	0.005	3.74	0.03	0.22	0.002
	145.30	Herbivore (Broadleaf plants)	17.34	0.1	1.04	0.007	5.73	0.04	0.34	0.002
Reproduction	17.70	Insectivore	8.47	0.5	0.51	0.03	5.85	0.3	0.35	0.02
	17.70	Granivore (grain and seeds)	1.31	0.07	0.08	0.004	0.63	0.04	0.04	0.002
	17.70	Frugivore (fruit)	2.62	0.1	0.16	0.009	1.25	0.07	0.08	0.004
	17.70	Herbivore (short grass)	18.74	**1.1**	1.12	0.06	6.65	0.4	0.40	0.02
	17.70	Herbivore (long grass)	11.44	0.6	0.69	0.04	3.74	0.2	0.22	0.01
	17.70	Herbivore (Broadleaf plants)	17.34	1.0	1.04	0.06	5.73	0.3	0.34	0.02

Table 9 Screening Level Risk Assessment for Aquatic Organisms Exposed to Ascernity Fungicide (seasonal maximum: 980 g a.i./ha)

Organism	Exposure	Endpoint Value[1] (ug ai/L)	EEC (ug ai/L)	RQ	LOC Exceeded
FRESHWATER SPECIES					
Daphnia magna	acute	385	118	0.3	No
	chronic	5.6	118	**21**	**Yes**
Rainbow Trout	acute	81	118	**1.5**	**Yes**
Fathead Minnow	chronic	8.7	118	**14**	**Yes**
Amphibians	acute	81	632	**7.8**	**Yes**
	chronic	8.7	632	**73**	**Yes**
Freshwater alga (diatom)	acute	50	118	**2.4**	**Yes**
Vascular plant (duckweed)	acute	900	118	0.1	No
MARINE SPECIES					
Marine Invertebrate (mysid)	acute	75	118	**1.6**	**Yes**
	chronic	4.6	118	**26**	**Yes**
Sheepshead minnow	acute	81.9	118	**1.4**	**Yes**
	chronic	8.8	118	**13**	**Yes**
Marine alga (diatom)	acute	215	118	0.5	No

[1] Source of Ecotoxicity Endpoint Values: Table 10 in ERC 2011-06

Table 10 Screening Level Risk Assessment for Aquatic Organisms Exposed to Instrata II A Fungicide (seasonal maximum: 250 g a.i./ha)

Organism	Exposure	Endpoint Value[1] (ug ai/L)	EEC (ug ai/L)	RQ	LOC Exceeded
FRESHWATER SPECIES					
Daphnia magna	acute	385	31	0.1	No
	chronic	5.6	31	**5.6**	**Yes**
Rainbow Trout	acute	81	31	0.4	No
Fathead Minnow	chronic	8.7	31	**3.6**	**Yes**
Amphibians	acute	81	167	**2.1**	**Yes**
	chronic	8.7	167	**19**	**Yes**
Freshwater alga (diatom)	acute	50	31	0.6	No
Vascular plant (duckweed)	acute	900	31	0.03	No
MARINE SPECIES					
Marine Invertebrate (mysid)	acute	75	31	0.4	No
	chronic	4.6	31	6.8	Yes
Sheepshead minnow	acute	81.9	31	0.4	No

Organism	Exposure	Endpoint Value[1] (ug ai/L)	EEC (ug ai/L)	RQ	LOC Exceeded
	chronic	8.8	31	3.6	Yes
Marine alga (diatom)	acute	215	31	0.1	No

[1] Source of Ecotoxicity Endpoint Values: Table 10 in ERC 2011-06

Table 11 Refined Risk Assessment for Non-Target Aquatic Organisms Exposed to Drift of Ascernity Fungicide (Difenoconazole)

	ORGANISM									
	Daphnia magna (chronic)	Rainbow Trout (acute)	Fathead Minnow (chronic)	Amphibian (acute)	Amphibian (chronic)	Freshwater algae (acute)	Mysid Shrimp (acute)	Mysid Shrimp (chronic)	Sheepshead Minnow (acute)	Sheepshead Minnow (chronic)
Screening Level Information										
Ecotox Endpoint (ug/L)	5.6	81	8.7	81	8.7	50	75	4.6	81.9	8.8
Screening Level EEC (ug/L)	118	118	118	632	632	118	118	118	118	118
Ground Boom (Field) Sprayer Medium (6% drift)										
EEC Refined for Drift (ug/L)	7.1	7.1	7.1	37.9	37.9	7.1	7.1	7.1	7.1	7.1
RQ Refined for Drift	1.3	0.1	0.8	0.5	4.4	0.1	0.1	1.5	0.1	0.8
RQ Exceeded	Yes	No	No	No	Yes	No	No	Yes	No	No

