Registration Decision RD2012-17

Penflufen

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Registration Decision for Penflufen

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 the technical product PENFLUFEN TC and its associated end-use products PEN 240FS, PENRED 240FS, PENPRO 118FS, PENPROME 177FS and PENTRI 308FS, containing the fungicidal active ingredient penflufen, for control of various seed-, seedling- and soil-borne diseases on oilseed and cereal grain crops, legume vegetables, alfalfa and potatoes.

It should be noted that, although full registration is granted for the end-use product PENPROME 177FS, conditional registration is granted for the use of PENPROME 177FS on small grains due to the registration status of this use for the precedent prothioconazole seed-treatment product, JAU 6476 100 FS Seed Treatment Fungicide (Registration Number 30101).

The PMRA, under the authority of the *Pest Control Products Act* and Regulations, is granting conditional registration for the sale and use of the end-use products PENCLO 273.5FS and PENCLOTRIME 310.68FS due to the registration status of the precedent clothianidin seed treatment products, Titan ST Insecticide (Registration Number 27449) and Prosper FX Flowable Insecticide and Fungicide Seed Treatment (Registration Number 29159).

An evaluation of available scientific information found that, under the approved conditions of use, the penflufen products have value and do 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 PRD2012-02, *Penflufen*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for penflufen and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of comments received during the consultation process as well as the PMRA's response to these comments. This decision is consistent with the proposed registration decision stated in PRD2012-02, *Penflufen.*

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2012-02, *Penflufen* that contains a detailed evaluation of the information submitted in support of this registration.

[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.*

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 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 Penflufen?

Penflufen is a systemic, xylem-mobile fungicide. This active ingredient belongs to the Group 7 of the Fungicide Resistance Action Committee. Penflufen is classified as a succinate dehydrogenase inhibitor (SDHI) and interferes with fungal respiration. Seven penflufen-containing products are granted registration.

Health Considerations

Can Approved Uses Of Penflufen Affect Human Health?

Penflufen is unlikely to affect your health when used according to label directions.

Potential exposure to penflufen 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.

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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".

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.

In laboratory animals, the technical grade active ingredient penflufen was of low acute toxicity by the oral, dermal and inhalation routes. Penflufen was minimally irritating to the eye and non-irritating to the skin, and did not cause an allergic skin reaction.

The acute toxicity of the seven end-use products PEN 240FS, PENRED 240FS, PENPRO 118FS, PENCLO 273.5FS, PENCLOTRIME 310.68FS, PENPROME 177FS and PENTRI 308FS containing penflufen was low via the oral, dermal and inhalation routes of exposure. All the end-use products were non- to minimally irritating to the eye and non-irritating to the skin, and did not cause allergic skin reactions.

There was no indication that the technical grade active ingredient penflufen caused damage to the nervous system. There was a low level of concern for effects on the immune system. Health effects in animals given repeated doses of penflufen over a long period of time were decreases in body weight, and changes to the liver, thyroid, blood, adrenals and kidneys.

There was no evidence to suggest that penflufen damaged genetic material. Penflufen did, however, cause brain, ovarian and blood-related tumours in rats. The cancer risk assessment was conducted based on the ovarian tumours found in rats, as this was protective of the other tumour types.

Penflufen did not cause birth defects in animals. A decreased number of pups per dam at birth as observed at a dose that was toxic to the maternal animals. When penflufen was given to pregnant or nursing animals, effects indicating a delay in development in the fetus and juvenile animal (for example, decreased fetal weight, incomplete ossification and delay in sexual maturation) were observed at doses that were toxic to the mother, indicating that the young do not appear to be more sensitive to penflufen than the adult animal.

The risk assessment protects against the effects of penflufen 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 water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and infants less than one year old, the subpopulation which would ingest the most penflufen relative to body weight, are expected to be exposed to less than 6% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from penflufen is not of concern for all population subgroups. The lifetime cancer risk from the use of penflufen on cereal grains, oilseeds, legume vegetables, potato and alfalfa is considered acceptable.

