Proposed Special Review Decision PSRD2022-03

Special Review of Picoxystrobin and Its Associated End-use Products: Proposed Decision for Consultation

Consultation Document

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1.0 Introduction

Health Canada's Pest Management Regulatory Agency (PMRA) initiated a special review of picoxystrobin in 2019 under subsection 17(2) of the *Pest Control Products Act* based on the decision made by the European Union in 2017 (Official Journal of the European Union, 2017).

Pursuant to subsection 18(4) of the *Pest Control Products Act*, the PMRA has evaluated the aspects of concern that prompted the special review of pest control products containing picoxystrobin. The aspects of concern for this special review are relevant to human health and the environment.

2.0 Uses of picoxystrobin in Canada

Picoxystrobin is a fungicide registered for foliar ground or aerial use on canola, dry legumes, cereals, corn, soybeans, potatoes, sunflowers, onions, sugar beets, almonds, alfalfa, grass grown for seed, and peanuts. Picoxystrobin is also registered for seed treatment use on canola, rapeseed, and mustard. All registered pest control products containing picoxystrobin (Appendix I) are considered in the special review.

3.0 Aspects of concern that prompted the special review

The European Union published the Implementing Regulation (EU) 2017/1455 on 10 August 2017 concerning the non-renewal of approval of the active substance picoxystrobin. Based on a review of the European Commission (2017) decision, Health Canada has identified the following aspects of concern that prompted the special review:

Human health

- Potential genotoxicity of the metabolite IN-H8612.[1]

Environment

- Potential for risk to aquatic invertebrates exposed to picoxystrobin.
- Potential for risk to earthworms exposed to picoxystrobin.
- Potential for risk to earthworm-eating mammals exposed to the metabolite IN-QDY63.[2]

[1] The metabolite IN-H8612 is alternatively referred to as Metabolite 11 and Compound 24. See Appendix 2 for a summary of the chemical structure and name information.

[2] The metabolite IN-QDY63 is alternatively referred to as Compound 8 and R408509. See Appendix 2 for a summary of the chemical structure and name information.

4.0 Evaluation of the aspects of concern that prompted the special review

Following the initiation of the special review, Health Canada requested information related to the aspects of concern from provinces and other relevant federal government departments and agencies in accordance with subsection 18(2) of the *Pest Control Products Act*. No information was received.

To evaluate the aspects of concern for picoxystrobin, Health Canada considered currently available relevant scientific information, which includes existing reviews, food residue information, drinking water information, additional requested toxicology information for the metabolites, information from the European Food Safety Authority (EFSA), the European Union decision and information from the Joint Meeting on Pesticide Residues (JMPR).

4.1 Assessment of aspect of concern related to human health

4.1.1 Toxicology and potential genotoxicity of the metabolite IN-H8612

As part of the special review, the potential genotoxicity of metabolite IN-H8612 was considered. Toxicology studies including acute oral and 28-day oral toxicity studies, and three genotoxicity studies: a bacterial reverse mutation assay, an in vitro chromosomal aberration assay in human lymphocytes, and an in vivo mouse bone marrow micronucleus test, were submitted to Health Canada to assess the aspect of concern of this compound.

Based on the review of this information, metabolite IN-H8612 is of low acute toxicity in rats. In the 28-day dietary toxicity study in rats, systemic toxicity was observed, including decreases in spleen weights and white blood cell parameters, and increased weight and histopathology findings in the thymus. There were also increases in the incidence of hydronephrosis, blood present in urine, and urine pH, and decreased urine specific gravity. Histopathology findings in the uterus, as well as increased time to tail flick were also observed. A no observed adverse effect level (NOAEL) of 58 mg/kg bw/day was established for both sexes in this study.

Based on the available acute and repeat-dose toxicity data, IN-H8612 and picoxystrobin are considered of similar toxicity, although unique kidney effects in the short-term oral toxicity study with IN-H8612 were noted.

