

Evaluation Report for Category B, Subcategory B.4.1 Application

Application Number: 2006-7815
Application: B.4.1 (Conversion to full registration without consultation)
Product: Zoxium 80W Agricultural Fungicide
Registration Number: 26840
Active ingredients (a.i.): Zoxamide (ZOX)
PMRA Document Number : **1836620**

Purpose of Application

The purpose of these applications was to convert the registration of Zoxamide Technical Fungicide (Registration Number 26841), Zoxium 80W Agricultural Fungicide (Registration Number 26840) and Gavel 75DF Agricultural Fungicide (Registration Number 26842) and from conditional to full. These products were granted conditional registration in Canada and the detailed review supporting the conditional registration can be found in Regulatory Note REG2001-09, *Zoxamide Technical Fungicide, Zoxium 80W Agricultural Fungicide and Gavel 75DF Agricultural Fungicide*.

This document will present the evaluation of the information provided in support of the conversion of the registration of Zoxium 80W Agricultural Fungicide from conditional to full.

Chemistry Assessment

Zoxium 80W Agricultural Fungicide is formulated as a wettable powder containing the technical grade active ingredient zoxamide at a nominal concentration of 80 %w/w. This end-use product has a bulk density of 0.22-0.30 g/mL and pH of 8.8. The chemistry requirements for Zoxium 80W Agricultural Fungicide are complete.

Health Assessments

The Zoxium 80W Agricultural Fungicide formulation was considered to be of low acute toxicity by oral, dermal and inhalation routes in rats (oral and dermal LD₅₀ >5000 mg/kg bw; inhalation LC₅₀ >3.8 mg/L). When tested on rabbits, the formulation was moderately irritating to the skin and minimally irritating when instilled into the eyes. Results of skin sensitization testing in guinea pigs were positive. Consequently, the statements “Warning – Skin Irritant” and “Potential Skin Sensitizer” are required on the label.

Occupational risks are not of concern when Zoxium 80W Agricultural Fungicide is used according to label directions, which include protective measures.

A preliminary occupational risk assessment of the active ingredient zoxamide is presented in REG2001-09. An updated occupational risk assessment, taking into consideration revised areas-treated-per-day and transfer co-efficients, indicates that no changes are required to the registered label directions, except for the addition of a statement not to use human flaggers when applying by air.

Direct skin contact can occur with zoxamide when farmers and pesticide applicators are mixing, loading or applying Zoxium 80W Agricultural Fungicide, and when field workers re-enter freshly treated fields. Therefore, the label specifies that anyone mixing, loading and applying Zoxium 80W Agricultural Fungicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes; additionally, a NIOSH-approved respirator, and chemical-resistant apron are necessary when cleaning equipment, mixing or loading. Taking into consideration these label requirements, and that occupational exposure is expected to be short to intermediate duration, risk to farmers, applicators or workers is not a concern.

For bystanders, the exposure is expected to be much less than that of field workers. Therefore, health risks to bystanders are not of concern.

Environmental Assessment

The previously outstanding information on persistence of zoxamide in a sediment and water system, and the potential for bioaccumulation in biota (*n*-octanol-water partitioning coefficient) of four major metabolites (RH-127450, RH-24549, RH-141288 and RH-139432) have been submitted to the PMRA and were found to be satisfactory for review.

There were concerns regarding the potential for four transformation products to bioaccumulate in organisms. The *n*-octanol-water partitioning coefficient ($\log K_{ow}$) was determined empirically or by using the Quantitative Structure Activity Relationship (QSAR) for these four major metabolites. The values obtained were 3.5 (measured) and 4.10 (QSAR predicted) for RH-127450, and 2.57 (QSAR predicted) and 2.7 (measured) for RH-139432. For RH-24549 and RH-141288, the partitioning coefficients were determined using QSAR only, with values of 3.71 (pH 4) and -0.43 (pH 7) for RH-24549, and 3.55 for RH-141288. These values are below the TSMP Track-1 cut-off criterion of ≥ 5.0 . These four transformation products are expected to have a low potential to bioaccumulate in biota.

