Health Canada Santé Canada

Canada

Consumer Product Safety

Consultation Document on Dithiopyr - Proposed Re-evaluation Decision - PRVD2009-01

Notice to the reader: The online consultation is now closed. Comments and suggestions received during the public consultation period are being considered in the finalization of this document. The final report will be made available as soon as possible.

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The text provided on this page reflects only the body of the report. To obtain an electronic copy of the complete document, including appendices (PRVD2009-01, Proposed Re-evaluation Decision: Dithiopyr, please contact our publications office.

Should you require further information please contact the Pest Management Information Service.

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Overview

Proposed Re-evaluation Decision for Dithiopyr

After a re evaluation of the herbicide dithiopyr, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing dithiopyr for sale and use in Canada.

An evaluation of available scientific information found that under the proposed conditions of use, products containing dithiopyr have value and do not present unacceptable risks to human health or the environment. As a condition of the continued registration of dithiopyr, new risk reduction measures are proposed for the labels of all products. No additional data are being requested at this time

The PMRA's pesticide re-evaluation program considers potential risks as well as the value of pesticide products to ensure they meet modern standards established to protect human health andthe environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure. Re-evaluation draws on data fromregistrants, published scientific reports, information from other regulatory agencies and any other relevant information available.

This proposal affects all end-use products containing dithiopyr registered in Canada. Once the final re-evaluation decision is made, registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for dithiopyr and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessment of dithiopyr.

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document. Please forward all comments to Publications (see contact information on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation 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 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 or proposed conditions of registration.[2] The Act also requires that products have value[3] when used according to the 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 hazard and risk-assessment methods as well as policies that are rigorous and modern. These methods consider the unique characteristics of sensitive subpopulations in both humans (e.g. children) and organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present 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 PMRA's website

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy [TSMP]).

Before making a re-evaluation decision on dithiopyr, the PMRA will consider all comments received from the public in response to this consultation document.[4] The PMRA will then publish a Re-evaluation Decision document[5] on dithiopyr, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and the PMRA's response to these comments.

For more details on the information presented in this overview, please refer to the Science Evaluation of this consultation document.

What Is Dithiopyr?

Dithiopyr is a selective turf herbicide. It is registered for pre-emergence and early postemergence control of crabgrass (large or smooth) on turf in Ontario and Quebec. Dithiopyr is to be applied once per year with ground equipment including hose, handgun or boom sprayer by trained and certified applicators.

Health Considerations

Can Approved Uses of Dithiopyr Affect Human Health?

Dithiopyr is unlikely to affect your health when used according to the revised label directions.

Potential exposure to dithiopyr may occur through the drinking water, when handling and applying the product or when entering treated areas such as residential turf and golf courses. When assessing health risks, two key factors are considered: the levels at which no health effects occur in animal testing 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 (e.g. 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 dithiopyr products are used according to label directions.

Dithiopyr induced mild but transient eye and dermal irritation in rabbits and was not a sensitizer in guinea pigs. Consequently, no statements are required on the label of the technical product.

Dithiopyr did not cause cancer in animals, was not genotoxic or teratogenic and showed no signs of neurotoxicity. The liver and kidneys were the main targets of toxicity by the oral route in mice, rats and dogs. Effects on liver weights were also seen following exposure via the dermal route in rats. There is a low level of concern for potential prenatal and postnatal toxicity associated with dithiopyr.

The risk assessment protects against these effects 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

Dietary risks from water are not of concern.

As dithiopyr is not registered for use on food, exposure and risk from food consumption is considered negligible. Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Human exposure to dithiopyr was estimated from residues in drinking water and ranged from 6.5% of the acceptable daily intake for the general population to 21.2% of the acceptable daily intake for infants. An acute drinking water assessment was not performed as no acute endpoints were identified, due to the low acute toxicity of dithiopyr.

Risks in Residential and Other Non occupational Environments

Non occupational risks are not of concern.

Risks to homeowners applying the domestic product are not of concern. Postapplication risks to adults, youths and children entering treated lawns and turf following commercial and homeowner application are not of concern.

Aggregate risks are not of concern.

Aggregate risks to homeowners and children from drinking water and residential exposures are not of concern

Occupational Risks From Handling Dithiopyr

Occupational risks are not of concern.

Risk estimates associated with applying, mixing and loading activities are not of concern and additional personal protective equipment are not required beyond what is currently specified on the label.

Postapplication risks are not of concern.

Risks to workers re-entering turf treated with dithiopyr are not of concern. The minimum 12 hour restricted-entry interval (REI) is proposed for all uses, with the exception of golf courses where entry is restricted until after the spray has dried.

Environmental Considerations

What Happens When Dithiopyr Is Introduced Into the Environment?

Dithiopyr poses a potential risk to terrestrial and aquatic plants; therefore, additional risk-reduction measures need to be observed.

When dithiopyr is released into the environment, some of it can be found in soil and surface water. However, dithiopyr readily volatilizes from turf grass, is broken down by soil microbes and undergoes phototransformation in water. Thus, dithiopyr is not expected to persist in the environment. Laboratory and field studies indicate that dithiopyr is not mobile in soil. There is limited potential for leaching and groundwater contamination and runoff can occur, although the concentrations are low.

When dithiopyr is used for weed control in turf grass, there is a potential that non-target plant species on land and in water may be exposed to the chemical as a result of spray drift or runoff. Some of plant species are sensitive to the chemical and would be adversely affected. To minimize the potential exposure, strips of land between the agricultural field and the nontarget terrestrial or aquatic areas must be left unsprayed. The width of these buffer zones will be specified on the product label. Dithiopyr presents negligible risk to wild birds and mammals, bees and other arthropods. Dithiopyr poses risk to terrestrial plants and aquatic organisms like fish, amphibians and algae. The concentrations are very low in runoff and do not pose a concern for aquatic environments.

Value Considerations

What Is the Value of Dithiopyr?

Dithiopyr controls crabgrass in turf.

Crabgrass is a troublesome weed in turf. Dithiopyr provides both pre-emergence and early postemergence control of crabgrass in established turf. It provides a wider application window than alternative crabgrass control products used on turf. In addition, the application rate of dithiopyr is usually lower than that of alternative crabgrass control products.