The genotoxicity studies conducted with IN-H8612 were all found to be negative when considering the weight of evidence.

IN-H8612 was observed to be negative in the bacterial reverse mutation assay.

For the in vivo micronucleus study, EFSA had previously concluded that “the clastogenic and aneugenic potential of metabolite IN-H8612, found as a residue, cannot be excluded as equivocal results were observed in the in vivo micronucleus test” (EFSA, 2016).

However, based on suggested practices for evaluating in vivo micronucleus assays in scientific literature, the determination of a positive result should include statistically significant dose-related increases in micronucleated polychromatic erythrocyte (MNPCE) frequency (at any time point), with at least one value significantly exceeding the historical vehicle control range (Krishna and Hayashi, 2000).

Although there was a small dose-related increase in MNPCE frequency observed in the micronucleus study, none of the values attained statistical significance at any of the dose levels tested. Furthermore, the MNPCE values of the test substance-treated animals were within the recent historical control range from the conducting laboratory. There was also evidence that IN-H8612 had been tested at adequate dose levels in the study based on the observation of significant clinical signs of toxicity at the highest dose level tested. Therefore, according to criteria outlined in the published literature, as well as those set out by the testing laboratory, the micronucleus study was determined to be negative.

The results from the initial experiments in the in vitro chromosomal aberration assay in human lymphocytes showed an increase in chromosome aberrations at high concentrations. However, the culture medium had lower than normal physiological pH, creating an artificially cytotoxic environment (Scott et al., and Morita et al., 1992). When the culture medium was brought to a more neutral pH, the clastogenic observations were eliminated, or reduced to within solvent control historical levels. As the clastogenic findings all occurred under non-ideal conditions, it was concluded that the effects in the initial experiments were not related to treatment. Therefore, it was concluded that IN-H8612 did not induce treatment-related chromosomal aberrations in primary human lymphocyte cultures under conditions that reflect normal physiological pH.

4.1.2 Toxicology and potential genotoxicity of the metabolite IN-QDY63

Although toxicological concerns for metabolite IN-QDY63 were not one of the human health aspects of concern identified by EFSA, the review of the available toxicology data for this metabolite was considered for the environmental aspects of concern. Toxicology studies assessed include acute oral and 90-day oral toxicity studies in rats, and a complete battery of genotoxicity studies with an additional bacterial reverse mutation assay study.

IN-QDY63 was of moderate toxicity in the acute oral toxicity study in the rat. It was noted, however, that there was a disparity in the level of acute toxicity between the in vivo unscheduled DNA synthesis (UDS) assay and the acute LD50 assay, both of which used the same strain of rat. In the acute LD_{50} assay, all animals died at a dose level of 500 mg/kg bw (with a resulting LD_{50} of 387 mg/kg bw), while in the UDS assay, all animals survived up to a dose level of 1250 mg/kg bw in the main assay, and only a single mortality was observed in the preliminary assay in which rats were dosed with 2000 mg/kg bw. Comparisons of the study protocols identified potential differences that could contribute to this disparity, including those related to the vehicle, purity, date of study conduct, the age of the rats used in the studies, and fasting practices. Despite the disparity in the acute toxicity data for IN-QDY63, there remains some indication of increased acute toxicity for this metabolite compared to picoxystrobin, which was found to have an acute oral LD_{50} of greater than 5000 mg/kg bw.

In the 90-day dietary toxicity study in rats conducted with IN-QDY63, effects on the kidney, along with quantitative clinical chemistry and qualitative urinalysis findings, were observed in males at the highest dose level tested. NOAELs of 14 and 53 mg/kg bw/day were established for males and females, respectively, in this study.

The weight of evidence indicated that IN-QDY63 does not have genotoxic potential. Although there was a positive finding in the in vitro chromosome aberration study, negative findings were observed in the remaining in vitro and in vivo studies.

