Proposed Registration Decision PRD2017-15

Oxathiapiprolin, DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment

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Overview

Proposed Registration Decision for Oxathiapiprolin

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 DuPont Zorvec Technical Fungicide, DuPont Lumisena Fungicide Seed Treatment, and Plenaris 200FS Seed Treatment, containing the technical grade active ingredient oxathiapiprolin. DuPont Lumisena Fungicide Seed Treatment, is intended for control of downy mildew in sunflowers and Phytophthora root and stem rot in soybeans. Plenaris 200FS Seed Treatment, from Syngenta Canada Inc., is proposed for control of downy mildew in sunflowers.

Oxathiapiprolin was granted full registration in 2015 to control various oomycete diseases on field and vegetable crops; bulb vegetables, brassica (cole) leafy vegetables, cucurbit vegetables, fruiting vegetables, leafy vegetables, ginseng, tobacco, succulent shelled and edible-podded peas, and tuberous and corm vegetables including potatoes. For further details see the Proposed Registration Decision PRD2015-22, *Oxathiapiprolin* and the Registration Decision RD2015-29, *Oxathiapiprolin.*

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 DuPont Zorvec Technical Fungicide, DuPont Lumisena Fungicide Seed Treatment, and Plenaris 200FS Seed Treatment, containing the technical grade active ingredient oxathiapiprolin.

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.

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

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

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

Before making a final registration decision on oxathiapiprolin, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on oxathiapiprolin, DuPont Lumisena Fungicide Seed Treatment, and Plenaris 200FS Seed Treatment 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 Oxathiapiprolin?

Oxathiapiprolin is a conventional fungicide and the sole active ingredient in DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment. DuPont Lumisena Fungicide Seed Treatment is to be used as a seed treatment for early season control of Phytophthora seed rot, pre-emergence and post-emergence damping off in soybeans and systemic downy mildew in sunflowers. Plenaris 200FS Seed Treatment will be used as a seed treatment for control of systemic downy mildew on sunflowers.

Oxathiapiprolin belongs to a new mode of action group and works by interfering with lipid formation and transportation in susceptible pathogens. Oxathiapiprolin is already registered in Canada for use on agricultural crops against several fungal pathogens.

Health Considerations

Can Approved Uses of Oxathiapiprolin Affect Human Health?

DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment, containing oxathiapiprolin, are unlikely to affect your health when used according to label directions.

Potential exposure to oxathiapiprolin may occur through the diet (food and water) or when handling and applying the products. 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

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

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

dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose 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 pesticide-containing products are used according to label directions.

In laboratory animals, oxathiapiprolin was of low acute toxicity by the oral, dermal and inhalation routes of exposure. It was non-irritating to skin, minimally irritating to eyes and did not cause an allergic skin reaction.

Plenaris 200FS Seed Treatment and DuPont Lumisena Fungicide Seed Treatment were of low acute toxicity via the oral, dermal, and inhalation routes of exposure. They were non-irritating to the eyes and skin and did not cause an allergic skin reaction.

Registrant supplied short- and long-term (lifetime) animal toxicity studies were assessed for the potential of oxathiapiprolin to cause neurotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, genetic damage, and various other effects. There was evidence that the young animal was more sensitive than the adult animal. The most sensitive endpoints used for risk assessment were effects on body weight and delayed sexual maturation.

The risk assessment protects against these findings as well as any other potential effects by ensuring that the level of exposure to humans is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

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

Aggregate dietary intake estimates (food plus drinking water) revealed that the general population and infants less than one year old, the subpopulation which would ingest the most oxathiapiprolin relative to body weight, are expected to be exposed to $\leq 1.1\%$ of the acceptable daily intake. Based on these estimates, the chronic dietary risk from oxathiapiprolin is not of health concern for all population subgroups.

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

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.

Residue trials conducted throughout Canada and the United States using oxathiapiprolin on soybeans and sunflowers are acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this consultation document.

Occupational Risks From Handling DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment

Occupational risks are not of concern when the above end-use products containing oxathiapiprolin are used according to the label directions, which include protective measures.

Workers in commercial seed treatment facilities and farmers planting or handling soybean or sunflower seed treated with DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment can come into direct contact with oxathiapiprolin through residues on the skin and through inhaling dust. Therefore, the label states that workers mixing/loading, applying or performing other activities that involve handling treated seed in commercial seed treatment facilities must wear long-sleeved shirt, long pants, chemical-resistant gloves, and shoes plus socks. Workers performing clean-up and repair activities in commercial seed treatment facilities must wear coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, and shoes plus socks. Seeds can only be treated in closed treatment systems. Farmers planting or handling treated seed must wear long-sleeved shirt, long pants, chemical-resistant gloves and shoes plus socks.

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 Oxathiapiprolin Is Introduced Into the Environment?

When used according to label directions for seed treatment, oxathiapiprolin is not expected to pose risks of concern to the environment.

Oxathiapiprolin can enter the environment when it is used as a fungicide for the control of oomycete diseases in a variety of field and vegetable crops. It can enter into plant tissues and be distributed throughout the plant because it is systemic.

Oxathiapiprolin can persist in the environment and has a potential to carry-over to the following growing season. It does not readily break down by reacting with water or sunlight. Oxathiapiprolin is not volatile and is unlikely to enter the atmosphere.

Oxathiapiprolin is not likely to accumulate in plant and fish tissues.

In water, oxathiapiprolin will move to sediments where it will be broken down by microbes. In general, once oxathiapiprolin enters the aquatic environment, it will begin to breakdown and is unlikely to be persistent in water and sediments.

Oxathiapiprolin will not be expected to pose risks of concern to aquatic non-target organisms.

Oxathiapiprolin, when used as a seed treatment, presents a negligible risk to terrestrial and aquatic non-target organisms since it is unlikely that organisms will be exposed to high enough concentrations to cause harm. Standard precautionary label statements relevant to the seed treatment use will be required on the labels.

Value Considerations

What Is the Value of DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Fungicide Seed Treatment?

DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment will provide growers with a new mode of action to control early season fungal diseases on certain crops.

There are alternatives registered for control of Phytophthora seed rot, pre-emergence and post-emergence damping-off in soybeans and downy mildew in sunflowers. Oxathiapiprolin is the first active ingredient classified under a recently established mode of action group. Registration of products containing oxathiapiprolin will provide growers with a new mode of action for managing the listed diseases.

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 DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Workers mixing, loading and applying in commercial seed treatment facilities must use closed treatment systems only.

Environment

Environmental risk mitigation measures and label statements required on the existing end use product labels are required, where applicable. In addition, standard precautionary label statements relevant to the new seed treatment use for soybean and sunflower to be used in commercial and on-farm treatment facilities will be required on the label.

What Additional Scientific Information is Being Requested?

Chemistry

The following studies are required to complete the chemistry database for this product:

Analytical data from at least five batches of technical grade active ingredient representing full-scale production at each manufacturing site, once available (expected timeframe 1 year).