Acute dietary (food and water) estimates for the general population and all population subgroups were less than 6% of the acute reference dose, and are not of health concern. The highest exposed subpopulation was infants less than one year old.

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 penflufen on potatoes, beans, peas, soybeans, wheat, barley, sweet corn, field corn, sunflower, canola and cotton were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation of PRD2012-02, *Penflufen*.

Risks In Residential And Other Non-Occupational Environments

Bystander exposure should be negligible since the potential for drift is expected to be minimal. Application is limited to agricultural crops only when there is low risk of drift to areas of human habitation or activity, such as houses, cottages, schools and recreational areas, taking into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

Occupational Risks From Handling Penflufen Products

Occupational risks are not of concern when penflufen products are used according to the label directions, which include protective measures.

Workers treating seed with penflufen products in commercial seed treatment facilities, workers treating seed on-farm and workers planting treated seed can come into direct contact with penflufen residues on the skin. Therefore, anyone treating seed with seed treatment products containing penflufen or bagging treated seed, handling bags of treated seed or cleaning equipment used to treat seed must wear a long-sleeved shirt, long pants and chemical-resistant gloves. Closed transfer is required for seeds treated at commercial seed treatment facilities. For products co-formulated with other active ingredients, the personal protective measures required

reflect those required for other seed treatment products containing the same active ingredients. Taking into consideration these precautionary measures, the number of applications and the expectation of the exposure period for handlers and workers, the risk to these individuals is not a concern.

Environmental Considerations

What Happens When Penflufen Is Introduced Into The Environment?

Penflufen enters the environment when used as an in-furrow treatment on potato seed pieces and as a seed treatment for various crops. Once in the terrestrial environment, penflufen moderately binds to soil particles and has moderate to low potential for leaching. Penflufen is moderately persistent to persistent in soil. In aquatic systems, penflufen will move from the water column into the sediment where it will persist. Residues of penflufen are not expected to be found in air due to low volatility.

Penflufen is toxic to aquatic organisms; however, based on the use of penflufen as a seed treatment and in-furrow application, the potential for exposure to non-target organisms is expected to be limited. Risks to both non-target terrestrial and aquatic organisms from the use of penflufen were determined to be acceptable.

Value Considerations

What Is The Value Of Penflufen Products?

Penflufen products are formulated as seed treatments for control of seed, seedling and soil-borne diseases on various oilseed and cereal grain crops, legume vegetables, alfalfa and potatoes. Penflufen represents an effective disease management tool and would also be the first fungicide registered for certain diseases on crops such as winter wheat, sunflower, safflower, flax, crambe and borage. A number of the penflufen fungicides contain a combination of actives in order to achieve effective resistance management and/or to increase the spectrum of controlled pests.

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 on the product labels to address the potential risks related to the hazards of penflufen are as follows.

Key Risk-Reduction Measures

Human Health

Anyone treating seed with penflufen or bagging treated seed, handling bags of treated seed or cleaning equipment used to treat seed must wear a long-sleeved shirt, long pants and chemical-resistant gloves.

Closed transfer is required for seeds treated at commercial seed treatment facilities.

Environment

Standard precautionary measures are required to minimize potential exposure of aquatic habitat. Treated seeds must be incorporated into the soil as a standard precautionary measure to minimize potential exposure of birds and mammals that might feed on exposed seed.

Other Information

The relevant test data on which the decision is based (as referenced in this document and PRD2012-02, *Penflufen*) 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[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, healthcanada.gc.ca/pmra) or contact the PMRA's Pest Management Information Service.