For the rat in vivo micronucleus assay, EFSA highlighted a concern regarding whether the compound reached the target site and determined that the results of the assay were, therefore, not conclusive. However, EFSA guidance on interpretation of genotoxicity assays indicates that evidence of systemic toxicity can act as a surrogate for a direct measure of the test compound reaching the bone marrow (EFSA, 2017). There was ample evidence of systemic toxicity for this compound in other repeat-dose studies conducted in the rat, and in the preliminary in vivo micronucleus study (which included clinical signs of toxicity and a sacrifice due to moribund condition). Therefore, as there was no treatment-related increase in the frequency of MNPCEs observed in this study, the study can be classified as negative. And as noted above, the overall weight of evidence indicated that IN-QDY63 does not have genotoxic potential.

Overall, there is indication of increased toxicity for IN-QDY63 on an acute basis when the study results are compared to those of the parent compound, picoxystrobin. There is also some indication of increased toxicity on a repeat-dose basis when comparing the results of the 90-day oral toxicity studies with IN-QDY63 and picoxystrobin. In the IN-QDY63 study, the NOAEL for males was lower (14 mg/kg bw/day, compared to 42 mg/kg bw/day for picoxystrobin), and kidney findings were observed in males that were not observed in the picoxystrobin toxicology database.

4.1.3 Potential dietary risk

Following the review of the toxicity data for metabolites IN-H8612 and IN-QDY63, there are indications that the metabolites are of similar or increased toxicity when compared to the parent, picoxystrobin. The current residue definition for plant and animal commodities for dietary exposure and risk assessment in Canada includes the parent, picoxystrobin, only. Metabolite IN-QDY63 is included in the residue definition for drinking water, along with the parent and Compound 2 and 3. According to the environmental fate data, IN-H8612 was not detected in soil or water and is not expected to be present in drinking water.

EFSA (EFSA, 2016) and JMPR (JMPR, 2016) concluded that the residue definition for enforcement in plant and animal commodities should be the parent, picoxystrobin, only. EFSA did not propose a residue definition for risk assessment since the conclusion regarding the clastogenic potential of the metabolite IN-H8612 could not be excluded (EFSA, 2016). JMPR did not identify any toxicological concern regarding any of the major metabolites in food producing animals (JMPR, 2012). For plant metabolism, JMPR found metabolite IN-H8612 in significant proportions in the soybean and tomato metabolism studies (JMPR, 2016).

IN-H8612, similar in toxicity to that of picoxystrobin, is found in plant/animal commodities at greater than 10% of the total radioactive residue. IN-QDY63, approximately 3-fold more toxic than picoxystrobin, is a minor metabolite.

In Canada, the most recent acute and chronic (non-cancer) dietary exposure assessments were conducted in 2018 using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™, Version 4.02, 05-10-c) program which incorporates food consumption data from the National Health and Nutritional Examination Survey, What We Eat in America (NHANES/ WWEIA) dietary survey for the years 2005-2010 available through CDC's National Center for Health Statistics (NCHS). The assessment was conducted to support the addition of the new uses on potatoes, sunflowers, bulb vegetables, sugar beets, almond, alfalfa, peanuts, and grass grown for seed.

Acute dietary risk

The acute reference dose (ARfD) for picoxystrobin was determined to be 0.67 mg/kg bw for the general population based on a lowest observed adverse effect level (LOAEL) of 200 mg/kg bw/day from an acute neurotoxicity study in rats and a composite assessment factor of 300. An additional 3-fold uncertainty fact was applied due to the lack of NOAEL (Canada, 2012). The acute dietary risk assessment was conducted using Canadian maximum residue limits (MRLs) and default processing factors, where applicable.

