Registration Decision RD2016-07

Difenoconazole

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Registration Decision Statement[1] for Difenoconazole

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Difenoconazole Technical Fungicide and Inspire Fungicide, containing the technical grade active ingredient difenoconazole, to control or suppress fungal diseases on a variety of fruit and vegetable crops.

This decision is consistent with the Proposed Registration Decision PRD2015-29, *Difenoconazole,* which contains a detailed evaluation of the information submitted in support of this registration. The evaluation found that, under the approved conditions of use, the products have value and do not present an unacceptable risk to human health or the environment. See Appendix I for a summary of comments received during the consultation process as well as the PMRA's response to these comments.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2015-29, *Difenoconazole)* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[2] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticide and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service

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

[2] As per subsection 35(1) of the *Pest Control Products Act.*

Appendix I Comments and Responses

In response to the consultation document PRD2015-29, *Difenoconazole*, a number of comments were received from non-government organizations. A summary of the comments received, along with the Agency responses are provided below.

1. Disappointment was expressed that the PMRA is proposing to register the technical active difenoconazole and Inspire Fungicide, a pest control product that contains it, without a special review.

PMRA Response

The PMRA is aware of the 1998 Norway decision on difenoconazole, and has previously considered it to determine if a special review is required under subsection 17(1) and subsection 17 (2) of the *Pest Control Products Act.*

In evaluating the need for special review, the PMRA took into consideration the available information from Norway pertaining to the concerns identified in the 1998 decision (i.e. persistence in the environment, bioaccumulation and toxicity to aquatic organisms), as well as the PMRA information on environmental fate from laboratory/field studies, and aquatic toxicity studies.

Based on the analysis, the PMRA concluded that there are no reasonable grounds to believe that the health or environmental risks of products containing difenoconazole currently registered in Canada are, or their value is, unacceptable under current conditions of use. On this basis, a special review was not required under subsection 17(1) of the *Pest Control Products Act*.

Further, as seed treated with difenoconazole (for sowing) was granted import authorization in Norway, the PMRA determined that the criteria under subsection 17(2) of the *Pest Control Products Act* were not met and, as such, no special review was required under subsection 17(2). Additional details are included in Re-evaluation Note REV2015-02, *Special Review Update for Difenoconazole*. PMRA acknowledges that the decision in relation to subsection 17(2) is currently before the Federal Court and is waiting for the decision to be rendered.

2. A comment was made, as follows, on the persistence of difenoconazole in soils:

With respect to persistence, Norway's PIC Form cites a half-life in excess of one year 'in many cases' as one of the reasons for Norway's decision to ban difenoconazole. Specifically, Norway reports a half-life in soil of difenoconazole from 142 days to 4.4 years (or about 1600 days), and in water of 324 to 860 days.

The upper half-life ranges of difenoconazole, as reported by the PMRA in the Science Management Committee Briefing of December 19, 2014, also exceed a year. The half-life range report by the PMRA due to aerobic biotransformation is from 103 to 1600 days, based on a field study the half-life range is from 28 to 892 days, and in aerobic aquatic systems, the half-life

range is from 307 days to 494 days. In its PRD2015-29 document, PMRA also recognizes that difenoconazole has the potential to persist in soil.

However, in contrast to Norway's conclusion, the PMRA in its PRD2015-29 document considers that difenoconazole "... has the potential to carryover from one growing season to the next with repeated yearly applications.", which is a significantly shorter range of time, and offered no further explanation as to what evidence would support this surprising and new consideration on the length of persistence difenoconazole in soils.

Despite that the PMRA identification of difenoconazole's half-life ranges is similar to Norway's reporting on half-life ranges, it is proposing to register the technical active of difenoconazole and Inspire Fungicide, without a special review.

PMRA Response

The advisory statement, "has the potential to carryover from one growing season to the next with repeated yearly applications," does not indicate or refer to a shorter dissipation time (DT_{50}) for difenoconazole under field conditions. It is intended solely as an environmental hazard statement to mitigate the accumulation of difenoconazole in soil from successive yearly applications. It should be noted that percent carryover to the next season is based on the soil concentration of difenoconazole measured over the course of at least one growing season and does not imply that 50% of the residues persist into the next growing season. This statement is placed on product labels if 30% or more of the pesticide is observed at the end of the first use season.