Next Steps

Before making a final registration decision on oxathiapiprolin, 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 note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to Publications (contact information on the cover page of this document). 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 oxathiapiprolin (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

Oxathiapiprolin

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Refer to PRD2015-22, *Oxathiapiprolin*.

1.2 Physical and Chemical Properties of the Active Ingredient and End-Use Product

Technical Product—Oxathiapiprolin Technical

Refer to PRD2015-22, *Oxathiapiprolin*.

End-use Product—DuPont Lumisena Fungicide Seed Treatment

Property	Result
Colour	White opaque
Odour	Chemical odour
Physical state	Liquid
Formulation type	Suspension concentrate (PMRA formulation type = suspension)
Guarantee	200 g/L
Container material and description	1–1500 L HDPE plastic
Density	1.06–1.08 g/mL
pH of 1% dispersion in water	4.0–7.0
Oxidizing or reducing action	Not oxidizing or reducing
Storage stability	Stable after storage for 14 days at 54°C
Corrosion characteristics	Not corrosive to its commercial packaging
Explodability	Not explosive

End-use Product—Plenaris 200FS Seed Treatment

Property	Result
Colour	White opaque
Odour	Chemical odour
Physical state	Liquid
Formulation type	Suspension concentrate (PMRA formulation type = suspension)

Property	Result
Guarantee	200 g/L
Container material and description	1–1500 L HDPE plastic
Density	1.06–1.08 g/mL
pH of 1% dispersion in water	4.0–7.0
Oxidizing or reducing action	Not oxidizing or reducing
Storage stability	Stable after storage for 14 days at 54°C
Corrosion characteristics	Not corrosive to its commercial packaging
Explodability	Not explosive

1.3 Directions for Use

DuPont Lumisena Fungicide Seed Treatment is to be used as a seed treatment for early season control of Phytophthora seed rot, pre-emergence and post-emergence damping off in soybeans and systemic downy mildew in sunflowers. Plenaris 200FS Seed Treatment will be used as a seed treatment for control of systemic downy mildew on sunflowers only. In sunflowers, both products are to be applied at a rate of 9.37–18.75 mL product/200 000 seeds. In soybean, DuPont Lumisena Fungicide Seed Treatment is to be applied at a rate of 8.4–16.8 mL product/140 000 seeds.

1.4 Mode of Action

Oxathiapiprolin has recently been reclassified to a new mode of action group (Group # 49) by the Fungicide Resistance Action Committee. Oxathiapiprolin works by interfering with lipid formation and transportation in susceptible fungi, thus interfering with cell membrane integrity and function.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

Refer to PRD2015-22, *Oxathiapiprolin*.

2.2 Method for Formulation Analysis

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

2.3 Methods for Residue Analysis

Refer to PRD2015-22, *Oxathiapiprolin*.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicology database for oxathiapiprolin and the end-use products DuPont Zorvec Epicaltrin Fungicide and OXTP 200 SC Fungicide was conducted previously and is summarized in PRD2015-22, *Oxathiapiprolin*. The database for oxathiapiprolin and the end-use products DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to oxathiapiprolin.

The acute toxicity of DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment was low via the oral, dermal and inhalation routes of exposure in rats. These products were non-irritating to the eyes and skin of rabbits and were not a skin sensitizer in guinea pigs by the Maximization method.

Results of the toxicology studies conducted on laboratory animals with oxathiapiprolin, as well as the toxicology reference values for use in human health risk assessment can be found in PRD2015-22, *Oxathiapiprolin*. The toxicology reference values are reproduced in Appendix I, Table 1 of this document.

3.1.1 Incident Reports Related to Human and Animal Health

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. In addition, the general public, medical community, government and non-governmental organizations are able to report pesticide incidents directly to the PMRA.

As of 16 June 2017, no human or domestic animal incident reports involving oxathiapiprolin had been submitted to the PMRA.

3.2 Occupational and Residential Risk Assessment

3.2.1 Toxicological Endpoints

Occupational exposure to oxathiapiprolin is characterized as intermediate term for workers in commercial seed treatment facilities and short term for planters. Exposure is predominantly by the dermal and inhalation routes. Due to a lack of toxicological effects in the short-term repeat dose dermal toxicity study in rats up to the limit dose of testing, low dermal absorption values and the low concern for effects at the limit dose of testing in dietary/gavage toxicity studies, dermal exposure endpoints were not selected. Therefore, only inhalation exposure was assessed.

3.2.1.1 Dermal Absorption

A rat in vivo dermal absorption study was reviewed with the initial registration of oxathiapiprolin but a dermal absorption factor (DAF) was not established since no dermal endpoints were established and a dermal risk assessment was not required (PRD2015-22, *Oxathiapiprolin*).

3.2.2 Occupational Exposure and Risk

3.2.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Soybean seed and sunflower seed can be treated with DuPont Lumisena Fungicide Seed Treatment in commercial seed treatment facilities and planted using conventional seeding equipment. Furthermore, sunflower seed can be treated with Plenaris 200FS Seed Treatment in commercial seed treatment facilities and planted using conventional seeding equipment. Worker exposure to oxathiapiprolin in commercial facilities is expected to be intermediate term in duration and occur primarily by the dermal and inhalation routes. Since no dermal endpoints have been established for oxathiapiprolin, only the inhalation exposure was assessed.

Chemical-specific data for assessing treater/applicator, bagger/sewer/stacker and cleaner exposures during pesticide handling activities were not submitted. For assessing exposure during seed treatment in commercial operations with closed chemical transfer, a surrogate passive dosimetry study (2012; PMRA document number 2313613) measuring the dermal and inhalation exposure of treaters/applicators, baggers/sewers/stackers and cleaners at commercial facilities treating wheat seed was used. In the study, workers were treating wheat seed with Jockey Fungicide, containing fluquinconazole and prochloraz, at target rates of 75 and 14 g a.i./100 kg seed, respectively. The monitoring period for treaters (n = 7) and cleaners (n = 8) was less than 35 minutes, whereas the monitoring period for baggers (n = 22) ranged from 3 to 8 hours. Although not required for this assessment, dermal exposure for each worker was measured by passive dosimetry using a combination of an inner whole body dosimeter, hand rinses, and face/neck wipes. The inner dosimeter was worn underneath worker clothing. Treaters wore a long-sleeved shirt, long pants and nitrile gloves. Cleaners wore Tyvek coveralls over a long-sleeved shirt, long pants and nitrile gloves. Baggers wore a long-sleeved shirt and long pants. Inhalation exposure for each worker was measured by means of a personal air sampling pump with an IOM multi-dust sampler with a glass fibre filter. Treater and bagger exposure values were normalized for the amount of active ingredient handled. Exposure values for cleaners were normalized for the application rate used in the study. Since the application rate from the study (14 g a.i./100 kg seed) and for the proposed use (6.9-13.8 g a.i./100 kg seed for soybean and 15.7-31.4 g a.i./100 kg seed for sunflowers) are similar, risk estimates for cleaners were calculated using normalized exposure values from the Jockey Fungicide study. In addition, cleaner exposure was monitored for only 9–33 minutes in the study; as such, the risk estimates for cleaner and treater were combined to take into account workers who conduct both tasks during the workday. For the Jockey Fungicide study, the arithmetic mean was used for all activities since there were an adequate number of replicates and the recoveries were sufficient. The highest value of the two actives monitored in the surrogate study was chosen for risk assessment purposes since it should not underestimate exposure.