Table 12 Refined Risk Assessment for Non-Target Aquatic Organisms Exposed to Drift of Instrata II A Fungicide (Difenoconazole)

	ORGANISM						
	Daphnia magna (chronic)	Fathead Minnow (chronic)	Amphibian (acute)	Amphibian (chronic)	Freshwater algae (acute)	Mysid Shrimp (chronic)	Sheepshead Minnow (chronic)
Screening Level Information							
Ecotox Endpoint (ug/L)	5.6	8.7	81	8.7	50	4.6	8.8
Screening Level EEC (ug/L)	31	31	167	167	31	31	31
Ground Boom (Field) Sprayer Medium (6% drift)							
EEC Refined for Drift (ug/L)	1.9	1.9	10	10	1.9	1.9	1.9
RQ Refined for Drift	0.3	0.2	0.1	1.2	< 0.1	0.4	0.2
RQ Exceeded	No	No	No	Yes	No	No	No

Table 13 Refined Risk Assessment for Non-Target Aquatic Organisms Exposed to Run-off of Ascernity Fungicide (Difenoconazole)

	ORGANISM									
	Daphnia magna (21-d chronic)	Rainbow Trout (96-h acute)	Fathead Minnow (30-d chronic)	Amphibian (96-h acute)	Amphibian (30-d chronic)	Freshwater Algae (72-h acute)	Mysid Shrimp (96-h acute)	Mysid Shrimp (28-d chronic)	Sheepshead Minnow 96-h acute)	Sheepshead Minnow (chronic)
Screening Level Information										
Ecotox Endpoint (ug/L)	5.6	81	8.7	81	8.7	50	75	4.6	81.9	8.8
Screening Level EEC (ug/L)	118	118	118	632	632	118	118	118	118	118
Refined Assessment for Run-off										
EEC Refined for Run-off (ug/L)	21	25	21	33	23	25	25	21	25	21
RQ Refined for Run-off	3.8	0.3	2.4	0.4	2.6	0.5	0.3	4.6	0.3	2.4
RQ Exceeded	Yes	No	Yes	No	Yes	No	No	Yes	No	Yes

Table 14 Refined Risk Assessment for Non-Target Aquatic Organisms Exposed to Run-off of Instrata II A Fungicide (Difenoconazole)

	ORGANISM					
	Daphnia magna (21-d chronic)	Fathead Minnow (30-d chronic)	Amphibian (96-h acute)	Amphibian (30-d chronic)	Mysid Shrimp (28-d chronic)	Sheepshead Minnow (chronic)
Screening Level Information						
Ecotox Endpoint (ug/L)	5.6	8.7	81	8.7	4.6	8.8
Screening Level EEC (ug/L)	31	31	167	167	31	31
Refined Assessment for Run-off						
EEC Refined for Run-off (ug/L)	0.66	0.66	1.4	0.75	0.66	0.66
RQ Refined for Run-off	0.1	0.08	0.02	0.09	0.1	0.08
RQ Exceeded	No	No	No	No	No	No

Table 15 Registered Alternatives as of June 5, 2014

Disease	Active Ingredient (Mode of Action Group)
Dollar spot (*Sclerotinia homeocarpa*)	thiophanate-methyl (1), iprodione (2), propiconazole (3), myclobutanil (3), triticonazole (3), boscalid (7), penthiopyrad (7), pyraclostrobin (11), fluoxastrobin (11), *Bacillus subtilis* (44), chlorothalonil (M), mineral oil (NC)
Anthracnose (*Colletotrichum cereale*)	propiconazole (3), triticonazole (3), penthiopyrad (7), azoxystrobin (11), trifloxystrobin (11), *Bacillus subtilis* (44), fosetyl-Al (U)
Brown patch (*Rhizoctonia solani*)	thiophanate-methyl (1), iprodione (2), propiconazole (3), myclobutanil (3), penthiopyrad (7), azoxystrobin (11), pyraclostrobin (11), *Bacillus subtilis* (44), chlorothalonil (M),

Disease	Active Ingredient (Mode of Action Group)
	captan (M)
Microdochium patch (*Microdochium nivale*)	iprodione (2), propiconazole (3), triticonazole (3), azoxystrobin (11), pyraclostrobin (11), trifloxystrobin (11), chlorothalonil + propiconazole (M+3)
Red thread (*Laetisaria fuciformis*)	propiconazole (3), propiconazole + azoxystrobin (3+11), propiconazole + chlorothalonil (3+M)
Pink snow mould (*Microdochium nivale*)	thiophanate-methyl (1), iprodione (2), propiconazole (3), triticonazole (3), azoxystrobin (11), pyraclostrobin (11), trifloxystrobin (11), chlorothalonil (M), mineral oil (NC), *Typhula phacorrhiza* (NC)
Grey snow mould (*Typhula incarnata, T. ishikariensis*)	iprodione (2), propiconazole (3), myclobutanil (3), triticonazole (3), azoxystrobin (11), pyraclostrobin (11), trifloxystrobin (11), chlorothalonil (M), mineral oil (NC), *Typhula phacorrhiza* (NC)