Environmental persistence does not mean that a pesticide poses risk to the environment. Persistence is a concern if there is a potential for risk (i.e. exposure levels exceed a level of concern). The risk assessment conducted by the PMRA, which considers persistence, exposure and toxicity indicates that potential risks are below the level of concern. In addition, mitigation measures are specified on the label in order to further reduce exposure and, thus, the risk. The Norwegian review did not consider exposure.

3. A comment was made, as follows, on the bioaccumulation of difenoconazole:

With respect to bioaccumulation, unlike Norway, the PMRA reports that difenoconazole is not expected to accumulate significantly in the tissues of organisms under field conditions, according to the Science Management Committee Briefing and to PRD2015-29. Norway's PIC Form reports a Bioaccumulation Factor ("BCF") range from 330 to 420 in whole fish. The PMRA's Science Management Committee Briefing reports a BCF of 330X in whole fish.

PMRA Response

Bioaccumulation is a general term describing a process by which substances are accumulated by organisms directly from the surrounding media and through consumption of food containing the substances.

The purpose of conducting a bioaccumulation assessment is to determine if bioaccumulation occurs and whether it occurs to a degree that is a concern to the environment and/or human health. The potential for a substance to bioaccumulate can be expressed in terms of the bioconcentration factor (BCF), the bioaccumulation factor (BAF) or, for lipophilic substances, the octanol-water partition coefficient (K_{ow}).

The Government of Canada defines the critical bioaccumulation criterion in the *Persistence & Bioaccumulation Regulations* and in the *Toxic Substances Management Policy* (TSMP). It is identical to the bioaccumulation criteria from the Stockholm Convention.

Bioaccumulation Endpoint	Criteria
BAF[1]	>5 000
BCF[1]	>5 000
LogK_{ow}	≥5

[1] whole body, wet weight

Internationally, other jurisdictions such as the European Chemical Agency (ECHA under the European Union's regulation *Registration, Evaluation, Authorisation and Restriction of Chemicals* (REACH)) and the United States (under the *Toxic Substances Control Act*) have also established bioaccumulation criteria.

Bioaccumulation Endpoint	REACH criteria	US TSCA criteria
BCF – bioaccumulative	>2 000	>1 000
BCF – very bioaccumulative	>5 000	>5 000

In the bioconcentration study, the bioconcentration factors (BCF) for difenoconazole in bluegill edible and nonedible tissue were 170X and 570X, respectively. The whole body BCF was 330X. By day-14 of the depuration phase, the bluegill had eliminated 96%, 98% and 97% of the difenoconazole residues in edible, nonedible and whole body tissue, respectively, that were present on the last day of exposure (day 28 of exposure). Based on the low BCFs and the observed depuration, difenoconazole is not expected to bioaccumulate significantly in organisms under field conditions.

Difenoconazole does not meet the TSMP Track 1 criterion for bioaccumulation, as its octanol-water partition coefficient (log K_{ow} = 4.4) is below the criterion (log K_{ow} = 5.0) and the highest BCF in fish of 330X (wet weight, whole fish) does not meet or exceed the BCF criterion (BCF = 5000).

Difenoconazole does not meet other internationally-adopted critical bioaccumulation criteria (for example, REACH, TSCA). The low BCF values reported in the studies indicate that organisms in the field may accumulate low levels of difenoconazole residues, but these are well below levels that may cause effects or require regulatory action.

4. A comment was made, as follows, on the toxicity of difenoconazole to aquatic organisms:

With respect to toxicity in aquatic organisms, similar to Norway, the PMRA has identified its toxicity to certain aquatic organisms as a concern. Yet despite this, the PMRA continues to register difenoconazole as an active ingredient in many pest control products.