Measures to Minimize Risk

Additional Key Risk-Reduction Measures

Human Health

- Additional label statements to clarify the maximum number of applications per year

- A restricted-entry interval to protect workers entering treated sites

Environment

- Precautionary statements and buffer zones to protect non-target terrestrial and aquatic habitats and terrestrial and aquatic habitats that may contain sensitive species

Next Steps

Before making a re-evaluation decision on dithiopyr, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision, which will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

Other Information

At the time that the re-evaluation decision is made, the PMRA will publish an Evaluation Report on dithiopyr in the context of this re-evaluation decision (based on the Science Evaluation section of this consultation document). In addition, the test data on which the decision is based will also be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

1.0 Introduction

Dithiopyr is a selective turf herbicide. It belongs to the pyridine chemical family and is classified as a Group 3 herbicide. Dithiopyr is an inhibitor of microtubule assembly, inhibiting plant cell divisions.

Following the re-evaluation announcement for dithiopyr, Dow AgroSciences Canada Inc., the registrant of the technical grade active ingredient and primary data provider in Canada, indicated support for all uses included on the label of the Commercial Class end-use product. There are no Domestic Class end-use products containing dithiopyr.

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2.0 The Active Substance, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name Dithiopyr

Function Herbicide

Chemical family Pyridine

Chemical name

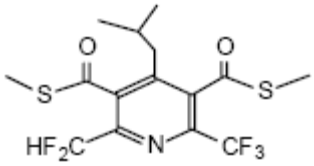
1 International Union of Pure and Applied Chemistry (IUPAC)
S,S'-dimethyl 2-difluoromethyl-4-isobutyl-6- trifluoromethylpyridine-3,5-dicarbothioate

2 Chemical Abstracts Service (CAS)

CAS Registry Number 97886-45-8

Molecular formula $C_{15}H_{16}F_5NO_2S_2$

Structural formula



Molecular weight 401.4 amu

Identity of relevant impurities of human health or environmental concern
Based on the manufacturing process used, impurities of human health or environmental concern as identified in the *Canada Gazette*, Part II, Vol. 139, No. 24, SI/2005-114 (30 November 2005), including TSMP Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property Result

Vapour pressure at 25°C 0.53 mPa

Ultraviolet (UV)/visible spectrum Not provided

Solubility in water at 20°C 1.4 mg/L

***n*-octanol-water partition coefficient** 4.75

Dissociation constant Not applicable

2.3 Description of Registered Dithiopyr Uses

Appendix I lists all dithiopyr products that are registered under the authority of the *Pest Control Products Act*, including one technical grade active ingredient, one manufacturing concentrate and one commercial class end-use product.

Appendix II lists all uses for which dithiopyr is presently registered. The registrant supported all uses when the re-evaluation was initiated; therefore, all uses were considered in the health and environmental risk assessments.

Uses of dithiopyr belong to a single use-site category, being turf. Dithiopyr is mainly used on golf courses and residential lawns in Ontario and Quebec.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for dithiopyr was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes with the exception of an in vivo chromosomal aberration study. All of the toxicity studies were conducted in accordance with accepted international testing protocols and good laboratory practice in place at that time. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to this chemical pest control product.

In acute toxicity studies, dithiopyr is of low toxicity by the oral, dermal and inhalation routes of exposure. Dithiopyr induced mild but transient eye and dermal irritation in rabbits and was not a sensitizer in guinea pigs.

Results from toxicokinetic studies indicated that absorption was dose-dependent in rats; the higher the dose, the lower the fraction absorbed. Dithiopyr was rapidly and extensively metabolized by rats with the major end-products being carboxylic acids and thioacids. Study results indicate that whether administered by oral

or intravenous dose, fat retains the greatest fraction of dithiopyr. Delayed clearance of dithiopyr was noted with the majority of radioactivity eliminated between 72 and 96 hours postdosing.

Both the urinary and fecal metabolic profiles differed between sexes following acute exposure. Metabolic profiles also differed in the male animals depending on whether the route of exposure was oral or intravenous; however, diacids IV and V were continuously detected. Despite the route, dosage or dosing regimen, female rats routinely excreted more carbon 14 (^{14}C) through urine than their male counterparts. Conversely, male rats appeared to have more active biliary excretion of dithiopyr. Neither the metabolic pattern nor the distribution of metabolites in rats were changed following repeat dose protocols.

In repeat-dose dietary studies in rats and mice, dose-related alterations were noted in organ weights and histopathology predominantly involving the liver and kidneys. Altered pathology mainly involving the liver and the kidneys was also noted in repeat-dose studies in dogs exposed orally (by capsule) to dithiopyr. Increased liver weights were also seen following exposure via the dermal route in rats. Repeat-dose inhalation studies were not available. Throughout the subchronic oral studies, decreased food efficiency, elevated alkaline phosphatase, reduced hemoglobin and reduced hematocrit levels were common findings, with both liver and kidney appearing to be the target organs. No gender sensitivities were seen in repeat-dose dietary studies. Comparison of the dietary short and long-term toxicity studies suggested a pronounced increase in toxicity with increased duration of dosing.

In the multigeneration rat reproduction study, no effects were noted in either the parents or offspring at the lowest dose examined. However, at the next dosage level, alterations in liver pathology were noted in pups from both generations that were not seen in the parental animals at the same dose level. A high incidence of white spots on the surface of liver lobes was noted in mid-dose (males only) and high-dose pups from both generations. Among mid-dose and high-dose second filial generation (F_2) pups dying during lactation days 0 to 4 or culled on lactation day 4, an increased incidence of focal hepatocellular necrosis and fibrosis was noted. F_2 pups that died during lactation days 5 to 21 or were killed after weaning experienced a high incidence of fibrosis and mineralization with no signs of necrosis. First filial generation (F_1) pups at weaning showed a treatment-related increase in fibrosis, but not necrosis, as adults these animals showed neither fibrosis nor necrosis.

The white spots on the liver surface were identified as focal hepatocellular necrosis and fibrosis/mineralization. While the pups were growing, the incidence of necrosis appeared to be tapering off with no signs of necrosis identified in the weanlings. In contrast, the incidence of fibrosis/mineralization in the weanlings was increased. Based on these findings, the theory was put forward by the study author that necrotic lesions were followed by fibrosis and mineralization during the growth of pups, with the lesions becoming small and obscure by the time of weaning. Given these pathological alterations occurring in the F_2 pups were more severe than the hepatic lesions noted in the parental animals and occurred at doses eliciting minimal parental systemic toxicity, there is evidence of sensitivity of the young to dithiopyr. No information is available to indicate whether this sensitivity would be present with other routes of dosing.