When considering exposure from picoxystrobin only, the acute dietary risk from food uses ranged from 0.22% to 1.0% of the ARfD for the general population and all subpopulations. Exposure from food and drinking water (EEC value = 27 µg a.i./L) ranged from 0.35% to 1.64% of the ARfD for all population subgroups, and therefore was shown to be acceptable. Although the inclusion of metabolites IN-H8612 and IN-QDY63 in the residue definition for food may increase exposure; the acute risk is expected to be acceptable based on the current low risk estimates from exposure to picoxystrobin only.

Chronic non-cancer dietary risk

The acceptable daily intake (ADI) for picoxystrobin was determined to be 0.046 mg/kg bw/day, based on a NOAEL of 4.6 mg/kg bw/day from a 1-year dietary toxicity study in the dog and a composite assessment factor of 100 (Canada, 2012). The chronic dietary risk assessment was conducted using Canadian MRLs and default processing factors, where applicable.

When considering exposure from picoxystrobin only, the chronic dietary risk from food uses ranged from 1.3% to 5.6% of the ADI for the general population and all subpopulations. Exposure from food and drinking water (EEC value= 8.1 µg a.i./L) ranged from 1.7% to 6.9% of the ADI for all population subgroups, and therefore was shown to be acceptable. Although the inclusion of metabolites IN-H8612 and IN-QDY63 in the residue definition for food may increase exposure; the chronic risk is expected to be acceptable based on the current low risk estimates from exposure to picoxystrobin.

Chronic cancer dietary risk

A cancer dietary exposure assessment was not required as picoxystrobin did not cause cancer at dose levels that were relevant to the human health risk assessment.

4.1.4 Potential occupational risk

Mixer, loader, and applicator risk

Workers mixing, loading, and applying picoxystrobin are not expected to be exposed to metabolites IN-H8612 and IN-QDY63, as these metabolites are formed by plant and animal metabolism.

Postapplication risk

There is a possibility for workers entering treated areas to be potentially exposed to the plant metabolite IN-H8612 and/or IN-QDY63 through the dermal route while performing activities such as scouting, irrigating, detasseling, hand harvesting, and thinning. The results of the most recent postapplication assessment for picoxystrobin indicated that the calculated margins of exposure (MOEs) ranged from 24 200 to 2 110 000 for all activities, exceeding the target MOE of 100 on day 0 (Canada, 2018). IN-H8612 and picoxystrobin are considered of similar toxicity based on the available data and IN-QDY63, although approximately 3-fold more than picoxystrobin, is a minor metabolite (see Section 4.1.1). Should workers be exposed to IN-H8612 and/or IN-QDY63 through postapplication activities, any additional risks will not exceed the level of concern based on the calculated exposure estimates for picoxystrobin. Therefore, an updated quantitative assessment for postapplication exposure was not conducted as part of this special review.

4.1.5 Assessment of aspect of concern related to human health: conclusions

Following the special review assessment of the available toxicity data on metabolites IN-H8612 and IN-QDY63, Health Canada has concluded that all micronucleus findings in question were considered negative and conclusive and that there are no genotoxicity concerns for metabolites IN-H8612 and IN-QDY63.

The acute and chronic (non-cancer) dietary risks (from exposure to picoxystrobin and its metabolites INQDY63 and IN-H8612) are expected to be acceptable under the current conditions of use. Additional risk mitigation measures are not required.

Workers mixing, loading, and applying picoxystrobin are not expected to be exposed to metabolites IN-H8612 and IN-QDY63. Potential risk from exposure to metabolite IN-H8612 for postapplication workers is considered acceptable under the current conditions of use.

Overall, Health Canada concludes that the human health risks relating to the aspect of concern are acceptable under the current conditions of use.