There were concerns regarding the potential for zoxamide to partition in sediments; data on the transformation of the compound in the sediment layer was requested by the PMRA. The registrant submitted a scientific rationale for the waiver of data on the biotransformation of zoxamide in an anaerobic sediment/water system. This rationale was based on the fact that zoxamide transforms both by abiotic and biotic mechanisms in soil and water, and that there is no significant difference in the rate of transformation of zoxamide in aerobic and anaerobic systems. Therefore, the results of the aerobic aquatic study and anaerobic soil study should provide sufficient information on the transformation of zoxamide in anaerobic sediment/water. A toxicity test on sediment-dwelling organisms showed these organisms to be less sensitive to

zoxamide than other aquatic species, such as the rainbow trout, and the risk assessments are based on the most sensitive species. Therefore, there is already a margin of safety to benthic organisms. The waiver request was accepted.

The risk assessment integrates the environmental exposure and ecotoxicity data to estimate the potential for adverse ecological effects. Since publication of REG2001-09, the PMRA has modified its environmental risk assessment process. Therefore, the environmental risk assessment of zoxamide was completely redone in accordance with current methods.

At the approved rates of use for Zoxium® 80W Agricultural Fungicide, risk was identified for non-target plant species, non-target freshwater and marine organisms. Therefore, buffer zones are required to mitigate the risks. Environmental hazard statements are required on the label for protection of aquatic organisms and non-target terrestrial plants.

Buffer zones are required for the protection of aquatic and terrestrial habitats. For Zoxium 80W Agricultural Fungicide, a buffer zone of one metre is required for terrestrial habitats. Meanwhile for aquatic freshwater and marine habitats, buffer zones vary from one metre to 150 metres, depending on the crop treated and the application type (field sprayer, airblast or aerial application).

Value Assessment

A value assessment was not required on this application.

Conclusion

The Agency has completed an assessment of the subject application and concluded that the applicant has met the required conditions to convert Zoxium 80W Agricultural Fungicide from conditional to a full registration.

References

PMRA Document Number: 712920

Reference: 2001. Gavel 75DF fungicide: delayed contact hypersensitivity (dose-response in water) study in guinea pigs. Laboratory Report No. 01R-148. Data Numbering Code 4.6.6.

PMRA Document Number: 712921

Reference: 2001. Zoxium 80W fungicide: delayed contact hypersensitivity (dose-response in water) study in guinea pigs. Laboratory Report No. 01R-231. Data Numbering Code 4.6.6.

PMRA Document Number: 1288703

Reference: 1997. Dermal Sensitization Study of RH-117,281 Purified in Guinea Pigs-Maximization Test (EU Guidelines. Report Number 95RC-260. Data Numbering Code 4.6.6.

PMRA Document Number: 712923

Reference: 2001, Storage Stability of RH-117281 Residues in raisin samples under conditions of frozen storage: Supplement to TR34-98-161, Data Numbering Code: 7.3

PMRA Document Number: 712924

Reference: 2001, Storage Stability of RH-117281 Residues in grape juice samples under conditions of frozen storage: Supplement to TR34-98-161, Data Numbering Code: 7.3

PMRA Document Number: 1191376

Reference: 2000. Tolerance Enforcement Method for Parent RH-7281 and Its Two Acid Metabolites, RH-1452 and RH-1455, in Potato Peel Waste. Data Numbering Code: 7.2.1

PMRA Document Number: 1193795

Reference: 2000. Tolerance Enforcement Method for Parent RH-7281 and Its Two Acid Metabolites, RH-1452 and RH-1455, in Potato Peel Waste. Data Numbering Code: 6.3

PMRA Document Number: 1193795

Reference: 1998. ¹⁴C-RH-117281: Nature of the Residue in Fruiting Grape Plants. Data Numbering Code: 6.3