Table 16 List of Supported Uses

Proposed claim	VRD comments
Control of pink snow mould (*Microdochium nivale*) on golf course turf at a rate of 31.7 ml Instrata II Fungicide Component A/100 m^2 + 34.8 ml Instrata II Fungicide Component B/100 m^2. Make one application in the late fall before snow cover when conditions are favourable for disease infection and prior to disease symptom expression.	Supported as proposed.
Control of grey snow mould (*Typhula incarnata, T. ishikariensis*) on golf course turf at a rate of 31.7 ml Instrata II Fungicide Component A/100 m^2 + 34.8 ml Instrata II Fungicide Component B/100 m^2. Make one application in the late fall before snow cover when conditions are favourable for disease infection and prior to disease symptom expression.	Supported as proposed.
Control of dollar spot (*Sclerotinia homeocarpa*) on golf course turf with Ascernity Fungicide applied at 31 ml/100 m^2 (or 3.1 L/ha) applied twice on a 14 – 21 day interval.	Supported as proposed.
Control of anthracnose (*Colletotrichum* spp.) on golf course turf with Ascernity Fungicide applied at 31 ml/100 m^2 (or 3.1 L/ha) applied twice on a 14-day interval.	Supported as proposed. Pathogen name amended to *Colletotrichum cereale*.
Control of microdochium patch (*Microdochium nivale*) on golf course turf with Ascernity Fungicide applied at 31 ml/100 m^2 (or 3.1 L/ha) applied twice on a 14-day interval.	Supported as proposed.
Control of red thread (*Laetisaria fuciformis*) on golf course turf with Ascernity Fungicide applied at 31 ml/100 m^2 (or 3.1 L/ha) applied twice on a 14-day interval.	Supported as proposed.
Control of brown patch (*Rhizoctonia solani*) on golf course turf with Ascernity Fungicide applied at 31 ml/100 m^2 (or 3.1 L/ha) applied twice on a 14 – 21 day interval.	Supported as proposed.
Tank mixes with Daconil 2787 Flowable Fungicide (Reg. No. 15724) and Daconil Ultrex Fungicide (Reg. No. 28354).	Supported as proposed.

Appendix II Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

Table 1 Differences Between MRLs in Canada and in Other Jurisdictions

Please refer to the Maximum Residue Limit Database in the Pesticides and Pest Management section of Health Canada's website for the established MRLs for difenoconazole.

References

A. List of Studies/Information Submitted by Registrant

1.0 Human and Animal Health

2115788	Agricultural Reentry Task Force (ARTF). 2008. Data Submitted by the ARTF to Support Revision of Agricultural Transfer Coefficients. Submission #2006-0257.
1563654 & 1563664	Merricks et al. 1999. Exposure of Professional Lawn Care Workers During the Mixing and Loading of Dry and Liquid Formulations and the Liquid Application of Turf Pesticides Utilizing A Surrogate Compound. OMA002. ORETF. Submission #2006-4038.

2.0 Environment

2334695	2012, Dissipation of Difenoconazole EC (250) Under Field Conditions in Turf and Bare Soil in New York, DACO: 8.3.2.2
2142300	2011, Difenoconazole - Toxicity Effects on the Vegetative Vigour of Ten Species of Plants, DACO: 9.8.4,9.8.6
2142303	2011, Difenoconazole - Toxicity Effects on the Seedling Emergence of Ten Species of Plants, DACO: 9.8.4,9.8.6

3.0 Value

2254199 2012, Trial Study Reports, DACO: 10.2.3.3,IIIA 6.1.2

2254197 2012, INSTRATA II Fungicide Co-pack of A19334A (SolatenoM, 24 g/L + Difenoconazole, 79 g/L) and A17856B (Fludioxonil 125 g/L) - DOCUMENT M-III, Section 7 - EFFICACY DATA AND INFORMATION – CANADA, DACO: 10.2.1, 10.2.2, 10.2.3.1, 10.2.3.3, 12.7, Document M-7

2254784 2012, Trial Study Reports, DACO: 10.2.3.3,IIIA 6.1.2

2254779 2012, Ascernity (A19188A) - Solatenol, 24 g/L + Difenoconazole, 79 g/L - Document M-III, Section 7 - Efficacy Data and Information - Canada, DACO: 12.7,Document M