In PRD2015-29, the PMRA acknowledges evidence of potential risk for aquatic organisms "through exposure from off-target spray drift and runoff entering aquatic systems resulting from the application of difenoconazole". However, in contrast to Norway's conclusion, the PMRA considers that risks to aquatic organisms are not a concern because the following precautionary statement is required on the label of products containing difenoconazole:

"The following label statements are required to mitigate exposure to non-target aquatic and terrestrial habitats:

- Label statements to mitigate the risk of spray drift to aquatic organisms
- Label statements to mitigate contamination of irrigation or drinking water supplies and aquatic habitats
- Buffer zones to mitigate the risk of spray drift to aquatic organisms
- Label statements to mitigate the risk of surface runoff from treated fields
- Label statement to mitigate accumulation in soil from repeated seasonal applications
- Label statement to mitigate the risk to beneficial arthropods

We find it difficult to understand – and PRD2015-29 does not explain – how a label statement to mitigate exposure to non-target aquatic habitats is considered adequate protection for aquatic organisms, when Norway concluded that risks to aquatic organisms were unacceptable, and banned difenoconazole.

PMRA Response

The PMRA risk assessment for difenoconazole indicated a negligible risk to low risk to non-target organisms based on conservative exposure scenarios. The actual label statements on the difenoconazole product label to mitigate these risks to non-target aquatic and terrestrial habitats are as follows:

- Toxic to certain beneficial insects. Minimize spray drift to reduce harmful effects on beneficial insects in habitats next to the application site such as hedgerows and woodland.

- Difenoconazole is persistent and may carryover. It is recommended that any products containing difenoconazole not be used in areas treated with this product during the previous season.

- 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.
- As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests.
- DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

Also, the statements for the mandatory requirement of spray buffer zones to reduce the risk to acceptable levels are as follows:

- Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.
- The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands), sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of application	**Crop**		**Buffer Zones (metres) Required for the Protection of:**			
			Freshwater Habitat of Depths:		**Estuarine/Marine Habitats of Depths:**	
			Less than 1 m	**Greater than 1 m**	**Less than 1 m**	**Greater than 1 m**
Field sprayer[1]	Brassica vegetables, bulb vegetables, curcubits, fruiting vegetables, potatoes, Chinese artichoke, Jerusalem artichoke, edible canna, sweet potato and sugar beets		3	1	1	1
Airblast	Pome fruit, grapes	Early growth stage	25	4	15	5
		Late growth stage	15	2	5	3

[1] For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy, the labelled buffer zone can be reduced by 30%.

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

Label statements and mandatory precautionary measures are used globally for pest control products to reduce environmental exposure to acceptable levels. For example, the European Food Safety Authority (EFSA) report, *Conclusion on the peer review of the pesticide risk assessment of the active substance difenoconazole* [EFSA Journal 2011; 9(1):1967], indicates that:

> "Risk mitigation measures corresponding to 14 m non-spray buffer zones and 5 m non-spray buffer zones were required to address the risk to aquatic organisms for the representative uses on pome fruit and carrots, respectively."

The mandatory precautions required by the PMRA are similar to those of EFSA, requiring maximum no-spray buffer zones of 25 m for pome fruit and grapes and 3 m for field vegetables, sweet potatoes and sugar beets, to reduce the aquatic risk to acceptable levels.

The EFSA report also indicated there were no "Critical Areas of Concern" identified with the all representative uses of difenoconazole.

Furthermore, consistent with the Canadian position, as of 15 December, 2014, difenoconazole is registered /approved in other OECD countries including the United States, European Union countries, Australia and New Zealand.

5. A comment was made, as follows, on the need to assess all difenoconazole containing products:

The PMRA is being urged by the commenters to further assess not only the above-referenced environmental concerns related to persistence, bioaccumulation and toxicity in aquatic organisms, but all environmental and health risks of all registered pest control products containing difenoconazole. That assessment, with the benefit of public input, would be of utmost importance.

As you know, we believe that a special review not just of difenoconazole, but of all registered pest control products containing it, is legally required. Currently, at least 26 pest control products containing difenoconazole are registered for use in Canada. However, here the PMRA has conducted only very limited evaluation of just the active ingredient and one end-use product, and not evaluated any of the other end-use products containing difenoconazole that are used in Canada.

Many of those other pest control products are seed treatment products that contain neonicotinoid ingredients, in addition to difenoconazole. These end-use products raise concerns about their harmful effects on bees and other pollinator species. None of the PMRA's past evaluations and registrations of difenoconazole, namely its Proposed Regulatory Decision Document PRDD99-01, *Difenoconazole* and the Regulatory Decision Document RDD2001-04, *Difenoconazole Fungicide*, evaluate the impacts of end-use seed treatment products on pollinator species. Since

then, registration in Canada of new seed treatment products containing difenoconazole and neonicotinoids has expanded rapidly, without evaluation of these effects.