The submitted dust-off data measured the dust off potential of Jockey Fungicide-treated wheat seed compared to Oxathiapiprolin 200FS treated soybean seed and sunflower seed. Oxathiapiprolin 200FS treated soybean seed and sunflower seed resulted in 10.04 and 17.10 g dust/100 kg seed, respectively. More dust was generated from Jockey Fungicide-treated wheat seed (29.80 g dust/100 kg seed). Therefore, the Jockey Fungicide study is not expected to underestimate the exposure for the proposed use of DuPont Lumisena Fungicide Seed Treatment on soybean seed and sunflower seed and Plenaris 200FS Seed Treatment on sunflower seed.

Table 3.2.2.1 presents the exposure estimates for commercial seed treatment of soybean seed and sunflower seed with DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment. The calculated margins of exposure (MOEs) were well above the target MOE of 100 and therefore not of concern.

Table 3.2.2.1 Non-cancer risk estimates for workers treating soybean and sunflower seed in commercial facilities with DuPont Lumisena Fungicide Seed Treatment and sunflower seed with Plenaris 200FS Seed Treatment

Worker task	Inhalation Unit exposure (µg/kg a.i. handled)	Application rate (kg a.i./kg seed)	Seed treated (kg seed/day)	Exposure (mg/kg bw/day)[2]	Calculated MOE[3]
Closed transfer commercial facilities (using Jockey Fungicide study unit exposure values)[1]					
Soybean					
Treater	0.016	0.000138	63000	1.7×10^{-6}	1.2×10^{7}
Bagger	0.89	0.000138	63000	9.7×10^{-5}	2.1×10^{5}
Cleaner*	0.64	0.000138	63000	1.1×10^{-4}	1.8×10^{5}
Treater + Cleaner †	-	0.000138	63000	1.1×10^{-4}	1.8×10^{5}
Sunflowers					
Treater	0.016	0.000314	195045	1.2×10^{-5}	1.6×10^{6}
Bagger	0.89	0.000314	195045	6.8×10^{-4}	29,356
Cleaner*	0.64	0.000314	195045	2.5×10^{-4}	79,618
Treater + Cleaner †	-	0.000314	195045	2.6×10^{-4}	76,336

[1] For closed transfer commercial facilities, the arithmetic mean values were used from the Jockey Fungicide study
[2] Exposure = (Inhalation exposure × Application rate × Seed treated per day)/(80 kg bw × 1000 µg/mg)
[3] Based on NOAEL = 20 mg /kg bw/day, target MOE = 100
* Cleaner unit exposure values are in (µg/ g a.i./100kg seed); as such,
exposure = (total unit exposure × application rate in g a.i./100 kg seed)/(80 kg bw × 1000 µg/mg); Soybean seed = 13.8 g a.i./100 kg seed; Sunflower seed = 31.4 g a.i./100 kg seed.
† Assuming that a worker both treats and cleans in the same workday.

3.2.2.2 Exposure and Risk Assessment for Planters of Treated Seed

Individuals have potential for exposure to oxathiapiprolin while planting and handling treated seed through dermal and inhalation routes. Exposure is expected to be short-term in duration. Since no dermal endpoints have been established for oxathiapiprolin, only the inhalation exposure was assessed.

Chemical specific data for assessing human exposure during planting of treated seed were not submitted. As such, surrogate exposure data have been used to estimate risk to workers planting treated seed.

Sunflower seed

Commercially treated sunflower seed is bagged. To address planting exposure from bagged sunflower seed, the Gaucho planting study was used as a surrogate (PMRA document number 1571553). In the study, 15 replicates were monitored while planting treated corn seed from bags. The seeds were treated with Gaucho FS 350 or Gaucho FS 600, containing imidacloprid. The workers in the study loaded treated seed from bags into the planter and sowed the seed using a closed cab tractor. Although not required for this assessment, dermal exposure for each worker was measured by passive dosimetry using a combination of an inner whole body dosimeter, hand rinses, and face/neck wipes. The inner dosimeter was worn underneath worker clothing. Workers wore a single layer and chemical-resistant gloves. Inhalation exposure was monitored using IOM samplers attached to a personal air sampling pump. For the purpose of estimating inhalation exposure when using open cab tractors, air samplers were fixed outside each window of the tractor cabin in approximately the height equivalent to the driver's head. The air samplers operated during the entire work day without differentiation between the loading and sowing phases. The estimated inhalation exposure from these tractor samplers was summed with the loading phase inhalation exposure (from the personal air samplers) to estimate the "inhalation open cab" unit exposure. The study was of good quality and had only minor limitations. As such, the arithmetic mean values from the study were adequate for risk assessment purposes.

The submitted dust off data showed that soybean seed and sunflower seed treated with Oxathiapiprolin 200FS were both significantly less dusty than Gaucho-treated corn seed. Therefore, the Gaucho surrogate study is not expected to underestimate planting exposure for sunflower seed.

Soybean seed

Commercially treated soybean seed can be bagged or stored as loose bulk. To address planting exposure from bagged and loose bulk soybean seed, the Austral Plus Net study was used as a surrogate (PMRA document number 2313627). In the study, 11 replicates were monitored while planting treated wheat seed from bags of various sizes as well as a bulk container. The seeds were treated with Austral Plus Net containing fludioxonil and tefluthrin. The workers in the study loaded treated seed from the bags or a container into the planter and sowed the seed using a closed cab tractor. Although not required for this assessment, dermal exposure for each worker was measured by passive dosimetry using a combination of an inner whole body dosimeter, hand rinses, and face/neck wipes. The inner dosimeter was worn underneath worker clothing. Workers wore a single layer and chemical-resistant gloves. Inhalation exposure was monitored using personal air sampling device (OVS sampling tubes) attached to a personal air sampling pump. The study was of good quality and had only minor limitations. As such, the arithmetic mean values from the study were adequate for risk assessment purposes.

The submitted dust off data did not measure the dust-off potential of Austral Plus Net treated wheat seed. However, Jockey Fungicide treated wheat seed had a higher dust-off potential than Oxathiapiprolin 200FS treated soybean seed and sunflower seed. Therefore, the Austral Plus Net study is not expected to underestimate the exposure for the proposed use of DuPont Lumisena Fungicide Seed Treatment on soybean seed and sunflower seed and Plenaris 200FS Seed Treatment on sunflower seed.