PMRA Document Number: 1193810

Reference: 1998. Metabolism of ¹⁴C-RH-117,281 in Lactating Goats. Data Numbering Code: 6.2

PMRA Document Number: 1193811

Reference: 1998. ¹⁴C-RH-117281: Nature of the Residue in Potato. Data Numbering Code: 6.3

PMRA Document Number: 1193825

Reference: 1998. Storage Stability of RH-117,281 Residues in Grapes, Grape Juice, Raisins and Potatoes Under Conditions of Frozen Storage. Data Numbering Code: 7.3

PMRA Document Number: 1193826

Reference: 1998. Magnitude of Residue of RH-7281 and Mancozeb in Potatoes Following Treatment with RH-7281 80W and an RH-7281/ Pre-mix Formulation. Data Numbering Code: 7.4.1

PMRA Document Number: 1193827

Reference: 1998. RH-117,281 80W and 2F Residue Studies in Potatoes and Potato Processed Fractions 1996 and 1997 Trials. Data Numbering Code: 7.4.1, 7.4.5

PMRA Document Number: 1193828

Reference: 1998. RH-117,281 80W and 2F Residue Studies in Potatoes and Potato Processed Fractions 1996 and 1997 Trials. Data Numbering Code: 7.4.1, 7.4.5

PMRA Document Number: 1193829

Reference: 1998. RH-117,281 80W and 2F Residue Studies in Grapes and Grape Process Fractions 1996 and 1997 Trials. Data Numbering Code: 7.4.1

PMRA Document Number: 1193830

Reference: 1998. RH-117,281 80W and 2F Residue Studies in Grapes and Grape Process Fractions 1996 and 1997 Trials. Data Numbering Code: 7.4.1

PMRA Document Number: 1193834

Reference: 1998. ¹⁴C-RH-117281: Confined Rotational Crop Study. Data Numbering Code: 7.4.3

PMRA Document Number: 1194286

Reference: 2000. Magnitude of Residue of RH-7281 and Mancozeb in Grapes Following Treatment with RH-7281 80W and RH-7281 MZ 75DF Formulation. Data Numbering Code: 7.4.1, 7.4.2

PMRA Document Number: 1194288

Reference: 1998. Preliminary Residue Analytical Method for Parent RH-7281 in Raisins. Data Numbering Code: 7.2.1

PMRA Document Number: 1194289

Reference: 1998. Tolerance Enforcement Method for RH-7281 and Its Two Acid Metabolites, RH-1452 and RH-1455, in Potato and Potato Processed Fractions. Data Numbering Code: 7.2.2

PMRA Document Number: 1194290

Reference: 1998. Tolerance Enforcement Method for RH-117,281 in Grapes and Processed Fractions. Data Numbering Code: 7.2.2

PMRA Document Number: 1194295

Reference: 1998. Stability of RH-141,455 and RH-141,452 Residues in Potatoes, Potato Chips and Potato Flakes Under Conditions of Frozen Storage. Data Numbering Code: 7.3

PMRA Document Number: 1194296

Reference: 1998. Storage Stability of RH-117,281 Residues in Grapes, Grape Juice, Raisins and Potatoes Under Conditions of Frozen Storage. Data Numbering Code: 7.3

PMRA Document Number: 712925

Reference: 2001. Bioaccumulation Potential of Zoxamide and Metabolites (plus 5 references). Dow AgroSciences Inc. pp. 107. Data Numbering Code: 8.2.1.

PMRA Document Number: 712926

Reference: 2002. Scientific Justification to Support a Waiver Request for PMRA Data Numbering Code 8.2.3.5.6 (Anaerobic Sediment-Water Degradation) for Zoxamide. pp. 9. Data Numbering Code: 8.2.3.5.6

PMRA Document Number: 712927

Reference: 1997. Anaerobic soil Metabolism of [¹⁴C]RH-117281. Study No. XBL95010 Study report No. RPT00267. Report No. 34-97-43. pp. 123. Data Numbering Code: 8.2.3.4.4
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