4.2 Assessment of aspects of concern related to environment

4.2.1 Potential for risk to aquatic invertebrates exposed to Picoxystrobin

To assess the potential for adverse effects to aquatic invertebrates to picoxystrobin, previously established screening level estimated environmental concentrations (EECs) from 2012 in the aquatic environment based on a direct application to water following foliar application to sweet corn at rates of 132.5-225 g a.i./ha and dry legumes at rates of 150-225 g a.i./ha were used as the exposure estimates. A risk assessment of picoxystrobin (875 g a.i./ha maximum seasonal rate) and the five transformation products Compounds 2, 3, 7, 8 (IN-QDY63) and 26 was previously conducted for freshwater and marine aquatic organisms based on available toxicity data for each of the compounds to invertebrates (acute and chronic) (Canada, 2012).

Freshwater species

Acute exposure to picoxystrobin resulted in significant mortality in several freshwater species of aquatic invertebrates. Transformation products were much less acutely toxic than the parent to *Daphnia magna*. Chronic exposure to picoxystrobin resulted in reduced reproduction of *Daphnia magna* and significant reduction in emergence rate of the freshwater midge *Chironomus riparius*. The screening level risk quotients for acute and chronic exposure of freshwater invertebrates to picoxystrobin exceeded the level of concern. The refined risk quotients based on spray drift of picoxystrobin slightly exceeded the level of concern for acute exposure of freshwater invertebrates from aerial application to sweet corn, chronic exposure of *Daphnia magna* from aerial application to sweet corn and dry legumes and chronic exposure of the freshwater midge from aerial application to sweet corn. Thus, there is the potential for adverse effects to freshwater invertebrates exposed to picoxystrobin through spray drift from aerial application. Refined risk quotients based on runoff inputs did not exceed the level of concern for any freshwater invertebrate species, indicating that these organisms are not expected to be at risk from picoxystrobin runoff into water bodies. Screening level risk quotients for picoxystrobin transformation products did not exceed the level of concern for acute exposure to *Daphnia magna*. To address potential risks from exposure to freshwater invertebrates, mitigation measures were implemented on the current labels (see the section on risk mitigation measures below).

Marine/Estuarine species

Picoxystrobin was found to be acutely toxic to the Eastern oyster (*Crassostrea virginica*) and mysid shrimp (*Americamysis bahia*). Exposure to picoxystrobin for 29 days resulted in reduced reproduction of mysid shrimp. The screening level risk quotients based on acute, chronic and/or early life stage exposures of marine/estuarine invertebrates exceeded the level of concern. Refined risk quotients based on spray drift of picoxystrobin exceeded the level of concern for mysid shrimp (aerial and field sprayer application to sweet corn, aerial application to dry legumes) and Eastern oyster (aerial and field sprayer application to sweet corn and dry legumes). Thus, there is the potential for adverse effects to marine/estuarine invertebrates exposed to picoxystrobin through spray drift from aerial and field sprayer application.

Refined risk quotients based on runoff inputs did not exceed the level of concern indicating that a risk to marine/estuarine invertebrates is not expected from picoxystrobin runoff. To address potential risks from exposure to marine invertebrates, mitigation measures were implemented.

Risk mitigation measures

The following environmental hazard statements are on the registered products labels with foliar application (Reg. No. 30470 and 33522):

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

Furthermore, to mitigate potential risk via spray drift, spray buffer zones are required to protect sensitive aquatic habitats. These spray buffer zones are currently specified on picoxystrobin product labels.

Exposure of aquatic organisms through spray drift from seed treatment uses is not expected (Canada, 2015). The application rates from seed treatment uses are less than 0.5% of the application rates from foliar uses. The risk to aquatic organisms from run-off of picoxystrobin as a result of seed treatment uses is expected to be negligible given the risk is acceptable for the fol

The following environmental hazard statement is currently included on picoxystrobin product label with seed treatment application (Reg. No. 31805):

- Toxic to aquatic organisms.