Table 3.2.2.2 presents the exposure estimates for planting exposure for soybean and sunflower seed treated with DuPont Lumisena Fungicide Seed Treatment and sunflower seed treated with Plenaris 200FS Seed Treatment. The calculated MOEs were well above the target MOE of 100 and therefore, not of concern. Moreover, considering the magnitude of the calculated MOEs, it is expected that the risk from planting DuPont Lumisena Fungicide Seed Treatment treated soybean seed and sunflower seed and Plenaris 200FS Seed Treatment treated sunflower seed in open cab tractors is not of concern.

Table 3.2.2.2 Non-cancer risk estimates for workers planting soybean and sunflower seeds commercially treated with DuPont Lumisena Fungicide Seed Treatment and sunflower seeds commercially treated with Plenaris 200FS Seed Treatment

Worker task	Inhalation Unit exposure (µg/kg a.i. handled)[1]	Application rate (kg a.i./kg seed)	Seed planted (kg seed/day)	Exposure (mg/kg bw/day)[2]	Calculated MOE[3]
Planting commercially treated seed (using Gaucho study unit exposure values)[1]					
Soybean					
Planting (closed cab)	82.83	0.000138	9000	0.0013	15,553
Planting (open cab)	116.75	0.000138	9000	0.0018	11,034
Sunflower					
Planting (closed cab)	82.83	0.000314	1000	3.3×10^{-4}	61,518
Planting (open cab)	116.75	0.000314	1000	4.6×10^{-4}	43,645
Planting commercially treated seed (using Austral Plus Net study unit exposure values)					
Soybean					
Planting (closed cab)	360	0.000138	9000	0.0056	3578
Sunflower					
Planting (closed cab)	360	0.000314	1000	0.0014	14,154

[1] For planting commercial treated seed, the arithmetic mean values were used from the Gaucho and Austral Plus Net studies.
[2] Exposure = (Inhalation exposure × Application rate × Seed planted per day)/(80 kg bw × 1000 µg/mg)
[3] Based on NOAEL = 20 mg /kg bw/day, target MOE = 100

3.3 Bystander Exposure and Risk

Bystander exposure is considered to be negligible since the potential for drift is expected to be minimal.

3.4 Food Residues Exposure Assessment

3.4.1 Residues in Plant and Animal Foodstuffs

Please refer to PRD2015-22, *Oxathiapiprolin* for the complete review of residues of oxathiapiprolin in plants and animal foodstuffs.

In the context of the current submissions, crop field trials conducted throughout Canada and the United States using end-use products containing oxathiapiprolin at approved or exaggerated rates in or on soybeans and sunflowers are sufficient to support the proposed maximum residue limits. Processing studies for soybeans (refined oil) and sunflowers (refined oil) were not conducted as residues in the raw agricultural commodities from the supervised residue trials were all non-quantifiable when treated at exaggerated rates. Quantifiable residues are not expected to occur in livestock matrices with the current use pattern.

3.4.2 Dietary Risk Assessment

A chronic (non-cancer) dietary risk assessment was conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™).

3.4.2.1 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the basic chronic non-cancer analysis for oxathiapiprolin: 100% crop treated, default processing factors, residues of crop and animal commodities based on recommended MRL values. The basic chronic dietary exposure from all supported oxathiapiprolin food uses (alone) for the total population, including infants and children, and all representative population subgroups is less than 1% of the acceptable daily intake (ADI), and is therefore not of concern. Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that chronic dietary exposure to oxathiapiprolin from food and drinking water is ≤1.1% of the ADI for the total population. The highest exposure and risk estimate is for Children 1–2 years at 1.1% (0.043295 mg/kg bw/day) of the ADI.

3.4.2.2 Acute Dietary Exposure Results and Characterization

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

3.4.3 Aggregate Exposure and Risk

The aggregate risk for oxathiapiprolin consists of exposure from food and drinking water sources only, which is not of concern; there are no residential uses.

3.4.4 Maximum Residue Limits

Table 3.4.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Dry soybeans	0.01
Sunflower seeds	0.01
Eggs; fat, meat, and meat byproducts of poultry	0.01

Please refer to PRD2015-22, *Oxathiapiprolin* for a summary of the nature of the residues in animal and plant matrices, analytical methodologies, and freezer storage stability data. Field trial data and chronic dietary risk estimates are summarized in Appendix I.

4.0 Impact on the Environment

An environmental risk assessment for oxathiapiprolin use in seed treatment products was conducted. An environmental risk assessment for oxathiapiprolin uses in foliar and soil applied products was conducted previously for non-target terrestrial and aquatic organisms and is reported in PRD2015-22, *Oxathiapiprolin*.

4.1 Fate and Behaviour in the Environment

The properties of oxathiapiprolin and its environmental behaviour have been thoroughly reviewed and characterized previously. Please refer to PRD2015-22, *Oxathiapiprolin*, for further details.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative

application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the 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 is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

As a seed treatment, oxathiapiprolin can enter the environment through dislodging from treated seed surfaces during and after seeding. The potential for exposure to aquatic environments and non-target terrestrial plants via this application method is, however, considered to be reduced when compared to other forms of application (for example, broadcast spraying). The primary environmental concern for this risk assessment is for birds and small wild mammals as they may be exposed to oxathiapiprolin through direct ingestion of treated seeds and for bees as oxathiapiprolin can enter into plant tissues and be distributed throughout the plant because it is systemic.

It should be noted that the proposed maximum rate of application indicated in the proposed labels was converted into grams oxathiapiprolin per hectare, based on the number of seeds per kilogram and typical seeding rates. Therefore, the proposed maximum rate of application for each seed type is: 0.024 milligrams of oxathiapiprolin per seed, which is equivalent to 22.38 grams oxathiapiprolin per hectare for soybean, and 0.01875 milligrams of oxathiapiprolin per seed, which is equivalent to 3.38 grams oxathiapiprolin per hectare for sunflower.

4.2.1 Risks to Terrestrial Non-Target Organisms

Risk to Earthworms

Previous risk assessment to earthworms have been conducted at 140 and 560 grams oxathiapiprolin per hectare and identified that all acute and chronic screening level risk quotients for earthworms were below the level of concern for oxathiapiprolin and its soil transformation products. As the current proposed application rates are much lower (22.38 grams oxathiapiprolin per hectare for soybean and 3.38 grams oxathiapiprolin per hectare for sunflower) than the currently registered application rates (140 and 560 grams oxathiapiprolin per hectare), it is unlikely that oxathiapiprolin will pose a risk of concern to earthworms.

No mitigation measures are therefore required for earthworms.

Risk to Birds and Mammals

Birds and mammals may be exposed to oxathiapiprolin through consumption of treated seeds when used as seed treatment. The previous risk assessment indicated that, when used as a foliar spray (or soil application), oxathiapiprolin poses a negligible risk for birds and mammals foraging on food items in fields treated up to the highest seasonal application rate of 560 g a.i./ha.

The risk assessment for birds and mammals was conducted for soybean and sunflower seeds using the same endpoints that were used in the original risk assessment presented in the PRD2015-22, *Oxathiapiprolin* (Appendix I, Table 13; page 102).

