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Registration Decision

RD2014-28

Halauxifen-Methyl

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Registration Decision for Halauxifen-Methyl

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 XDE-729 Methyl Technical Herbicide and its end-use products, GF-2685 Herbicide, Paradigm Herbicide and Pixxaro A Herbicide, containing the technical grade active ingredient halauxifen, present as methyl ester, for control of annual broadleaf weeds in cereal crops (spring wheat, winter wheat, durum wheat and spring barley). Halauxifen, present as methyl ester, is referred to as halauxifen-methyl in this Registration Decision document.

GF-2685 Herbicide is formulated with halauxifen-methyl and the safener, cloquintocet-mexyl. Paradigm Herbicide contains halauxifen-methyl and florasulam. Pixxaro A Herbicide is formulated with halauxifen-methyl, fluroxypyr and the safener cloquintocet-mexyl.

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.

These products were first proposed for registration in the consultation document¹ Proposed Registration Decision PRD2014-12, *Halauxifen-methyl*. This Registration Decision² describes this stage of the PMRA's regulatory process for halauxifen-methyl and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2014-12. This decision is consistent with the proposed registration decision stated in PRD2014-12.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2014-12, *Halauxifen-methyl* that contains a detailed evaluation of the information submitted in support of this registration.

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 acceptable³ 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 conditions of registration. The Act also requires that products have value⁴ when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

¹ "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

² "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

³ "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

⁴ "Value" as defined by subsection 2(1) of *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 (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is Halauxifen-Methyl?

Halauxifen-methyl is the first member of a new chemical class of synthetic auxin herbicides, the arylpicolinates. It belongs to the Weed Science Society of America (WSSA) Group 4 herbicides and to the Herbicide Resistance Action Committee (HRAC) Group O. Halauxifen-methyl mimics the effect of a persistent high dose of the natural plant hormone auxin, causing over-stimulation of specific auxin-regulated genes which result in the disruption of several growth processes in susceptible plants. Tissues that are undergoing active cell division and growth are particularly susceptible to injury.

Health Considerations

Can Approved Uses of Halauxifen-Methyl Affect Human Health?

Products containing halauxifen-methyl are unlikely to affect your health when used according to label directions.

Potential exposure to halauxifen-methyl may occur through the diet (food and water) or when handling and applying end-use 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 dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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

The majority of the toxicology data was conducted with the acid form of halauxifen-methyl, herein referred to as halauxifen acid. Acceptable bridging data were provided and halauxifen acid was considered to be the relevant compound for risk assessment purposes.

In laboratory animals, the technical grade active ingredient halauxifen-methyl was of low acute toxicity by the oral and dermal routes of exposure. It was non-irritating to the eyes and skin, and did not cause allergic skin reactions. Consequently, hazard signal words are not required on the label.

The associated end-use products, GF-2685 Herbicide, Paradigm Herbicide and Pixxaro A Herbicide, were of low acute toxicity via the oral, dermal and inhalation routes of exposure. Paradigm Herbicide was minimally irritating to eyes and skin. Pixxaro A Herbicide was moderately irritating to the eye and mildly irritating to the skin. Therefore, the hazard signal words “WARNING EYE AND SKIN IRRITANT” are required on the label. GF-2685 Herbicide was minimally irritating to the eye, but mildly irritating to the skin; consequently, the hazard signal words “CAUTION SKIN IRRITANT” must appear on the label. All of the end-use products caused allergic skin reactions and therefore, the hazard signal words “POTENTIAL SKIN SENSITIZER” are required on all the labels.

Health effects in animals given repeated doses of halauxifen-methyl included effects on the liver and thyroid. In animals given repeated doses of halauxifen acid, treatment-related effects were observed in the kidneys and urinary bladder.

Halauxifen acid did not cause cancer in animals and there was no evidence that halauxifen-methyl or halauxifen acid damages genetic material. There was no indication that halauxifen acid caused damage to the nervous system and halauxifen-methyl did not affect the immune system. There were no treatment-related effects on the ability to reproduce after treatment with halauxifen acid.

When halauxifen-methyl or halauxifen acid was given to pregnant animals, resorptions were observed in rats at doses that were toxic to the mother, indicating that the young do not appear to be more sensitive than the adult animal; however, some fetal loss occurred in rabbits at a dose considered to be only marginally toxic to the mother.

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

Residues in Water and Food

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

Aggregate dietary intake estimates (food plus drinking water) revealed that the general population and all subpopulations are expected to be exposed to <1% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from halauxifen-methyl is not of health concern for all population subgroups.

Halauxifen-methyl is not carcinogenic; therefore, a cancer dietary risk assessment is not required.

An acute dietary exposure assessment was not conducted since an acute reference dose (ARfD) was not established.

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 the United States and Canada using halauxifen-methyl on wheat (spring and winter varieties) and barley are acceptable. The MRLs for this active ingredient can be found in the Science Evaluation of the consultation document PRD2014-12.

The end-use products are also formulated with fluroxypyr, or florasulam, and/or with the safener cloquintocet-mexyl. Fluroxypyr, florasulam and cloquintocet-mexyl are already registered for foliar treatment use in Canada on wheat and barley.

Occupational Risks from Handling GF-2685 Herbicide, Paradigm Herbicide and Pixxaro A Herbicide

Occupational risks are not of concern when GF-2685 Herbicide, Paradigm Herbicide or Pixxaro A Herbicide is used according to the label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply GF-2685 Herbicide, Paradigm Herbicide or Pixxaro A Herbicide, as well as field workers re-entering freshly treated fields, can come into direct contact with halauxifen-methyl residues on the skin or through inhalation of spray mists. Therefore, the label specifies that anyone mixing/loading and applying Pixxaro A Herbicide, Paradigm Herbicide, or GF-2685 Herbicide must wear a long-sleeved shirt, long pants, shoes, socks and chemical-resistant gloves (gloves are not required during application). Mixer/loaders of Pixxaro A Herbicide must also wear eye protection. The label also requires that workers do not enter treated fields for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk to these individuals are not expected to be of concern.