4.2.2 Potential for risk to earthworms exposed to Picoxystrobin

Once picoxystrobin enters the terrestrial environment, it is expected to biotransform and adsorb to soil. Picoxystrobin and its transformation products are not expected to carry over in important amounts into the next growing season. Picoxystrobin does not appreciably bioconcentrate in fish. Previously, Health Canada concluded that picoxystrobin was acutely toxic to earthworms (Canada, 2012). The transformation products Compounds 2, 3 and 8 were much less toxic than the parent to earthworms. Earthworm reproduction was adversely affected by chronic exposure to picoxystrobin. The risk to earthworms resulting from acute and chronic exposure to picoxystrobin did not exceed the level of concern based on results of laboratory studies (Canada, 2012). The risk to earthworms from acute exposure to transformation products Compounds 2, 3 and 8 did not exceed the level of concern. Risk was assessed based on EECs for the highest use rate scenario on sweet corn.

Field studies indicate that application of picoxystrobin at rates representative of Canadian uses could result in earthworm mortalities of approximately 50% within a few days of application if irrigation or precipitation occurs following application. At all but one field site, earthworm populations recovered from the initial effects of picoxystrobin within one year of application.

A label statement to inform the users of the toxicity of picoxystrobin to earthworms is currently included on all picoxystrobin product labels with foliar application.

- Toxic to earthworms.

The seed treatment rate of 4.2 g a.i./ha is much lower than the seasonal maximum foliar application rate of (875 g a.i./ha). The seed treatment uses of picoxystrobin are expected to pose a negligible risk to earthworms and a hazard statement is not required on the registered picoxystrobin product label (Canada, 2015).

4.2.3 Potential for risk to earthworm-eating mammals exposed to metabolite IN-QDY63

IN-QDY63 has been identified as a minor transformation product in laboratory soil studies. In Canadian field studies, it has been identified at 5-13% of applied radioactivity. Based on dissipation in field studies, with half-lives of 12.5-133 days, IN-QDY63 is considered non-persistent to moderately persistent in soil. The following physical-chemical properties have been estimated in laboratory studies with IN-QDY63 (Canada, 2012):

- Water solubility: 6.8 mg/L at 20°C (low solubility)
- Henry's Law Constant: $<4 \times 10^4$ Pa·m^3/mol (slightly or non-volatile)
- Log K_{ow}: 4.2 at 20°C (potential to bioaccumulate)

EFSA (2016) also reported a K_{Foc} value range of 23-704 mL/g that showed pH dependence, indicating the potential for high mobility.

Based on mammalian toxicity data (Section 4.1.2), IN-QYD63 is more toxic to mammals than picoxystrobin. The lowest rat LD50 for IN-QYD63 is 387 mg/kg bw compared to >5000 mg/kg bw for picoxystrobin. No mammalian reproductive data was available for IN-QYD63; however, the results of the 90-day rat dietary studies showed a 3x difference in sublethal toxicity (lowest NOEL of 14 mg/kg bw/day for IN-QYD63, compared to 42 mg/kg bw/day for picoxystrobin).

Given the relatively low production of IN-QYD63 in soil and its reported physical-chemical properties, it is unlikely that concentrations of this transformation product would reach or exceed a level of concern for earthworm-eating mammals at the current highest seasonal application rate of picoxystrobin (1 kg a.i./ha).

The risk to mammals from ingestion of earthworms containing IN-QYD63 from currently registered uses of picoxystrobin is considered acceptable.

4.2.4 Assessment of aspect of concern related to the environment: conclusions

Potential risk to aquatic organisms and earthworms from exposure to picoxystrobin is considered acceptable under the current conditions of use. Environmental statements informing users of the potential toxicity to aquatic invertebrates and earthworms, as well as relevant mitigative measures such as spray buffer zones, are currently specified on picoxystrobin product labels.

The potential risk to earthworm-eating mammals exposed to IN-QDY63 is considered acceptable.

Overall, Health Canada concludes that the environmental risks relating to the aspects of concern are acceptable under the current conditions of use. Additional risk mitigation measures are not required.

5.0 Incident reports

As of 16 August 2022, no incident reports related to the aspects of concern for picoxystrobin have been submitted to Health Canada.