To characterize the risk to birds and mammals, the likelihood of exceeding the toxic effects endpoints through feeding on treated seed was considered. The exposure of birds and mammals to a pesticide through consumption of treated seed is a function of the amount of pesticide on the seed, the body weight and food ingestion rate of the animal, and the number of seeds available for consumption. To characterize the risk, both the estimated dietary exposures and toxicity endpoints must be expressed in the same units. In this risk assessment, exposure and toxicity were both expressed in mg a.i./kg bw, using the following equation:

EDE (Estimated daily exposure; expressed in mg a.i./kg bw) = EEC (mg a.i./kg seeds) × FIR (Food ingestion rate; expressed in kg seed/day) × BW (1/kg bw)

As an initial conservative screening level scenario, risk was characterized for generic small, medium, and large size classes of birds and wild mammals. For the screening level assessment, it was assumed that unlimited treated seed would be available for consumption over an extended time period and that 100% of the diet would consist of treated seed. In addition, the acute toxicity endpoints (acute oral and dietary) are divided by an uncertainty factor of 10 to account for potential differences in inter-species and intra-species sensitivity as well as varying protection levels (for example, community, population, individual). The chronic NOEL endpoint is used without an uncertainty factor. The most sensitive toxicity endpoint values used for the risk assessment of oxathiapiprolin to birds and mammals have previously been established (PRD2015-22, *Oxathiapiprolin*, Appendix I, Table 13; page 102) and was used for calculations of RQs.

The RQ was calculated by dividing the EDE by the endpoint toxicity. The LOC for the risk assessment is 1.

The screening level risk assessments on birds and mammals consuming sunflower and soybean seeds when treated with oxathiapiprolin are presented in Appendix I, Tables 4 and 5 respectively. All calculated RQs are <1 and do not exceed the LOC of 1. Therefore, all size classes of birds or mammals are not expected to be at risk from direct contact with treated sunflower seeds at the maximum proposed application rate 0.01875 milligrams of oxathiapiprolin per seed and with treated soybean seeds at the maximum proposed application rate of 0.024 milligrams of oxathiapiprolin per seed.

As indicated in the screening level risk assessments (Appendix I, Tables 4 and 5), exposure to treated seeds at the highest proposed application rate of oxathiapiprolin to sunflower and soybean seeds is not expected to elicit adverse effects to either birds or mammals in the field. As the risk is not expected to be a concern for either birds or mammals, no further risk characterization will be required at this time.

No mitigation measures are therefore required for birds and mammals.

Risk to pollinators

Previous risk assessments to pollinators (PRD2015-22, *Oxathiapiprolin*) have been conducted for both foliar and soil applications. The previous assessment considered acute oral and contact toxicity data, as well as higher tier tunnel studies which considered potential for brood effects and chronic effects from foliar spray at rates up to 3 × 180 g a.i./ha. It was concluded that both foliar and soil applications of oxathiapiprolin pose a negligible risk to honey bees (single application rates were each 280 g a.i./ha).

For the proposed new use, the maximum seed treatment application rate for soybean is 0.024 milligrams of oxathiapiprolin per seed (or 22.38 grams oxathiapiprolin per hectare). The maximum seed treatment application rate for sunflower is 0.01875 milligrams of oxathiapiprolin per seed (or 3.38 grams oxathiapiprolin per hectare). Because the product is systemic, seed treatments could result in oral exposure through translocation to pollen and nectar. Additionally, during planting of treated seed with certain planter types, pesticide containing dust could be emitted from planters and result in exposure. Exposure from seed treatment is expected to be much lower than exposure from soil treatment or foliar sprays which have much higher use rates, and were determined in the previous assessment to pose no risks of concern to bees. Risk estimates however, were conducted for seed treatment uses in order to confirm expectations.

The pollinator risk assessment for oxathiapiprolin seed treatment is conducted according to the Guidance for Assessing Pesticide Risk to Bees (2014). Oxathiapiprolin is considered to be practically non-toxic to adult bees based on laboratory toxicity studies.

Exposure via pollen and nectar

The acute oral LD_{50} is determined to be >40.26 µg a.i./bee [PRD2015-22, *Oxathiapiprolin* (Appendix I, Table 13; page 102)]. The dietary exposure for oxathiapiprolin seed treatment (oxathiapiprolin is a systemic fungicide), is estimated with the default conservative EEC value of 1 mg a.i./kg diet and a default food consumption rate for adult bees of 0.292 g diet per bee per day. The RQ value is computed using the equation below:

RQ= Default maximum exposure estimate × ingestion rate (0.292 g/bee/day) / the most sensitive 48-h oral toxicity LD_{50} (µg a.i./bee)/uncertainty factor
RQ = 1 mg a.i./kg seed × 0.292 g/bee/day ÷ >40.26 µg a.i./bee ÷ 1
RQ = <0.0073

Comparing the dietary exposure with the oral toxicity endpoint, the RQ for the dietary exposure is calculated to be <0.0073 which is below the LOC of 0.4 for bees.

Exposure to dust from treated seeds

The acute contact LD_{50} is determined to be >100 µg a.i./bee [PRD2015-22, *Oxathiapiprolin* (Appendix I; Table 13; page 102)]. For the contact exposure, considering oxathiapiprolin is practically non-toxic to adult bees (>100 µg a.i./bee), the risk of oxathiapiprolin to adult bees via contact exposure is considered to be negligible. Further supporting a negligible risk from contact exposure, the seed treatment application rate (3.38 g a.i./ha for sunflower and 22.38 g a.i./ha for soybean; based on number of seeds per kilogram and typical seeding rates) are much lower compared to the single maximum application rate of 280 g a.i./ha that was previously considered in the pollinator risk assessment for both foliar and soil applications, and determined to pose negligible risk to pollinators.

Overall, the proposed seed treatment with oxathiapiprolin fungicide is not expected to pose a risk to adult bees on both acute contact and oral bases.

No mitigation measures are therefore required for bees.

4.2.2 Risks to Aquatic Non-Target Organisms

A risk assessment for aquatic non-target organisms was previously conducted for oxathiapiprolin for both foliar and soil applications (see PRD2015-22, *Oxathiapiprolin,* for further details). The risk assessments were based on the maximum seasonal application rate for both foliar and soil applications. The maximum foliar application rate except for ginseng is 140 grams oxathiapiprolin per hectare. The maximum seasonal rate for foliar and soil application for ginseng is 560 grams oxathiapiprolin per hectare. Previous risk assessment identified that there were no risks to aquatic non-target organisms, either from a direct overspray or from spray drift/runoff. As the current proposed seed treatment application rates are much lower (22.38 grams oxathiapiprolin per hectare for soybean and 3.38 grams oxathiapiprolin per hectare for sunflower; based on number of seeds per kilogram and typical seeding rates) than the currently registered foliar and soil application rates (140 and 560 grams oxathiapiprolin per hectare), it is unlikely that this proposed major new use of oxathiapiprolin will pose a risk of concern to aquatic non-target organisms.