PMRA Response

The end-use products that contain difenoconazole with other active ingredients would not be captured in PRDD99-01 or RDD2001-04 as these documents pertain only to end-use products with difenoconazole alone. The environmental evaluations of the other active ingredients are available in the public documents for those actives (for example, PRVD2016-03, *Fludioxonil*). Products containing difenoconazole with other active ingredients were evaluated for environmental risk as are all other products containing more than one active ingredient.

It should be noted that difenconazole has low toxicity to bees, and the risk posed by difenoconazole to pollinators (bees) is negligible and is not a concern. Difenoconazole has a negligible contribution to the pollinator toxicity of end-use products that contain the neonicotinoid insecticides.

The PMRA has concluded that there are no reasonable grounds to believe that the environmental risks of products containing difenoconazole currently registered in Canada are unacceptable under current conditions of use. On this basis, the PMRA has determined that a special review is not required under subsection 17(1) of the *Pest Control Products Act*.

6. A comment was made, as follows, on human health and environmental risks of fungicide resistance:

A report by the Institute for Agriculture and Trade Policy from December 2014 entitled *Fungicide Resistance: Risk and Consequences in Modern Agriculture*, explains the risks of fungicide resistance: "Widespread and indiscriminate fungicide applications in modern agriculture have led to an increasing risk of fungicide resistance: reducing our ability to protect ourselves and our crops from the substantial, and sometimes catastrophic, effects of pathogenic fungi. This environmental and health risk should have been evaluated in PRD2015-29, and clearly must be evaluated in a special review of all registered pest control products containing difenoconazole."

PMRA Response

PMRA's mandate is to ensure that risks to human health and the environment are acceptable, and that there is value to registering a pesticide. Part of the value assessment is verifying that the directions for use of the product are consistent with the most current resistance management guidelines and recommendations available in North America, and globally. These use guidelines are set by the Fungicide Resistance Action Committee (FRAC, http://www.frac.info/), and are, in some cases, specific to a fungicide class, crop and disease.

To ensure the long term sustainability of difenoconazole, the PMRA ensures that product labels include resistance management statements which are reflective of FRAC recommendations. These label statements help prevent the onset of resistance, and include restrictions on the maximum number of seasonal or sequential applications allowed. In addition, on the label of

each difenoconazole product in Canada, the PMRA provides specific recommendations on resistance management, which are in accordance with Regulatory Directive DIR2013-04, *Pesticide Resistance Management Labelling Based on Target Site / Mode of Action*.

The precautionary measures implemented by PMRA to prevent the potential for fungal plant pathogens from developing resistance to difenoconazole will also aid in the prevention of the onset of resistance to triazole drugs in fungi that are potentially pathogenic to humans or other animals. Specifically, by prescribing the maximum number of seasonal or sequential applications of difenoconazole, pathogenic fungi present in the environment and within spray zones will not be exposed to the fungicide for sufficient duration to develop resistance to this pesticide or to related triazole compounds.

7. A comment was made on the requirement for a public consultation as set out in the Pest Control Products Act for conditionally registered products and that the conditional registration decision did not allow for any public participation.

PMRA Response

Conditional registrations have been granted on occasion when the scientific review determines that the risks of a pesticide are acceptable, but additional information is required to confirm the results of the risk assessment. Registrants are required to compile the additional information within a timeframe specified by PMRA. Under section 14 of the *Pest Control Product Regulations*, the consultation requirements in subsection 28(1) of the *Pest Control Products Act* do not apply when a conditional registration is first granted. That is why there was no consultation at the time the conditional registration was granted.

The additional information requested for difenoconazole has now been submitted to and reviewed by the PMRA. After completing this review, PMRA published the proposed decision to grant full registration for the foliar use of difenoconazole for public consultation under subsection 28(1) of the PCPA. The decision to grant full registration is supported based on the review of the additional information in conjunction with the information previously reviewed and summarized under Evaluation Report ERC2011-06, *Difenoconazole*, which included a full evaluation of the health and environmental effects of Inspire Fungicide as an end-use product.