Paradigm Herbicide is a co-formulation with florasulam, and Pixxaro A Herbicide is a co-formulation with fluroxypyr. In addition, the safener cloquintocet-mexyl is co-formulated in GF-2685 and Pixxaro A Herbicide. Florasulam, fluroxypyr and cloquintocet-mexyl are registered for use on wheat and barley. The precautions required to mitigate risk from the exposure of halauxifen-methyl are also adequate for the co-formulated active ingredients and safener. Florasulam, fluroxypyr and cloquintocet-mexyl will not be further discussed herein.

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 Halauxifen-Methyl Is Introduced Into the Environment?

Halauxifen-methyl can pose a risk to non-target terrestrial plants and aquatic vascular plants; therefore, statements on the product labels are required to inform users of the potential risks, and spray buffer zones are required during application.

Halauxifen-methyl enters the environment when applied to control broadleaf weeds on certain cereal crops. Halauxifen-methyl can break down by reacting with water or in the presence of soil microbes and is unlikely to persist in terrestrial systems. The properties of halauxifen-methyl and its transformation products, XDE-729 acid (X11393729) and X11449757, indicate some potential for movement through the soil. In field studies, the majority of halauxifen-methyl and its transformation products were measured in the top 30 cm of soil. Conservative modelling data indicates that levels of halauxifen-methyl and its transformation products that may reach groundwater are very low. In aquatic environments, halauxifen-methyl is rapidly broken down in the presence of sunlight, in the presence of microbes or by reacting with water. It is not expected to move into the sediment to a great extent or accumulate in aquatic organisms. Halauxifen-methyl is not expected to enter the atmosphere.

When used according to label directions, halauxifen-methyl is expected to pose a negligible risk to earthworms, bees, birds, small mammals, aquatic invertebrates, amphibians, algae and fish. Halauxifen-methyl may pose a risk to non-target terrestrial and aquatic plants. Risks to non-target terrestrial and aquatic plants can be mitigated with label statements and spray buffer zones to protect sensitive terrestrial and aquatic habitats. Label statements are required on the product labels to inform the users of the potential risks.

The use of the end-use product Paradigm Herbicide contains the active ingredients halauxifen-methyl and florasulam. Florasulam and its major soil transformation product, 5-hydroxy-XDE-570, have the potential to leach. Also, 5-hydroxy-XDE-570 has the potential to carry over into the next growing season. Label statements are required on the label for Paradigm Herbicide to inform users of the potential risks of leaching and carry-over.

The use of the end-use product Pixxaro A Herbicide contains aromatic petroleum distillates which are toxic to aquatic organisms. Label statements are required on the label for Pixxaro A Herbicide to inform users of the potential risks.

Value Considerations

What Is the Value of GF-2685 Herbicide, Paradigm Herbicide or Pixxaro A Herbicide?

Halauxifen-methyl is a postemergence herbicide that can be used at different rates of application to target specific weeds.

GF-2685 Herbicide, Paradigm Herbicide and Pixxaro A Herbicide provide control of important broadleaf weeds and may enable growers to control both broadleaf and grass weeds with a single pass in spring wheat, winter wheat, durum wheat, and barley when tank-mixed with various herbicides listed on the end-use product labels. Halauxifen-methyl has little residual activity following a postemergence application which allows for flexibility in crop rotation with numerous crops that can be seeded after an interval of 10 months following an application of any of the three end-use products.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions are required by law to be followed.

The key risk-reduction measures on the labels of GF-2685 Herbicide, Paradigm Herbicide or Pixxaro A Herbicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with halauxifen-methyl on the skin or through inhalation of spray mists, anyone mixing, loading and applying Pixxaro A Herbicide, Paradigm Herbicide or GF-2685 Herbicide must wear long-sleeved shirt, long pants, shoes, socks and chemical-resistant gloves (gloves are not required during application). Mixer/loaders of Pixxaro A Herbicide must also wear eye protection. In addition, standard label statements to protect against drift during application were added to the label.

Environment

Halauxifen-methyl can pose a risk to non-target terrestrial and aquatic plants. The use of the end-use products Paradigm Herbicide, containing the active ingredients halauxifen-methyl and florasulam, and Pixxaro A Herbicide, containing halauxifen-methyl and fluroxypyr present as methylheptyl ester, can also pose a risk to non-target terrestrial and aquatic plants. Label statements and spray buffer zones to protect sensitive terrestrial and aquatic habitats are to be specified on the labels.

To mitigate potential exposures to halauxifen-methyl via spray drift, spray buffer zones of 1 to 100 metres are required to protect sensitive terrestrial habitats, and spray buffer zones of 1 to 10 metres are required to protect sensitive aquatic habitats, depending on the end-use product and the method of application. These spray buffer zones are to be specified on the product labels.

Label statements are required on the label for Paradigm Herbicide to inform users of the potential risks of leaching of florasulam and its major soil transformation product, 5-hydroxy-XDE-570, and the potential for carry-over of 5-hydroxy-XDE-570.

Label statements are required on the label for Pixxaro A Herbicide to inform users of the potential risks to aquatic organisms from the aromatic petroleum distillates contained in the end-use product.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2014-12, *Halauxifen-methyl*) 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 objection⁵ 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 Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service.

⁵ As per subsection 35(1) of the *Pest Control Products Act*.