No additional mitigation measures are therefore required for aquatic non-target organisms.

4.3 Incident Reports Related to the Environment / Additional Considerations

Environmental incident reports are obtained from two main sources; the Canadian pesticide incident reporting system (including both mandatory reporting from the registrant and voluntary reporting from the public and other government departments) and the United States Environmental Protection Agency (USEPA) Ecological Incident Information System (EIIS). Specific information regarding the mandatory reporting system regulations that came into force on 26 April 2007 under the *Pest Control Products Act* can be found at https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/public/protecting-your-health-environment/report-pesticide-incident.html.

The USEPA's Ecological Incident Information System (EIIS) was also queried for environment incidents. None were located for the active oxathiapiprolin.

As of 16 June 2017, no environmental incident reports involving oxathiapiprolin had been submitted to the PMRA.

5.0 Value

5.1 Consideration of Benefits

There are alternatives registered for all disease claims (Appendix I, Table 6). However, DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment will provide users with a new mode of action to control oomycete diseases in soybean and sunflowers. This could be beneficial from a resistance management perspective. Although the risk of resistance in seed treatments in general is considered low, in the case where resistance to a seed treatment product is suspected, oxathiapiprolin will provide growers with an alternative mode of action. In the literature, there are reports of metalaxyl resistance for systemic downy mildew in sunflowers.

DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment could be part of an Integrated Pest Management program, which incorporates other management practices. Such practices include planting good-quality seed in well-drained, non-compacted fields and using varieties that would be tolerant to the labeled diseases.

DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment will be applied in a single pre-planting application and relatively small amounts will be applied. Therefore the overall risk of resistance development for these products is considered low.

5.2 Effectiveness Against Pests

In support of the Phytophthora claims on soybean and the downy mildew claim on sunflower, efficacy data from a total of four and twelve relevant trials were provided, respectively. Based on the results of these trials, it was demonstrated that DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment are effective at providing control of downy mildew in sunflower at a rate of 9.37-18.75 mL of product/200 000 seeds. It was also demonstrated that DuPont Lumisena Fungicide Seed Treatment is effective at providing control of Phytophthora seed rot, pre-emergence and post-emergence damping off in soybean at a rate of 8.4-16.8 mL of product/140 000 seeds.

5.3 Non-Safety Adverse Effects

Visual assessments of phytotoxicity were conducted in all trials. No phytotoxicity symptoms were observed.

5.4 Supported Uses

Based on the value information provided a claim of control of downy mildew (*Plasmopara halstedii*) on sunflower, at an application rate of 9.37–18.75 mL of product/200 000 seeds, is supported on both the DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment labels.

Based on the value information provided a claim of control of Phytophthora seed rot, pre-emergence and post-emergence damping off (*Phytopththora sojae*) in soybean, at an application rate of 8.4-16.8 mL of product/140 000 seeds, is supported on the DuPont Lumisena Fungicide Seed Treatment label.

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), bioaccumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act* (Appendix I, Table 10)].

During the original review process, oxathiapiprolin and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03 and evaluated against the Track 1 criteria (PRD2015-22, *Oxathiapiprolin*). The TSMP conclusions reached at that time apply to the current submission:

- Oxathiapiprolin Technical does not meet all Track 1 criteria, nor does it form any transformation products that meet all Track 1 criteria, and therefore is not considered a Track 1 substance.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the current revised environmental review process, contaminants in the technical (DuPont Zorvec Technical Fungicide) and formulants and contaminants in the end-use products (DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment) were compared against the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern maintained in the *Canada Gazette*. The list is used as described in the PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including: DIR99-03 and DIR2006-02, 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 oxathiapiprolin and the end use products DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02. Refer to PRD2015-22, *Oxathiapiprolin,* for more information on the Toxic Substances Management Policy Considerations (TSMP) considerations.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for oxathiapiprolin is adequate to define the majority of toxic effects that may result from exposure. The most sensitive endpoints for risk assessment were decreased body weight and body-weight gain and delayed sexual maturation in male rat offspring. These effects on offspring occurred in the absence of maternal toxicity and only at the limit dose of testing. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Workers treating seed with DuPont Lumisena Fungicide Seed Treatment or Plenaris 200FS Seed Treatment and workers planting treated seed are not expected to be exposed to levels of oxathiapiprolin that will result in an unacceptable risk when DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment are used according to label directions.

The personal protective equipment for mixers/loaders, applicators and baggers in commercial seed treatment facilities is a long-sleeved shirt, long pants, chemical-resistant gloves and shoes plus socks. Cleaners in commercial seed treatment facilities must wear coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves and shoes plus socks. Soybean seed and sunflower seed can only be treated in closed treatment systems. Farmers planting and handling treated seed must wear a long-sleeved shirt, long pants, chemical-resistant gloves and shoes plus socks.

The nature of the residues in plants and animals is adequately understood. The residue definition for enforcement is oxathiapiprolin in plant products and in animal matrices. The proposed use of oxathiapiprolin on soybeans and sunflowers does not constitute a risk of concern for chronic dietary exposure (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend MRLs. The PMRA recommends that the following MRLs be specified for residues of oxathiapiprolin.

Commodity	Recommended MRL (ppm)
Dry soybeans	0.01
Sunflower seeds	0.01
Eggs; fat, meat, and meat byproducts of poultry	0.01

7.2 Environmental Risk

When used for seed treatment on sunflower and soybean, oxathiapiprolin and its end-use products, DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment, are not expected to pose risks of concern to terrestrial and aquatic non-target organisms.

7.3 Value

DuPont Lumisena Fungicide Seed Treatment and Plenaris 200FS Seed Treatment will provide users with a new mode of action to control oomycete diseases in soybean and sunflowers.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of DuPont Zorvec Technical Fungicide, DuPont Lumisena Fungicide Seed Treatment, and Plenaris 200FS Seed Treatment, containing the technical grade active ingredient oxathiapiprolin, to control downy mildew in sunflower and Phytophthora root and stem rot in soybean.

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.