6.0 Proposed special review decision for Picoxystrobin

The evaluation of available relevant scientific information related to the aspects of concern for human health and the environment indicates that potential risks (human health and environment) from the use of picoxystrobin pest control products are considered acceptable under the current conditions of use. No additional risk mitigation measures are proposed. On this basis, Health Canada, under the authority of the *Pest Control Products Act*, is proposing to confirm the current registration of picoxystrobin products for sale and use in Canada pursuant to subsection 21(1) of the *Pest Control Product Act*.

This proposed special review decision is a consultation document.[3] Health Canada 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 (please see contact information on the cover page of this document).

7.0 Next steps

Before making a special review decision on picoxystrobin, Health Canada will consider all comments received from the public in response to this consultation document. A science-based approach will be applied in making a final decision on picoxystrobin. Health Canada will then publish a special review decision document, which will include the decision, the reasons for it, a summary of the comments received on the proposed decision, and Health Canada's response to these comments.

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

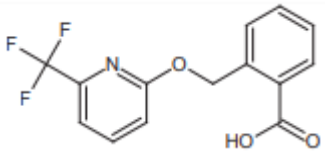
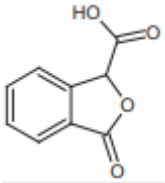
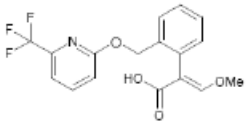
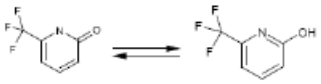
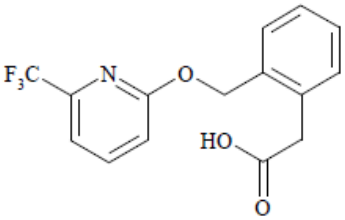
Appendix I Registered products containing Picoxystrobin as of 1 September 2022

Table 1 Registered products containing picoxystrobin as of 1 September 2022

Registration Number	Marketing Class	Registrant	Product Name
30469	Technical	Corteva Agriscience Canada Company	Picoxystrobin Technical Fungicide
31569	Technical		Dupont Acapela MUP
30470	Commercial		Dupont Acapela Fungicide
31805	Commercial		DPX-YT669 250FS Fungicide Seed Treatment
33522	Commercial		Cerefit A Fungicide
34528	Commercial		Lumitreo

Appendix II Identification of relevant Picoxystrobin Metabolites

Table 1 Identification of relevant picoxystrobin metabolites

EU Code[4]	PMRA Code[5] or US EPA Code[6]	Chemical Name[7]	Structural formula[8], [9]
IN-QDY63	Compound 8/ R408509	2-({[6-(trifluoromethyl)pyridin-2-yl]oxy}methyl)benzoic acid	
IN-H8612	Metabolite 11/ Compound 24	3-oxo-1,3-dihydro-2-benzofuran-1-carboxylic acid	
IN-QDY62	Compound 2/ R403092	(*E*)-3-methoxy-2-{2-[6-(trifluoromethyl)pyridin-2-yloxymethyl]phenyl}acrylic acid	
IN-QDK50	Compound 3/ R403814	6-(trifluoromethyl)pyridin-1*H*-2-one (6-(trifluoromethyl) pyrindin-2-ol (preferred name))	
Compound 7	R408631	2-[2-[6-trifluoromethyl) pyridin-2-yloxymethyl] phenyl] acetic acid	

4 Peer review of the pesticide risk assessment of the active substance picoxystrobin, EFSA 2016

5 Picoxystrobin – Food Residues Input to Agency Documentation, PRD2012-10

6 US EPA 2012. Page 38-39

7 Peer review of the pesticide risk assessment of the active substance picoxystrobin, EFSA 2016

8 Peer review of the pesticide risk assessment of the active substance picoxystrobin, EFSA 2016

9 US EPA 2012. Page 38-39.

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