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

Appendix I Comments and Responses

1. Comments on the efficacy of PENCLOTRIME 310.68FS and PENTRI 308FS

Comment:

The commenter suggested that the proposed decision to reject the claims for control of seed-borne blackleg and *Alternaria* spp. on canola, rapeseed and mustard (PENCLOTRIME 310.68FS) as well as for suppression of seed-borne anthracnose and *Ascochyta* spp. on legume vegetables (PENTRI 308FS) be reconsidered. Seed-borne bioassays on blotter paper or in petri plates had been submitted in support of these claims.

No data from field performance trials were submitted, but the commenter suggested that the submitted laboratory trials were adequate to characterize the products' efficacy. They stated that soil-borne pathogens will often act together as disease complexes in the field, making it difficult to characterize to what the improved level of plant establishment is attributable. In addition, the commenter indicated that the registered fungicides used in field research as blanket treatments will also control soil-borne pathogens. Conducting seed-borne bioassays would thus allow for the exclusion of confounding factors found under field conditions and focus on the fungicidal activity of the active ingredient on the seed-borne pathogen of interest. Scientific papers showing a correlation between the control of seed-borne inoculum under laboratory conditions, improved stand establishment and field performances were cited in the commenter's rationale. The commenter also argued that the PMRA had previously accepted seed-borne disease claims for other seed treatment products based solely on supporting laboratory data.

Response:

In the submitted laboratory trials, PENCLOTRIME 310.68FS or PENTRI 308FS adequately controlled or suppressed seed-borne blackleg, *Alternaria* spp. and *Ascochyta* spp. under moderate to high disease pressure, while providing statistically comparable levels of protection as the commercial standards. However, PENTRI 308FS did not significantly reduce seed-borne anthracnose in one bioassay plate study on dry bean (38% reduction).

The proposed claims were not supported initially given that efficacy data must demonstrate a consistent, commercially acceptable level of control under expected crop production and pest management practices. In vitro assays, while indicative of the antifungal activity of PENCLOTRIME 310.68FS or PENTRI 308FS against seed-borne pathogens, are not representative of such practices. The PMRA recognizes the experimental challenges associated with seed-borne diseases, but notes that other soil-borne pathogens exhibiting similar restrictions were tested under field conditions in the data package and were adequately controlled by the seed treatments.

Nevertheless, the PMRA understands that only seed-borne phases are claimed by the applicant. The fungicide seed treatments PENCLOTRIME 310.68FS and PENTRI 308FS are intended to decrease the chances of the pathogens surviving on the seed as well as prevent seed to seedling transmission and addition of inoculum in the field. The cited studies also do add to the weight of evidence that seed-borne bioassays are correlated to field performance. Furthermore, the PMRA recognizes that seed-borne disease claims were previously accepted for other seed treatment products based solely on supporting laboratory data; however, comparison of data packages supporting different products must be viewed cautiously, as the context of each data package is unique.

Based on the additional published information and rationale provided by the commenter, the PMRA determined that the claims for the control of seed-borne blackleg and *Alternaria* spp. on canola, rapeseed and mustard (PENCLOTRIME 310.68FS) as well as for suppression of seed-borne *Ascochyta* spp. on legume vegetables (PENTRI 308FS) have value and will not pose unacceptable health or environmental risk. The claim for control of seed-borne anthracnose was not supported due to inadequate levels of control in the submitted value data.

References

PMRA Document Number: 2162901
Reference: Kharbanda PD, 1992, Performance of fungicides to control blackleg of canola, Canadian Journal of Plant Pathology 14: 169-176, DACO: 10.6

PMRA Document Number: 2162902
Reference: Maude RB, Humpherson-Jones FM, Shuring CG, 1984, Treatments to control Phoma and Alternaria infections of brassica seeds, Plant Pathology 33: 525-535, DACO: 10.6

PMRA Document Number:2162903
Reference:Shrestha SK, Mathur SB, Munk L, 2000, Alternaria brassicae in seeds of rapeseed and mustard, its location in seeds, transmission from seeds to seedlings and control, Seed Sci & Technol 28: 75-84, DACO: 10.6