List of Abbreviations

µg	micrograms
°C	degrees celsius
a.i.	active ingredient
ADI	acceptable daily intake
AHETF	Agricultural Handlers Exposure Task Force
atm	atmosphere
bw	body weight
BW	generic body weight
CAF	composite assessment factor
DAF	dermal absorption factor
EEC	estimated environmental concentration
EDE	estimated daily exposure
EIIS	Ecological Incident Information System
FDA	*Food and Drugs Act*
FIR	food ingestion rate
g	gram
GI	gastro-intestinal tract
h	hour
HDPE	high density polyethylene
ha	hectare(s)
HAFT	highest average field trial
IOM	Institute of Occupational Medicine
kg	kilogram
L	litre
LAFT	lowest average field trial
LD_{50}	lethal dose 50%
LOC	level of concern
LOQ	limit of quantitation
mg	milligram
mL	millilitre
M	multi-site mode of action
MOE	margin of exposure
MRL	maximum residue limit
NAFTA	North American Free Trade Agreement
NOAEL	no observed adverse effect level
NOEL	no observed effect level
NR	not reported
OVS	OSHA Versatile Sampler
PHI	preharvest interval
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PRD	Proposed Registration Decision
RQ	risk quotient
SC	soluble concentrate

TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency

Appendix I Tables and Figures

Table 1 Toxicology Reference Values for Use in Health Risk Assessment for Oxathiapiprolin

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary	No relevant endpoint identified		
Repeated dietary	Rat oral (dietary) 2-generation reproductive toxicity	NOAEL = 411 mg/kg bw/day Decreased offspring body weight, body-weight gain and increased time to preputial separation	100
	ADI = 4 mg/kg bw/day		
Short, intermediate and long-term dermal	No relevant endpoint identified		
Short and intermediate-term inhalation	Rat oral (dietary) 2-generation reproductive toxicity	Adjusted NOAEL[2] = 20 mg/kg bw/day Decreased offspring body weight, body-weight gain and increased time to preputial separation	100
Cancer	No evidence of carcinogenicity		

[1] CAF (composite assessment factor) refers to a total of uncertainty and *Pest Control Products Act* factors for dietary risk assessment; MOE refers to a target margin of exposure for occupational assessment.
[2] Since GI absorption was only approximately 5% at high dose levels and compound absorption by the inhalation route is assumed to be 100%, the original oral NOAEL of 411 mg/kg bw/day was multiplied by a 5% correction factor to obtain a systemic NOAEL (411*0.05=20) for inhalation exposure scenarios.

Table 2 Integrated Food Residue Chemistry Summary

CROP FIELD TRIALS & RESIDUE DECLINE ON SOYBEANS			PMRA # 2600655					
Field trials were conducted in 2014 in the United States. Trials were conducted in NAFTA Growing Regions 2 (1 trial), 4 (1 trial) and 5 (4 trials) and for a total of 6 trials. DPX-QGU42-239, a suspension concentrate, was applied as a single preplant seed treatment application at a rate of 0.0625 – 0.0841 mg a.i./seed or 0.2515 – 0.2528 mg a.i./seed. Soybean forage, hay, and seed from the progeny crops grown from treated seeds were harvested at preharvest intervals (PHIs) of 41 – 75 days (forage and hay) and 126 – 151 days (seed).								
Commodity	**Total Application Rate (mg a.i./seed)**	**PHI (days)**	**Residue Levels (ppm)**					
			n	**LAFT**	**HAFT**	**Median**	**Mean**	**SD**
Oxathiapiprolin								
Soybean Forage	0.0625 – 0.0841	41 – 75	5	<0.010	<0.010	0.010	0.010	0
	0.2515 – 0.2528	41 – 53	3	<0.010	<0.010	0.010	0.010	0
Soybean Hay	0.0625 – 0.0841	41 – 75	5	<0.010	<0.010	0.010	0.010	0
	0.2515 – 0.2528	41 – 53	3	<0.010	<0.010	0.010	0.010	0
Soybean Seed	0.0625 – 0.0841	126 – 151	5	<0.010	<0.010	0.010	0.010	0
	0.2515 – 0.2528	126 – 151	3	<0.010	<0.010	0.010	0.010	0
LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation. Values based on per-trial averages. For computation, values < LOQ are assumed to be at the LOQ (0.010 ppm). n = number of independent field trials.								

CROP FIELD TRIALS & RESIDUE DECLINE ON SUNFLOWERS								PMRA # 2600656
Field trials were conducted in 2014 in Canada and the United States. Trials were conducted in NAFTA Growing Regions 5 (4 trials), 7 (2 trials), 8 (1 trial) and 14 (1 trial) for a total of 8 trials. DPX-QGU42-239, a suspension concentrate, was applied as a single preplant seed treatment application at a rate of 0.01877 – 0.0212 mg a.i./seed. Sunflower seed from the progeny crops grown from treated seeds were harvested at preharvest intervals (PHIs) of 105 – 148 days.								
Commodity	**Total Application Rate (mg a.i./seed)**	**PHI (days)**	**Residue Levels (ppm)**					
			n	**LAFT**	**HAFT**	**Median**	**Mean**	**SD**
Oxathiapiprolin								
Sunflower seed	0.01877 – 0.0212	105 – 148	8	<0.010	<0.010	0.010	0.010	0
LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation. Values based on per-trial averages. For computation, values < LOQ are assumed to be at the LOQ (0.010 ppm). n = number of independent field trials.								

Table 3 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

DIETARY RISK FROM FOOD AND WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Alone	**Food and Water**
Basic chronic non-cancer dietary exposure analysis **ADI = 4 mg/kg bw/day** **Estimated chronic drinking water concentration = 507 Φg/L**	**All infants < 1 year**	0.2	0.4
	Children 1–2 years	0.1	1.1
	Children 3 to 5 years	0.3	0.7
	Children 6–12 years	0.3	0.6
	Youth 13–19 years	0.2	0.4
	Adults 20–49 years	0.1	0.3
	Adults 50+ years	0.2	0.4
	Females 13-49 years	0.2	0.4
	Total population	0.2	0.4

Table 4 Oxathiapiprolin Screening Level Risk Assessment on Birds and Mammals: Consuming Sunflower Seed[1]

Toxicity Test	Screening Level Toxicity Endpoint[2] (mg a.i./kg bw/day)	EDE[3] (mg a.i./kg bw)	RQ[4]	LOC[5] exceeded?
Small bird (0.02 kg)				
Acute	225.00	95.227	0.423	No
Dietary	128.00	95.227	0.744	No
Reproduction	106.70	95.227	0.8925	No
Medium sized bird (0.10 kg)				
Acute	225.00	74.802	0.332	No
Dietary	128.00	74.802	0.584	No

Reproduction	106.70	74.802	0.701	No
Large sized bird (1.00 kg)				
Acute	225.00	21.808	0.097	No
Dietary	128.00	21.808	0.170	No
Reproduction	106.70	21.808	0.204	No
Small mammal (0.015 kg)				
Acute	500.00	54.420	0.109	No
Reproduction	411.40	54.420	0.132	No
Medium sized mammal (0.035 kg)				
Acute	500.00	46.801	0.094	No
Reproduction	411.40	46.801	0.114	No
Large sized mammal (1.00 kg)				
Acute	500.00	25.769	0.052	No
Reproduction	411.40	25.769	0.063	No

[1] The proposed maximum application rate for oxathiapiprolin for use as seed treatment in sunflower = 0.01875 mg a.i./seed. The screening level assessment, assumes that 100% of the sunflower seeds are available for consumption.

