Registration Decision RD2015-05

Metconazole

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Registration Decision for Metconazole

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 Metconazole Technical Fungicide and Caramba Fungicide containing the technical grade active ingredient metconazole, to control or suppress important diseases of cereal crops, soybeans and sugar beets.

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 document[1] Proposed Registration Decision PRD2014-24, *Metconazole*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for metconazole and summarizes the Agency's decision, and the reasons for it. The PMRA received no comments on PRD2014-24. This decision is consistent with the proposed registration decision stated in PRD2014-24, which was to convert Metconazole Technical Fungicide and Caramba Fungicide from conditional registration to full registration for Use Site Categories 13 and 14 (Terrestrial Food and Feed Crops).

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2014-24, which 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 acceptable[3] 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 value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the

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 the *Pest Control Products Act.*

4 "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".

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.

What Is Metconazole?

Metconazole is a triazole fungicide (Group 3) that inhibits sterol biosynthesis. The end-use product, Caramba Fungicide, is a chemical fungicide that contains 90 g/L metconazole formulated as an emusulfiable concentrate for use on cereals, soybeans and sugar beets to control or to suppress certain foliar fungal diseases.

Health Considerations

Can Approved Uses of Metconazole Affect Human Health?

Products containing Metconazole are unlikely to affect your health when used according to label directions.

Potential exposure to metconazole may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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

The technical grade active ingredient, metconazole, was moderately toxic to rats and highly toxic to mice when given as a single oral dose. It was of low acute dermal toxicity to rats and rabbits and of low inhalation toxicity to rats. It was moderately irritating to the eyes and non-irritating to the skin of rabbits. It was not a potential skin sensitizer to guinea pigs. The signal words, "DANGER – POISON" and "EYE IRRITANT" have been included on the label in light of these findings. The end-use product, Caramba Fungicide, was found to be of low oral, dermal and inhalation toxicity in rats. It was moderately irritating to the eyes and minimally irritating to the skin of rabbits and not a dermal sensitizer in guinea pigs. The label statements "WARNING – EYE IRRITANT" and "Causes eye irritation", "DO NOT get in eyes" are required.

Health effects in animals given repeated daily doses of metconazole over longer periods of time were decreased body weights, effects in blood (regenerative anemia) and microscopic changes to the liver, spleen and adrenal glands. There was no evidence that metconazole damaged genetic material. Skin tumours in male mice were observed following oral administration. There was no evidence of cancer in rats.

When metconazole was orally or dermally administered to pregnant rabbits, cranio-facial malformations were observed in fetuses. Limb-flexure malformations were observed in fetuses when metconazole was administered dermally to pregnant rabbits. These effects were observed at doses that were not toxic to the mother, indicating that the fetus is more sensitive to metconazole than the adult animal. Due to the serious nature of these endpoints, extra protective factors were applied during the risk assessment to further reduce the allowable level of human exposure to metconazole.

The risk assessment protects against the above effects by ensuring that the level of human exposure is well below the lowest dose at which the above 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, females 13-49 years old, and infants less than one year old, the subpopulation that would ingest the most metconazole relative to body weight, are expected to be exposed to less than 56% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from metconazole is not of health concern for all population subgroups. There are no lifetime cancer risks of concern from the use of metconazole.

The acute dietary (food plus drinking water) intake estimate for females 13-49 years old was approximately 82% of the acute reference dose, and is not of health concern.

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

The storage stability study, analytical methodology data and rationale to waive confirmatory trials conducted on wheat, barley, rye and oats in Canada submitted to support the conversion from conditional to full registration are adequate. The MRLs of 0.15 ppm in/on wheat and sugar beet roots, 2.5 ppm in/on barley, 1.0 ppm in/on oats, 0.25 ppm in/on rye and 0.05 ppm in/on dry soybeans specified for metconazole do not need to be revised as a result of this assessment. Refer to Health Canada's MRL database for a list of the MRLs established for this active ingredient.

Occupational Risks From Handling Caramba Fungicide

Occupational risks are not of concern when Caramba Fungicide is used according to the proposed label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Caramba Fungicide as well as field workers re-entering freshly treated fields can come in direct contact with metconazole residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying Caramba Fungicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and footwear during mixing/loading, application, clean up and repair. In addition, wearing goggles or a face shield is required during mixing/loading. Gloves are not required during application. For workers handling more than 300 L of Caramba Fungicide per day, a closed mixing/loading system is required. 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, there are no risks of concern (cancer and non-cancer).

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 Metconazole Is Introduced Into the Environment?

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

Caramba Fungicide, containing metconazole, enters the environment when used as a foliar-treatment fungicide on agricultural crops including cereals, soybeans and sugar beets. While metconazole generally breaks down relatively slowly, it can break down more rapidly in the presence of microorganisms in both aquatic and terrestrial environments. Metconazole dissolves readily in water and has the potential to move through soil and thus could reach groundwater under certain conditions. Specific instructions are provided on product labels to prevent carryover, groundwater contamination and runoff into aquatic habitats. Metconazole is unlikely to enter the atmosphere and be transported to areas far removed from where it was applied.

Metconazole is not expected to accumulate in the tissues of organisms.

Metconazole presents a negligible risk to terrestrial invertebrates including earthworms and honeybees, and freshwater invertebrates. At high enough concentrations it could pose a risk to certain non-target organisms (terrestrial plants, small wild mammals, amphibians, freshwater fish, freshwater plants, marine invertebrates); as such, spray buffer zones are specified on the label to protect terrestrial, freshwater and estuarine/marine habitats adjacent to treated areas. Toxicity statements are also specified on the product label for terrestrial plants, mammals and aquatic organisms.

Value Considerations

What Is the Value of Caramba Fungicide?

Caramba Fungicide controls or suppresses important diseases of cereal crops, soybeans and sugar beets.

Caramba Fungicide offers Canadian growers an additional option for rotation with current products. Caramba Fungicide can be an important tool when used in an Integrated Pest Management (IPM) program in conjunction with other elements such as resistant varieties, cultural controls and predictive models.

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 must be followed by law.

The key risk-reduction measures on the label of Caramba Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with Caramba Fungicide on the skin or through inhalation of spray mists, anyone mixing, loading and applying Caramba Fungicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and footwear during mixing/loading, application, clean up and repair. In addition, wearing goggles or a face shield is required during mixing/loading. Gloves are not required during application. For workers handling more than 300 L of Caramba Fungicide per day, a closed mixing/loading system is required. In addition, standard label statements to protect against drift during application were added to the label.

Environment

Refer to ERC-2011-02, *Metconazole* for the measures to minimize environmental risk from metconazole exposure resulting from the use of Caramba Fungicide. The only amendment to the previously reported measures is the size of spray buffer zones has been updated to 50 m for aerial application and 2 m for ground application to protect sensitive aquatic habitats.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2014-24) are available for public inspection, upon application, in the PMRA Reading Room (located in Ottawa). For more information, please contact the PMRA 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[5] 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 Health Canada's website (Request a Reconsideration of Decision), or contact the PMRA Pest Management Information Service.

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