Dithiopyr's effects on reproductive parameters in the multigeneration rat reproduction study were limited to decreased birth weights. Dithiopyr did not induce developmental changes or teratogenic effects in either rats or rabbits following in utero exposure, even at maternally toxic doses. Effects on the endocrine system were noted in the adrenals, thyroid and pituitary but only at high dose levels which elicited significant systemic toxicity.

Dithiopyr was considered non-mutagenic based on the negative results obtained in Ames tests (*Salmonella* strains TA98, 100, 1535, 1537 and 1538) with and without metabolic activation, a Chinese Hamster Ovary/Hypoxanthine-Guanine Phosphoribosyl Transferase gene mutation assay, an in vitro cytogenetic assay and an in vitro hepatocyte DNA repair (unscheduled DNA synthesis) assay. Dithiopyr did not show evidence of carcinogenicity in the mouse or rat.

A single oral dose of dithiopyr given to rabbits in a pharmacology study did not affect respiration rate, blood pressure, heart rate or electrocardiogram results.

Results of the acute and chronic tests conducted on laboratory animals with Dithiopyr Technical, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Appendix III, Table 1 and 2.

Pest Control Products Act Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects. This factor should take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the exposure of and toxicity to infants and children, extensive data were available for dithiopyr. Data of high quality were available for dithiopyr and included a developmental toxicity study in rats, a developmental toxicity study in rabbits and a multigeneration reproduction study in rats.

With respect to potential prenatal and postnatal toxicity, developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of fetuses to in utero exposure. In the two-generation rat reproduction study, sensitivity of the young was noted based on the presence of hepatic alterations (white spots, focal hepatocellular necrosis) in pups that were more severe than the lesions noted in the parental animals. However, as the pups aged, the presence of these hepatic lesions improved to the point that they were undetectable in adult animals. Given the hepatic lesions appeared to have no long-term implications, there is a low level of concern for potential prenatal and postnatal toxicity associated with dithiopyr.

3.2 Occupational and Non-occupational Risk Assessment

Occupational and non-occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects. However, MOEs less than the target MOE require measures to mitigate (reduce) risk.

Risks from different routes of exposure were aggregated using an aggregate risk index (ARI). Risks greater than one do not require risk mitigation. If the calculated ARI is less than one, it does not necessarily mean that exposure will result in adverse effects. However, ARIs less than one require measures to mitigate (reduce) risk.

3.2.1 Toxicology Endpoint Selection for Occupational and Non-Occupational Risk-Assessment

Acute Endpoints

Due to the low acute toxicity of dithiopyr, toxicological endpoints for an acute dermal and inhalation risk assessment are not required.

Short-Term and Intermediate-Term Dermal Risk Assessments

For residential and occupational short-term dermal assessment relative to the use pattern (1-30 days), the NOAEL of 1000 mg/kg bw/day (the highest dose tested) from the 21-day dermal toxicity study in rabbits was selected. Given the dermal toxicity study was conducted solely on adult animals, there is uncertainty whether or not the sensitivity observed with oral exposures to the young would also be manifested via the dermal route. The multigeneration reproduction study in rats revealed that sensitivity may occur in the fetus or nursing infant as a result of an indirect exposure via the mother.

This is a concern because the population (including workers) could include pregnant or lactating women, who could potentially pass an indirect dose of dithiopyr to their offspring. Given the lack of appropriate dermal data (to confirm or refute the sensitivity), a threefold uncertainty factor in the form of a database deficiency is considered appropriate to protect the young. The target MOE selected for all populations when using this study is 300, accounting for standard uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for

intraspecies variability and an additional 3-fold uncertainty factor for database deficiency. For residential exposure, the *Pest Control Products Act* factor was reduced to onefold as database uncertainties were subsumed under the applied uncertainty factors.

For occupational intermediate-term dermal assessment relative to the use pattern (1 month to several months), the NOAEL of 1000 mg/kg bw/day (the highest dose tested) from the 21-day dermal toxicity study in rabbits was selected. The target MOE selected when using this study is 1000, thus accounting for standard uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and an additional 10-fold uncertainty factor. The latter factor was employed for the lack of information on sensitivity of the young by the dermal route and extrapolation of the results from a short-term study to a longer-term exposure scenario.

Short-Term and Intermediate-Term Inhalation Risk Assessments

As there are no repeat-dose inhalation studies available for inhalation risk exposure, it is appropriate to assume that absorption via inhalation exposure is equivalent to oral absorption.

For residential and occupational short-term and intermediate-term exposure (up to 3 months), the 13-week dietary toxicity study in the rat was chosen with a NOAEL of 0.7 mg/kg bw/day. As this study NOAEL was lower than that of the multigeneration reproduction study (NOAEL of 1.9 mg/kg bw/day) in which sensitivity of the young was observed, the NOAEL was considered protective of the effects noted in the young animals. The target MOE selected for all populations when using this study is 100, accounting for standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. For residential exposure, the *Pest Control Products Act* factor was reduced to onefold as the toxicity database was considered complete and there was a low level of concern for potential prenatal and postnatal toxicity with dithiopyr.

Non-Dietary Short-term Oral Ingestion

For assessing non-dietary short-term oral ingestion in children entering treated lawns and turf (1-7 days), the offspring NOAEL of 1.9 mg/kg bw/day in a two-generation rat reproduction study (liver pathology at 16.4 mg/kg bw/day) was chosen with a target MOE of 100 (10-fold uncertainty factor for interspecies extrapolation and 10-fold uncertainty factor for intraspecies variability). The *Pest Control Products Act* factor was reduced to onefold as the toxicity database was considered complete and there was a low level of concern for potential prenatal and postnatal toxicity with dithiopyr.

Endpoint for Biomonitoring Risk Assessment

Where exposure (short-term to intermediate-term) has been assessed via biomonitoring, the selected toxicological endpoint is the NOAEL of 0.7 mg/kg bw/day from the 13-week dietary toxicity study in the rat, with a target MOE of 100. Biomonitoring studies take into account contributions from dermal, inhalation and oral (including non-dietary incidental oral) routes of exposure. Thus, exposure and risk assessments using this endpoint are considered more protective than the route-specific endpoints and accompanying MOEs.

Dermal Absorption

A dermal absorption value was not required for this assessment as dermal toxicity studies were selected for the dermal risk assessment.

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3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to dithiopyr through mixing, loading or applying the pesticide and/or when entering a treated site to conduct activities such as scouting and/or handling of treated turf.

Mixer, Loader and Applicator Exposure and Risk Assessment

There are potential exposures to mixers, loaders, and applicators. The following supported uses were assessed:

- Mixing/loading emulsifiable concentrates
- Groundboom application to golf courses and sod farms
- Mixing/loading/applying by backpack to residential turf, golf courses and sod farms
- Mixing/loading/applying by turf gun to residential turf, golf courses and sod farms

Based on the number of applications, workers applying dithiopyr would generally have a short-term to intermediate-term (one to several months) duration of exposure. The PMRA estimated handler exposure based on the following level of personal protection:

- Baseline personal protective equipment (PPE) - long pants, a long-sleeved shirt, shoes plus socks and chemical-resistant gloves (unless specified otherwise). For groundboom application, this scenario does not include gloves as the data quality were better for non-gloved scenarios than gloved scenarios.

Mixer/loader/applicator exposure estimates are based on the best available data at this time.

A chemical-specific handler biomonitoring study was submitted for dithiopyr. This study was conducted with commercial applicators applying dithiopyr to residential turf. Eighteen lawn care specialists applied dithiopyr at a rate of 1.12 kg a.i./ha to approximately 0.8 ha of residential turf during the course of a normal working day. A spray gun attached to large tank on a truck was used for application. All workers wore long pants and short-sleeved shirts and some also wore a variety of other protective equipment such as face shields, safety glasses and hats. Only two of the applicators reported wearing gloves during application, although all wore gloves during mixing and loading (open-pour). Complete 24-hour urine samples were collected from each worker for three days following application. A monkey pharmacokinetic study conducted using dithiopyr was submitted to the PMRA. The study was considered acceptable and was used to interpret the biomonitoring study results. Worker exposure ranged from 0.0260 to 0.216 µg/kg bw/day. The maximum exposure value was used in the risk assessment for workers using turf guns on residential lawns; this is considered to be a high-end estimate of exposure. As the application rate used in the biomonitoring study is twice that registered in Canada, the exposure from this study is considered to be conservative relative to the potential exposure to Canadian applicators.

For those scenarios where no acceptable chemical-specific handler exposure data were submitted, dermal and inhalation exposures were estimated using data from the Pesticide Handlers Exposure Database (PHED), Version 1.1. The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of PPE.

Occupational risk estimates associated with applying, mixing and loading dithiopyr for application to residential and commercial turf meet the target MOE, and ARIs are greater than one at baseline PPE. Therefore, risk to workers handling dithiopyr was not of concern. See Appendix IV for risk estimate calculations.

Postapplication Worker Exposure and Risk Assessment

The postapplication occupational risk assessment considered exposures to workers entering treated turf. Based on the dithiopyr use pattern, there is potential for short-term (< 30 days) postapplication exposure to dithiopyr residues for workers.

Chemical-specific turf transferrable residue (TTR) data and activity-specific transfer coefficients (TCs) were used to estimate postapplication exposure resulting from contact with treated turf at various times after application. TTR data include the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant. A TC is a factor that relates worker exposure to transferrable residues. TCs are specific to a given crop and activity combination (e.g. hand harvesting apples or scouting late season corn)

and reflect standard agricultural work clothing worn by adult workers. Postapplication exposure activities include harvesting, thinning, pruning, scouting and irrigating.

For workers entering a treated site, REIs are calculated to determine the minimum length of time required before people can safely re-enter. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE (i.e. > 300 for short-term dermal exposure scenarios for dithiopyr). See Appendix IV for risk estimate calculations.

A TTR study performed using both granular and liquid formulations to turf was submitted to the PMRA. Maximum liquid and granular mean TTR values from the day of application were used to estimate occupational and residential postapplication exposure.

All postapplication scenarios had MOEs that were above the target MOE on the day of application and therefore not of concern. Mitigation beyond the minimum 12-hour REI is not required. See Appendix IV for risk estimate calculations.

A turf volatility study was submitted to the PMRA. This study reported that up to 38% of the applied product can volatilize within 30 days of application. Although this study was considered unacceptable for risk-assessment purposes due to major limitations including low recovery and minimal study validation, these data were considered in a screening level assessment, the results of which would determine if further data would be required. The maximum concentration of volatilized dithiopyr measured in the study (7.82 µg/m^3) was used to conduct an inhalation-specific risk assessment. As the application rate used in this study is twice that which is registered in Canada, the dithiopyr air concentration is considered to be a high-end estimate. Inhalation exposure was then aggregated with the maximum dermal MOE from entry on the day of application. The MOE for the conservative inhalation exposure scenario was above the target MOE. When combined with the highest dermal MOEs, the resulting ARI was greater than one. Thus, postapplication risk is not of concern. See Appendix IV for risk estimate calculations.

3.2.3 Non-Occupational Exposure and Risk Assessment

Non-occupational risk assessment involves estimating risks to the general population, including children, during or after pesticide application, and assumes that homeowners wear short pants, a short-sleeved shirt and no gloves. Increased clothing will decrease the exposure and risk to homeowners during or after application.

Residential Mixer, Loader and Applicator Exposure and Risk Assessment

Dithiopyr is also included in some pesticide-fertilizer products regulated by the Canadian Food Inspection Agency.

Homeowners can apply granular pesticide-fertilizer products in the spring and early summer to residential turf. Given homeowners can only apply the product once during the spring and early summer, they have potential for short-term exposure to dithiopyr.

There is the potential for homeowners to mix, load and apply domestic class pesticide-fertilizer products. The following supported uses were assessed:

- Loading granular pesticide-fertilizer
- Applying granules by hand to residential turf
- Mixing/loading/applying granules by push-rotary spreader to residential turf
- Mixing/loading/applying granules by belly grinder to residential turf

No acceptable chemical-specific handler exposure data were submitted for homeowners applying dithiopyr on turf; therefore, dermal and inhalation exposures were estimated using data from the PHED, Version 1.1, and Outdoor Residential Exposure Task Force (ORETF) studies. The ORETF studies monitored exposure to workers and homeowners mixing/loading and applying pest control products to turf. Monitoring was conducted using passive dosimetry, including hand washes, face/neck wipes and personal air samplers.

Non-occupational risk estimates associated with mixing, loading and applying dithiopyr to residential turf meets the target MOE and ARIs are greater than one, thus residential use was not of concern. See Appendix IV for risk estimate calculations.

Postapplication Non-Occupational Exposure and Risk Assessment

There is potential for short-term exposure to adults, youth and children entering treated lawns and turf. Adults and youth have the potential for dermal and inhalation exposure, while children also have the potential for incidental oral exposure. It is assumed that people enter the treated area immediately after application.

Dermal Exposure

Dermal postapplication exposure is estimated in the same way as occupational postapplication exposure where a chemical-specific TTR data and activity-specific TCs are used.

A TTR study performed using both granular and liquid formulations to turf was submitted to the PMRA. Maximum liquid and granular mean TTR values from the day of application were used to estimate residential postapplication exposure.

A chemical-specific passive dosimetry study for postapplication activities on turf performed in conjunction with the TTR study was also submitted to the PMRA. Ninety-six participants were monitored for dermal exposure performing various activities (specifically children's activity patterns) on turf treated with liquid or granular formulation. Dermal exposure was monitored using whole body dosimeters. The highest mean exposure values from granular and liquid formulations were used in the postapplication risk assessment for residential turf. As this study was conducted with adults, exposures were normalized for body weight and surface area for youth and children.

Dermal MOEs were above the target MOE for all scenarios and subpopulations and therefore not of concern. See Appendix IV for risk estimate calculations.

Inhalation Exposure

A turf volatility study was submitted to the PMRA. This study reported that up to 38% of the applied product can volatilize within 30 days of application. Although this study was considered unacceptable for risk assessment purposes due to major limitations including low recovery and minimal study validation, these data were considered in a screening level risk assessment to assess potential inhalation exposure for residential post-application activities on treated turf, the results of which would determine if further data would be required. As there is no toxicological endpoint established for an acute inhalation scenario and only one application per year is permitted on residential turf, the average concentration of dithiopyr in air over 30 days was used in the residential postapplication assessment for both liquid and granular formulations. As the application rate used in this study is twice that which is registered in Canada, the dithiopyr air concentration used in this assessment is considered to be a high-end estimate.

The MOE for the inhalation exposure scenario was above the target MOE for all subpopulations and therefore not of concern. See Appendix IV for risk estimate calculations.

Incidental Oral Exposure

Incidental oral exposure through hand-to-mouth, object-to-mouth and ingestion of soil were assessed and aggregated for children; the resulting ARI was greater than one and therefore not of concern. Ingestion of granules is considered to be an acute episodic event and was not required as no acute endpoints were identified due to the low acute toxicity of dithiopyr.

Postapplication Risk: Total Exposure From All Routes

Exposure from all routes of postapplication exposure (dermal, inhalation and incidental oral) were aggregated for all subpopulations, where applicable. The resulting ARIs were greater than one for all scenarios and subpopulations, and therefore not of concern. See Appendix IV for risk estimate calculations.

3.3 Dietary Risk Assessment

As there are no registered food uses of dithiopyr, a dietary risk assessment was not required.

3.4 Exposure from Drinking Water

3.4.1 Determination of Acute Reference Dose

Due to the low acute toxicity of dithiopyr, an acute reference dose is not required.

3.4.2 Determination of Acceptable Daily Intake

To estimate dietary risk from repeat exposure (from drinking water), the most suitable study is a two-year chronic study in the rat. This study resulted in a NOAEL of 0.4 mg/kg bw/day based on the presence of altered liver pathology at the next dosage level of 3.6 mg/kg bw/day. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability are used. The *Pest Control Products Act* factor was reduced to 1-fold as the toxicity database was considered complete and there was a low level of concern for potential prenatal and postnatal toxicity with dithiopyr.

ADI = 0.4 mg/kg bw/day÷100 = 0.004 mg/kg bw/day

This acceptable daily intake (ADI) provides a margin of 250 000 to the developmental NOAEL and 475 to the lowest NOAEL for effects in offspring, for parental toxicity and for reproductive toxicity. It is thus considered protective of all populations including pregnant women, infants and children.

3.4.3 Concentrations in Drinking Water

Residues of dithiopyr in drinking water sources in Canada were estimated using the Leaching Estimation and Chemistry Model (LEACHM) and the Pesticide Root Zone Model/Exposure Analysis Modelling System (PRZM/EXAMS). Estimated environmental concentrations (EECs) of dithiopyr in groundwater were calculated using the LEACHM model to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using LEACHM are estimates of the flux, or movement, of pesticide into shallow groundwater (2 m or 5 m depth) with time. EECs of dithiopyr in surface water were calculated using the PRZM/EXAMS models, which simulate pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in two types of vulnerable drinking water sources, a small reservoir and a prairie dugout.

The EECs predicted by Level 1 modelling were high enough for Level 2 modelling to be conducted. The refinements used for Level 2 modelling were to use a scenario representing Ontario and Quebec only, because the current product registration is limited to those two provinces. For Level 2 surface water modelling, a turf scenario was used together with weather files from Ontario and Quebec instead of the standard Level 1 scenarios. As no dugouts are present in Ontario and Quebec, EECs in surface water were only generated for the reservoir. The Level 2 EECs are thus crop- and region-specific and do not allow for future use expansion into other crops or regions. Table 3.4.3.1 provides the Level 1 and Level 2 modelled EECs for dithiopyr in potential sources of drinking water.

The highest estimated yearly surface water EEC value (12.3 µg a.i./L) was used in the chronic drinking water risk assessment.

Table 3.4.3.1 Level 1 and 2 Estimated Environmental Concentrations of Dithiopyr in Potential Drinking Water Sources

Refinement Level	Groundwater EEC (µg a.i./L)		Surface Water EEC			
			Reservoir		Dugout	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]	Daily[5]	Yearly[6]
Level 1	19	19	28	5.6	63	54.9
Level 2 (Ontario and Quebec only)	12.3	12.3[6]	3.2	2	N/A[5]	N/A[5]

1 90th percentile of daily average concentrations.
2 90th percentile of yearly average concentrations.
3 90th percentile of yearly peak concentrations.
4 90th percentile of yearly average concentrations.
5 Dugout not included as regional scenarios for Ontario and Quebec only were used in Level 2 modelling.
6 Value used in drinking water chronic assessment.

Water Monitoring Data

Limited information on dithiopyr water monitoring data was available for Canada. Two datasets submitted to the PMRA contained data on various pesticide concentrations, including dithiopyr, in 8 Canadian tributaries of Lake Ontario in 2000 and 2001. Of the 195 samples analysed in these two datasets, dithiopyr was not detected.

American databases were searched for detections of dithiopyr. Both databases searched (the United States Geological Survey National Water Quality Assessment [NAWQA] Program and the United States Environmental Protection Agency [USEPA] Storage and Retrieval Database [STORET]) did not contain information on dithiopyr. The NAWQA Program does not have dithiopyr on the analyte list and no information was submitted to STORET for dithiopyr.

A study was conducted to investigate the impact of lawn-care pesticides on aquatic ecosystems. To determine the impact of lawn-care pesticides on aquatic ecosystems, various pesticides were analysed in the water of six American streams. The limits of quantitation for pesticides in water were set at 0.1 ng/L. Water samples were collected quarterly from the summer 2000 to the spring of 2002 (i.e. 6 samples) from each stream. Dithiopyr was detected in each stream (71-82% detection) with maximum concentrations ranging from 122.7-252.5 ng/L.

3.4.4 Drinking Water Exposure and Risk Assessment

For the chronic drinking water exposure assessment, the estimated dithiopyr concentration in drinking water is multiplied by the water consumption data for all relevant population subgroups to obtain an average daily pesticide exposure value. Dithiopyr concentration estimates in drinking water are based on the highest yearly surface water value modelled (12.3 µg a.i./L). The consumption data are based on the average daily water consumption of the general population and its subgroups. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic drinking water exposure is acceptable.

For all subpopulations, drinking water exposures were below the ADI and, therefore, not of concern. An acute drinking water assessment was not required, as acute endpoints were not identified due to the low acute toxicity of dithiopyr. See Appendix V for risk estimate calculations.

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3.5 Aggregate Exposure and Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from drinking water, residential and other non-occupational sources from all known or plausible exposure routes (oral, dermal and inhalation).

3.5.1 Aggregate Acute Risk and Exposure Assessment

Due to the low acute toxicity of dithiopyr, aggregate acute risk was not required as no acute endpoints were identified.

3.5.2 Aggregate Short-Term Exposure and Risk Assessment

Short-term aggregate exposure to dithiopyr may be comprised of drinking water and residential (dermal, inhalation and incidental oral) exposures. The relevant duration of exposure for this assessment would likely be for a period less than one month. Liver toxicity was the common toxic effect among all routes of exposure. For the dermal component, the NOAEL of 1000 mg/kg bw/day (highest dose tested) from the 21-day dermal toxicity study in rabbits was selected based on increased liver weights at that dose level. In the absence of repeat-dose inhalation data, it is assumed that liver toxicity would also be a critical endpoint by this route of exposure and thus deemed appropriate to default to oral studies for the inhalation component. Consequently, the NOAEL of 0.7 mg/kg bw/day from the 13-week oral toxicity study in rats is selected based on increased liver weights and liver pathology at the next higher dose level. This same study and NOAEL was selected to reflect the oral component (incidental oral exposure) of the aggregate assessment. The target MOE of 300 was chosen for the dermal exposure route to account for uncertainties associated with interspecies extrapolation (10-fold), intraspecies variability (10-fold) and the lack of information on sensitivity of the young by the dermal route (3-fold). The target MOE of 100 was considered appropriate for all other exposure routes and populations.

The chronic drinking water exposure is considered representative of a typical dietary exposure because it represents the average daily exposure over an individual's lifetime. This exposure was combined with short-term residential exposure estimated for children, youth and adults. Resulting ARIs were greater than one for all groups and, therefore, not of concern. See Appendix VI for risk estimate calculations.

3.6 Incident Reports

Starting on 26 April 2007, registrants are required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Incidents are classified into six major categories including effects on humans, effects on domestic animals and packaging failure. Incidents are further classified by severity, in the case of humans for instance, from minor effects such as skin rash, headache, etc., to major effects such as reproductive or developmental effects, life-threatening conditions or death.

The PMRA will examine incident reports and, where there are reasonable grounds to suggest that the health and environmental risks of the pesticide are no longer acceptable, appropriate measures will be taken, ranging from minor label changes to discontinuation of the product.

There were no incident reports submitted for dithiopyr as of 27 May 2008.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Based on its physical-chemical properties (Section 2.2), dithiopyr has low solubility in water, is not likely to volatilize from moist soil or water surfaces under field conditions and has a potential for bioaccumulation in organisms. Environmental fate data for dithiopyr are summarized in Table 1 of Appendix VIII. Dithiopyr is stable to hydrolysis at environmentally relevant pHs. Dithiopyr has high affinity to soil, therefore, is not mobile. Dithiopyr is stable to phototransformation in soil but undergoes phototransformation in the water and air. The major transformation products are the Monoacid, Reverse Monoacid and Diacid (Appendix IX). Dithiopyr is stable to biotransformation in aquatic environments being mostly absorbed into the sediment.

Laboratory studies on adsorption/desorption and soil column leaching indicate that dithiopyr is not mobile in soil. Field studies conducted in Canada detected residues of dithiopyr in only the top 15 cm deep soil layer. Canadian water monitoring data (Appendix VII) have shown no detections of dithiopyr in surface water and in groundwater.

4.2 Effects on Non-Target Species

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. EECs are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models that take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from terrestrial and aquatic habitats, including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (e.g. direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level risk quotient is below the level of concern, the risk is considered negligible, and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies and probabilistic risk-assessment methods. Refinements to the risk-assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Effects on Terrestrial Organisms

A risk assessment of dithiopyr to terrestrial organisms was based upon an evaluation of toxicity data on dithiopyr to earthworms (acute), bees (acute contact), two species of birds (acute oral, dietary and chronic), two species of mammals (acute oral, dietary and chronic) and ten species of terrestrial plants (seed germination, seedlings emergence and vegetative vigour). A summary of terrestrial toxicity data for dithiopyr is presented in Appendix VIII, Table 2. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with dithiopyr.

Dithiopyr demonstrated no adverse toxicological effects on terrestrial invertebrates and birds on an acute oral, dietary and reproductive basis. Dithiopyr has a potential adverse effect on mammals on chronic basis (dietary and reproductive). As dithiopyr is a herbicide, adverse effects to non-target terrestrial plants are expected. Plant emergence and vegetative vigour studies conducted with ten plant species indicated that, although the seeds of most plant species emerged successfully, plants exposed to dithiopyr did not follow normal growth patterns. No toxicity studies conducted with dithiopyr transformation products were available for review.

The screening level risk assessment in Appendix VIII, Table 3, indicated that exposure to dithiopyr does not pose a risk to terrestrial invertebrates or birds. However, the risk of chronic effects for mammals was identified. As a result, a refinement of the risk assessment was conducted taking into consideration the exposure concentrations of dithiopyr that could be present in terrestrial habitat directly adjacent to the application field through drift of spray. Spray drift data for a medium American Society of Agricultural Engineers (ASAE) droplet size, as is generally used in groundboom applications of herbicides, indicate the maximum amount of spray that will drift one metre down wind from the point of application during spraying is 6%. Using this percent drift, the off-site EECs for dithiopyr were calculated. Based on this refinement, dithiopyr exceedance of the LOC was reduced to 26 times from 427 times. However, taking under consideration that dissipation of dithiopyr from turf grass is relatively quick and that a peak concentration was used in the risk characterization, the expected exposure will be less than the effects endpoints of concern

shortly after application. Based on these considerations, the PMRA has concluded that there is minimal risk of chronic effects. Table 4 (Appendix VIII) summarizes the refined risk assessment from dithiopyr to mammals.

As would be expected, the herbicide dithiopyr poses a risk to non-target terrestrial plants. The screening level risk assessment indicated that RQ exceeded the LOC by as much as 192 times. As a result, a refinement of the risk assessment was conducted taking into consideration the concentrations of dithiopyr that could be present in terrestrial habitat directly adjacent to the application field through drift of spray. Based on this method of refinement, dithiopyr poses a reduced risk to non-target terrestrial plants directly adjacent to the application field. Exceedance of the LOC was reduced to 11.5 times from 192 times. Further refinement was conducted using Sensitivity Species Distribution (SSB) analysis which indicated that LOC exceedance was further reduced to 7. Buffer zones will be required to mitigate the risk of dithiopyr to non-target terrestrial plants. Appendix VIII, Table 4 summarizes the refined risk assessment from dithiopyr to non-target terrestrial plants.

4.2.2 Effects on Aquatic Organisms

Risk to aquatic organisms, acute and chronic, is based on an evaluation of toxicity data on dithiopyr for four freshwater species (one invertebrates, two fish and one algae). A summary of aquatic toxicity data for dithiopyr are presented in Appendix VIII, Table 2. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with dithiopyr.

Dithiopyr is toxic to freshwater invertebrates and fish on an acute basis. Dithiopyr shows toxic effects to fish in the early life-cycle study. Acute and early life-cycle toxic effects on amphibians are expected based on surrogate data from fish studies. As dithiopyr is a herbicide, adverse effects to non-target aquatic plants are also expected. Dithiopyr affected biomass and cell density of freshwater algae. Data on aquatic vascular plants were not available.

The risk assessment was conducted using data for the most sensitive freshwater organisms tested *Daphnia magna*, bluegill sunfish (*Lepomis macrochirus*), rainbow trout (*Oncorhynchus mykiss*) and green alga (*Selenastrum capricornutum*).

The screening level risk assessment indicated that dithiopyr does pose a risk to freshwater fish, amphibians (based on surrogate data from fish studies) and algae. The RQs exceeded LOCs by 1.25-8 times at the application rate of 558 g a.i./ha. Thus, a refined risk assessment was triggered. The refined assessment indicated negligible risk as the exceedance of the LOCs are less then 1 from spray drift and from runoff. Table 5 (Appendix VIII) summarizes the risk assessment from dithiopyr to aquatic organisms. In Appendix VIII, Tables 6 and 7 summarize the refined risk to aquatic organisms from dithiopyr spray drift and runoff, respectively.

5.0 Value

5.1 Value of Dithiopyr

Crabgrass is a troublesome weed in turf. Dithiopyr provides both pre-emergence and early postemergence control of crabgrass in established turf. It provides a wider application window than alternative crabgrass control products used in turf. In addition, the application rate of dithiopyr is usually lower than that of alternative crabgrass control products.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's *Toxic Substances Management Policy*, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the

environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, dithiopyr was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of dithiopyr were also considered, including major transformation products formed in the environment, microcontaminants in the technical product and formulants in the end-use products. Dithiopyr and its transformation products were evaluated against the following Track 1 criteria:

- persistence in soil ≥182 days;
- persistence in water ≥182 days;
- persistence in sediment ≥365 days;
- persistence in air ≥2 days;
- bioaccumulation log K_{ow} ≥5; or
- bioconcentration factor (BCF) ≥5000 (or bioaccumulation factor (BAF) ≥5000).

For dithiopyr or its transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met. The technical product and end-use product, including formulants, were assessed against the contaminants identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641-2643: List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern, Part 3 Contaminants of Health or Environmental Concern.

The PMRA has reached the following conclusions.

- Dithiopyr does not meet all Track 1 criteria. Dithiopyr does meet the Track 1 criteria for persistence because the half-life values in air (41 days), water/sediment (390-490 days) and soil (523-2300 days) exceed the TSMP Track 1 criteria for water, sediment and soil. Dithiopyr does not meet the Track 1 criterion for bioaccumulation as its *n*-octanol-water partition coefficient (log K_{ow} 4.75) and BCF (81-930) are below the Track 1 criterion. Although the Track 1 criterion is met for persistence, the Track 1 criterion for bioaccumulation is not met; therefore, dithiopyr does not meet all Track 1 criteria, and is not considered a Track 1 substance.
- Dithiopyr does not form any transformation products that meet the Track 1 criteria.
- There are no Track 1 formulants in the technical product or end-use product.
- There are no Track 1 contaminants in the technical product or end-use product.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, formulants and contaminants in the technical and end-use products are assessed against the formulants and contaminants identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641-2643: List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern. The following assessment refers to the formulants and contaminants in Part 1 and Part 2 of the list.

Technical grade dithiopyr and the end-use product Dimension Turf Herbicide do not contain any formulants or contaminants of health or environmental concern.

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7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for dithiopyr is adequate to define the majority of toxic effects that may result from exposure to dithiopyr. In rats and rabbits, dithiopyr was not carcinogenic, genotoxic, neurotoxic or teratogenic. There is low level of concern for potential prenatal and postnatal toxicity associated with dithiopyr. The liver and kidneys were the main targets of toxicity by the oral route in mice, rats and dogs.

Effects on liver weights were also seen following exposure via the dermal route in rats. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

7.1.1 Occupational Risk

Risk estimates associated with mixing and loading and applying dithiopyr are not of concern. Postapplication risks to workers are not of concern; the minimum 12-hour restricted-entry interval (REI) is proposed for all uses, with the exception of golf courses where entry is restricted until the spray has dried.

7.1.2 Dietary Risk from Food

Dithiopyr is not registered for use on food crops, so a dietary risk assessment was not conducted.

7.1.3 Dietary Risk from Drinking Water

Risk estimates for exposure from drinking water are not of concern. All subpopulations had an exposure estimate that was less than 100% of the ADI.

7.1.4 Residential Risk

Risk estimates associated with residential application and postapplication exposure are not of concern.

7.1.5 Aggregate Risk

An aggregate acute risk was not required as there are no acute toxic endpoints of concern. Aggregate (drinking water and residential) short-term risk was not of concern. All subpopulations had an ARI that was greater than one.

7.2 Environmental Risk

Dithiopyr absorbs very strongly to soil and particles; therefore, it is persistent in most soils and water/sediment systems. There is also a potential that dithiopyr may appear in surface water through runoff. The risk assessment of dithiopyr indicates that adverse effects on non-target terrestrial and aquatic organisms may occur. To reduce the effects of dithiopyr in the environment, mitigation in the form of precautionary label statements and buffer zones are required.

7.3 Value

From the value perspective, dithiopyr is acceptable for continued registration.

8.0 Proposed Regulatory Decision

The PMRA is proposing continued registration of products containing dithiopyr for sale and use in Canada provided new risk-reduction measures are adopted.

8.1 Proposed Regulatory Actions

8.1.1 Proposed Regulatory Action Related to Human Health

The PMRA has determined that the drinking water risks, worker and non-occupational risks during mixing, loading, application and after dithiopyr is applied are acceptable, provided that the mitigation measures listed in Appendix X are implemented.

8.1.1.1 Proposed Mitigation for Occupational Handlers

The following mitigation measures are required for all commercial class products containing dithiopyr.

- Only one application is permitted per season
- An REI of 12 hours for all crops except golf courses
- The REI for golf courses: Do not re-enter until spray has dried

8.1.1.2 Proposed Mitigation for Non-Occupational Handlers

All domestic class granular-fertilizer products containing dithiopyr must also be limited to one application per season.

8.1.2 Proposed Regulatory Action Related to Environment

The risk assessment has indicated that adverse effects on non-target terrestrial plants and aquatic organisms are expected. To reduce the effects of dithiopyr in the environment, mitigation in the form of precautionary label statements and buffer zones are required. Environmental mitigation statements are listed in Appendix X.

8.1.3 Proposed Regulatory Action Related to Value

At this time, no regulatory action is proposed for dithiopyr as a consequence of the value assessment.

8.2 Additional Data Requirements

No additional data are required for dithiopyr at this time.

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List of Abbreviations

↑
: increase

↓
: decrease

♂
: male

♀
: female

^{14}C
: carbon 14

ADI
: acceptable daily intake

a.i.
: active ingredient

ALP
: alkaline phosphatase

amu
: atomic mass unit(s)

ARI
: aggregate risk index

ASAE
: American Society of Agricultural Engineers

ATPD
: area treated per day

AUC
area under the curve
BAF
bioaccumulation factor
BCF
bioconcentration factor
BUN
blood urea nitrogen
bw
body weight
bwg
body-weight gain
°C
degree(s) Celsius
cm
centimetre(s)
CAF
composite assessment factor
CAS
Chemical Abstracts Service
CHO
Chinese hamster ovary cells
d
day(s)
DACO
data code
DNA
deoxyribonucleic acid
EC
emulsifiable concentrate
EC_{25}
effective concentration on 25% of the population
EC_{50}
effective concentration on 50% of the population
EEC
estimated environmental exposure concentration
F_0
parental generation
F_1
first filial generation
F_2
second filial generation
FC
food consumption
g
gram(s)
GD
gestation day
GI
gastrointestinal
GIT
gastrointestinal track
GOT
glutamate oxaloacetate transaminase
GPT
glutamic-pyruvic transaminase
ha
hectare(s)

HC_5
hazard concentration to 5%
HCT
hematocrit
HGB
hemoglobin
hr(s)
hour(s)
HGPRT
hypoxanthine-guanine phosphoribosyl transferase
i.p.
intraperitoneal
i.v.
intravenous
IUPAC
International Union of Pure and Applied Chemistry
K^+
potassium
K_d
adsorption coefficient
kg
kilogram(s)
K_{oc}
organic carbon partition coefficient
K_{ow}
n-octanol-water partition coefficient
L
litre(s)
LEACHM
Leaching Estimation and Chemistry Model
LC_{50}
lethal concentration to 50%
LD_{50}
lethal dose to 50%
LOAEL
lowest observed adverse effect level
LOC
level of concern
m
metre(s)
m^2
metre(s) square
m^3
metre(s) cube
MCH
mean corpuscular hemoglobin
MCV
mean corpuscular volume
mg
milligram(s)
M/L/A
mixers/loaders/applicators
mL
millilitre(s)
min
minutes
MOE

margin of exposure

mPa
milliPascal(s)

N/A
not applicable

NAWQA
National Water Quality Assessment (Program)

ng
nanogram(s)

NOAEL
no observed adverse effect level

NOEC
no observed effect concentration

NZW
New Zealand White

OC
organic carbon

OM
organic matter

ORETF
Outdoor Residential Exposure Task Force

pH
-log10 hydrogen ion concentration

PHED
Pesticide Handlers Exposure Database

PMRA
Pest Management Regulatory Agency

PND
postnatal day

PPE
personal protective equipment

ppm
parts per million

PRVD
Proposed Re-evaluation Decision

PRZM/EXAMS
Pesticide Root Zone Model/Exposure Analysis Modelling System

RBC
red blood cells

REI
restricted-entry interval

RQ
isk quotient

S9
mammalian metabolic activation system

SD
Sprague Dawley

STORET
Storage and Retrieval Database

SSD
sensitivity species distribution

TC
transfer coefficient

TSMP
Toxic Substances Management Policy

TTR
turf transferable residues

µg

microgram(s)

UDS

unscheduled

DNA

synthesis

USEPA

United States Environmental Protection Agency

UV

ultraviolet

wk

week

wt(s)

weight(s)

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

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

[3] "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."

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

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

Date Modified: 2009-07-03