[2] Toxicity endpoints (LD_{50} and NOEL) were taken from Proposed Registration Decision PRD2015-22, *Oxathiapiprolin* Appendix I, Table 13 (page 102),

[3] EDE (Estimated daily exposure; expressed in mg a.i./kg bw) = EEC (mg a.i./kg seeds) × FIR (in kg seed/day) × BW (1/kg bw). The number of seeds that are expected to be consumed by a generic-sized group of birds and mammals is calculated using a food ingestion rate (FIR) of 5.1, 19.9 and 58.1 g diet/day for 20, 100 and 1000 g birds, respectively, and 2.2, 4.4 and 68.7 g diet/day for 15, 35 and 1000 g mammals, respectively.

[4] RQ (Risk quotient) = EDE/Toxicity

[5] Level of concern (LOC) = 1 (for birds and mammals)

Table 5 Oxathiapiprolin Screening Level Risk Assessment on Birds and Mammals: Consuming Soybean Seed[1]

Toxicity Test	Screening Level Endpoint Toxicity[2] (mg a.i./kg bw/day)	EDE[3] (mg a.i./kg bw/day)	RQ[4]	LOC[5] exceeded?
Small bird (0.02 kg)				
Acute	225.00	45.099	0.200	No
Dietary	128.00	45.099	0.352	No
Reproduction	106.70	45.099	0.423	No
Medium sized bird (0.10 kg)				
Acute	225.00	35.426	0.157	No
Dietary	128.00	35.426	0.277	No
Reproduction	106.70	35.426	0.332	No

Large sized bird (1.00 kg)				
Acute	225.00	10.328	0.046	No
Dietary	128.00	10.328	0.081	No
Reproduction	106.70	10.328	0.097	No
Small mammal (0.015 kg)				
Acute	500.00	25.773	0.052	No
Reproduction	411.40	25.773	0.063	No
Medium sized mammal (0.035 kg)				
Acute	500.00	22.165	0.044	No
Reproduction	411.40	22.165	0.054	No
Large sized mammal (1.00 kg)				
Acute	500.00	12.204	0.024	No
Reproduction	411.40	12.204	0.030	No

[1] The proposed maximum application rate for oxathiapiprolin for use as seed treatment in soybean = 0.024 mg a.i./seed. The screening level assessment, assumes that 100% of the soybean seeds are available for consumption.

[2] Toxicity endpoints (LD_{50} and NOEL) were taken from Proposed Registration Decision PRD2015-22, *Oxathiapiprolin* (Appendix I, Table 13; page 102).

[3] EDE (Estimated daily exposure; expressed in mg a.i./kg bw) = EEC (mg a.i./kg seeds) × FIR (in kg seed/day) × BW (1/kg bw). The number of seeds that are expected to be consumed by a generic-sized group of birds and mammals is calculated using a food ingestion rate (FIR) of 5.1, 19.9 and 58.1 g diet/day for 20, 100 and 1000 g birds, respectively, and 2.2, 4.4 and 68.7 g diet/day for 15, 35 and 1000 g mammals, respectively.

[4] RQ (Risk quotient) = EDE/Toxicity

[5] Level of concern (LOC) = 1 (for birds and mammals)

Table 6 Registered Alternatives based on mode of action as of May 2017.

Crop	Disease	Conventional Mode of Action Group No.	Non-Conventional Mode of Action Group No.
soybean	Phytophthora seed rot	4, M+7,	~
	Phytophthora pre-emergence and post-emergence damping off	M, 4, 11, 12, M+7, 7+11	~
sunflower	systemic downy mildew	4, 11, 22	~

M=multi-site mode of action;

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

None

2.0 Human and Animal Health

PMRA Document Number	Reference
2313613	2012, Fluquinconazole and Prochloraz: Determination of Operator Exposure during Cereal Seed Treatment with "Jockey" Fungicide in Germany, United Kingdom and France, DACO: 5.3,5.4
1571553	2007, Determination of Operator Exposure to Imidacloprid During Loading/Sowing of Gaucho Treated Maize Seeds Under Realistic Field Conditions in Germany and Italy, DACO: 5.4
2313627	2013, Determination of Dermal and Inhalation Exposure to Operators During Loading and Sowing Seed Treated with Austral Plus Net Using Conventional or Pneumatic Sowing Machines, DACO: 5.3,5.4
2396870	2013, Agricultural Handler Exposure Task Force (AHETF) - Survey Results of Commercial and Downstream Seed Treating Facilities, DACO: 5.3,5.4
2600654	2015, Heubach Dust Test: Oxathiapiprolin-Containing Seed Treatment On Soybean And Sunflower Seed, DACO: 5.10,5.6,5.7,5.9,IIIA 7.4.1,IIIA 7.4.2,IIIA 7.5.1,IIIA 7.5.2,IIIA 7.5.3,IIIA 7.5.4
2600655	2015, Magnitude Of Residues Of Oxathiapiprolin And Its Metabolites In Raw And Processed Soybean Commodities Of Plants Grown From Seed Treated With Oxathiapiprolin (DPX-QGU42) 200 G/L SC - USA, 2014, DACO: 7.4.1,7.4.2,7.4.6,IIIA 8.3.1,IIIA 8.3.2,IIIA 8.3.3
2600656	2015, Magnitude Of Residues Of Oxathiapiprolin And Its Metabolites In Sunflower Seed Of Plants Grown From Seed Treated With Oxathiapiprolin (DPX-QGU42) 200G/L SC - USA AND CANADA 2014, DACO: 7.4.1,7.4.2,7.4.6,IIIA 8.3.1,IIIA 8.3.2,IIIA 8.3.3
2628968	Foreign review - Oxathiapiprolin Crop Field Trial - Soybean (forage, hay, seed), DACO: 12.5.7
2628976	Foreign review - Oxathiapiprolin Crop Field Trial - Sunflower (seed), DACO: 12.5.7

3.0 Environment

None

4.0 Value

2600657 2015, Biological Assessment Dossier For Dpx Qgu42 200 Fs Seed Treatment For Downy Mildew Control In Sunflowers And Phytopthora Sojae Control In Soybeans, Canada, DACO: 1.1, 10.1 (OECD), 10.2.1, 10.2.2, 10.2.3.1, 10.2.3.2, 10.2.3.3, 5.2, IIIA 3.1, IIIA 3.2, IIIA 3.3.1, IIIA 3.3.2, IIIA 3.3.3, IIIA 3.4, IIIA 3.5, IIIA 3.6

2625713 2016, Value Response For DPX QGU42 200 FS Seed Treatment For *Phytopthora Sojae* Control In Soybeans, Canada 2016, DACO: 10.1, 10.2, 10.2.3, 10.2.3.1, 10.2.3.3

B. Additional Information Considered

i) Published Information

1.0 Environment

Nagy, K.A., 1987. Field metabolic rate and food requirement scaling in mammals and birds. Ecological Monographs 57:111-128, 1987.

United States Environmental Protection Agency, Health Canada Pest Management Regulatory Agency, and California Department of Pesticide Regulation, 2014 Guidance for Assessing Pesticide Risk to Bees, June 19, 2014 (https://www.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf).