Proposed Re-evaluation Decision PRVD2010-13

Triforine

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Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario
K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the fungicide triforine, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the use of triforine on roses and ornamentals in Canada.

An evaluation of available scientific information found that products containing triforine for use on outdoor roses and ornamentals do not present unacceptable risks to human health or the environment when used according to label directions. For the currently registered food uses, the evaluation of the available scientific information found that the use of triforine does not pose risks of concern to occupational handlers, or to the environment, when used according to label directions. As a condition of the continued registration of products containing triforine, new risk-reduction measures must be included on the labels of all products. Additional data are being requested as a result of this re-evaluation.

Risks from dietary and aggregate exposure to triforine will be assessed by the PMRA in the future and will be communicated in a separate document. It should be noted that the registration status of triforine and its end-use products registered in Canada might change as a result of the outcome of these risk assessments.

This proposal affects all end-use products containing triforine registered in Canada. Once the re-evaluation decision is made, the 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 triforine 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 assessment of triforine.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

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

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health *and* the environment. Regulatory Directive DIR2001-03, *Pest Management Regulatory Agency Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

Triforine, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

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 (for example, the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in the 2008 RED, the USEPA concluded that triforine was eligible for continued registration provided risk-reduction measures were adopted. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED were an adequate basis for the re-evaluation of ornamental uses of triforine in Canada, when applied using hand-held equipment. Additional human health risk assessments (occupational exposure) were conducted by the PMRA in order to evaluate the eligibility for continued registration of the uses not covered by the USEPA RED. As noted above, a dietary risk assessment, including a consideration of aggregate exposure to triforine will be conducted by the PMRA in the future. The USEPA RED was also an adequate basis for the evaluation of ecological exposure and risk for all the registered uses of triforine in Canada.

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

What Is Triforine?

Triforine is a systemic fungicide that is used to control diseases such as black spot, rust, and powdery mildew in blueberries, cranberries, Saskatoon berries, stone fruits, apple nursery stocks and non-bearing apple trees, as well as on outdoor roses and ornamentals. Triforine is applied using airblast sprayer, groundboom and ground spray equipment by farm workers. In Eastern Canada only, it can be applied aerially on blueberries.

Health Considerations

Can Approved Uses of Triforine Affect Human Health?

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

People could be exposed to triforine by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which 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 exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that the use of triforine on roses and ornamentals was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required. Results from occupational risk assessments conducted by the PMRA indicated that the use of triforine on food crops was unlikely to affect the health of occupational handlers provided that risk-reduction measures were implemented.

Environmental Considerations

What Happens When Triforine Is Introduced Into the Environment?

Triforine is unlikely to affect non-target organisms when used according to the revised label directions.

Non-target organisms could be exposed to triforine in the environment. Environmental risk is assessed by the risk quotient method—the ratio of the estimated environmental concentration to the relevant effects endpoint of concern. In this screening level assessment, the resulting risk quotients are compared to corresponding levels of concern. A risk quotient less than the level of concern is considered a negligible risk to non-target organisms, whereas a risk quotient greater than the level of concern indicates some potential risks of concern.

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. As a result of the re-evaluation of triforine, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- Label statements to minimize bystander and domestic animal exposure
- Additional label statement prohibiting the use of triforine in greenhouses

Environment

- Additional advisory label statements to reduce potential surface and groundwater contamination
- Buffer zones to protect non-target, sensitive aquatic habitats
- Advisory label statements regarding potential toxicity to non-target organisms
- Changes to maximum number of yearly applications on roses and ornamentals

A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision.

What Additional Scientific Information Is Required?

In order for the PMRA to complete terrestrial buffer zone calculations and to confirm aquatic buffer zone calculations, data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of this active ingredient must provide these data or an acceptable scientific rationale to the PMRA within the timeline specified in the decision letter. Appendix I lists all data requirements.

Next Steps

Before making a re-evaluation decision on triforine, 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[2] document that 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.

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

Science Evaluation

1.0 Introduction

Triforine is a systemic fungicide, which acts by inhibition of sterol biosynthesis in fungal membranes.

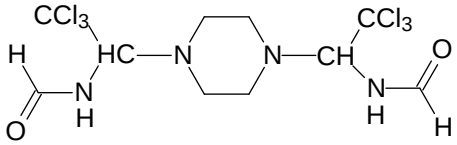
Following the re-evaluation announcement for triforine, the registrant of the technical grade active ingredient in Canada indicated that they intended to provide continued support for all uses included on the label of commercial class end-use product registered in Canada.

The PMRA used recent assessments of triforine from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for triforine, dated March 2008, as well as other information on the regulatory status of triforine in the United States can be found on the USEPA Pesticide Registration Status page at www.regulations.gov (Docket Folder EPA-HQ-OPP-2008-0196).

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity

Identity of the Technical Grade Active Ingredient

Common name	Triforine
Function	Fungicide
Chemical family	Piperazines
Chemical name	
1 International Union of Pure and Applied Chemistry (IUPAC)	N,N'-[piperazine-1,4-diylbis[(trichloromethyl)methylene]] diformamide
2 Chemical Abstracts Service (CAS)	N,N'-[1,4-piperazinediylbis(2,2,2-trichloroethylidene)]bis formamide
CAS Registry Number	26644-46-2
Molecular formula	$C_{10}H_{14}Cl_6N_4O_2$
Structural formula	
Molecular weight	434.96 amu

Purity of the technical grade active ingredient	99.15% nominal
Registration Number	20333

Based on the manufacturing process used, contaminants of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties

Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure	6.0×10^{-4} mm Hg
Henry's law constant	2.5 Pa m^3 mol^{-1}
Solubility in water	9 ppm
***n*-Octanol–water partition coefficient**	log K_{ow} = 2.2
Dissociation constant	10.6

2.3 Comparison of Use Patterns in Canada and the United States

Triforine is a systemic fungicide registered in Canada to control diseases such as black spot, rust, and powdery mildew. It acts by inhibition of sterol biosynthesis in fungal membranes. It is used on lowbush and highbush blueberries, cranberries, Saskatoon berries, stone fruits (cherries, peaches, plums and prunes), apple nursery stocks and non-bearing apple trees, as well as on outdoor roses and ornamentals. This product is formulated as an emulsifiable concentrate, and can be applied using airblast sprayer, groundboom and other conventional groundspray equipment and, in Eastern Canada only, it can be applied aerially on blueberries. In Canada, triforine can be applied as follows:

- at an application rate of 0.190 g a.i./L of water on roses and ornamentals (the maximum number of yearly applications is not specified on the label);
- up to three applications per year at a rate of 475 g a.i./ha on stone fruits;
- up to five applications per year at a rate of 475 g a.i./ha on apple nursery stocks and non-bearing apple trees;
- up to four applications per year at a rate of 570 g a.i./ha on cranberries and blueberries; and
- one application per year at a rate of 570 g a.i./ha on Saskatoon berries.

The American and Canadian use patterns were compared. The Canadian formulation type and the use of triforine on outdoor roses and ornamentals using hand-held equipment are encompassed by those registered in the United States. In the United States, products containing triforine can be purchased and used by homeowners, whereas domestic class products are not currently registered in Canada. The use of triforine on food crops (including apple nursery stocks and non-bearing apple trees) registered in Canada are not encompassed by the American use pattern. However, the maximum Canadian application rate is similar to the American maximum rate, which was used by the USEPA to assess ecological exposure and risk. Based on the above, it was concluded that the USEPA RED for triforine is an adequate basis for the re-evaluation of ornamental uses of triforine in Canada, when applied using hand-held equipment. The USEPA RED is also an adequate basis for the evaluation of ecological exposure and risk. Additional occupational exposure and risk assessments were conducted by the PMRA in order to evaluate the eligibility for continued registration of the uses not covered by the USEPA RED. A dietary risk assessment, including a consideration of aggregate exposure to triforine will be conducted by the PMRA in the future and will be communicated in a separate document.

All current uses are being supported by the registrant. Appendix II lists all triforine products that are registered as of 12 March 2010, under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In their 2008 RED, the USEPA concluded that the end-use products formulated with triforine met the safety standard under the American *Federal Insecticide, Fungicide and Rodenticide Act* and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended product labels.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to triforine may occur through consumption of food and water, while working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, the PMRA considers two key factors: the levels at which 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).

The USEPA's toxicological endpoints for assessing risk to human health are summarized in Appendix III. Triforine was classified as ''suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential'' by the USEPA. Therefore, quantification of human carcinogenic risk was not required for triforine. As noted above, a dietary risk assessment, including a consideration of aggregate exposure will be conducted by the PMRA in order to evaluate the acceptability of the food uses not covered by the USEPA RED. Should there be a revision of toxicological endpoints selected for risk assessments in the future, this may impact the occupational and residential exposure and risk assessments described below.

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure. This is compared to a target margin of exposure incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated margin of exposure is less than the target margin of exposure, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

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

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

The USEPA did not identify a dermal endpoint of concern, and did not expect long-term inhalation exposure based on the triforine use pattern. Therefore, occupational risk was not assessed for these routes of exposure.

Among the scenarios assessed in the RED, the following were considered relevant to the Canadian outdoor use of triforine on roses and ornamentals, when applied via hand-held equipment:

- mixing/loading and application of liquids using a high pressure handwand application;
- mixing/loading/applying liquids using a hose-end or low-pressure handwand sprayer (ground-directed garden applications);
- mixing/loading/applying liquids using a hose-end or low pressure handwand sprayer (tree/ornamental applications); and
- mixing/loading/applying liquids using a garden backpack sprayer or sprinkler can.

Handler exposure analyses were performed using surrogate data and assuming workers were wearing a long-sleeved shirt and long pants. Assessments were conducted using surrogate data from the Pesticide Handler Exposure Database (PHED) and the Outdoor Residential Exposure Task Force (ORETF). Short- and intermediate-term inhalation risks were based on maximum triforine application rates of 0.52 kg a.i./ha. Results indicated that occupational exposures and risks were not of concern. Margins of exposure ranged between 9700 and over one million.

The RED adequately addressed exposure scenarios associated with the use of products containing triforine on outdoor roses and ornamentals in Canada, when applied using hand-held equipment, and conclusions derived from the RED apply to the Canadian situation.

The PMRA generated short- and intermediate-term inhalation margins of exposure for the Canadian uses of triforine on blueberries, cranberries, Saskatoon berries, stone fruits, and apple nursery stocks and nonbearing apple trees, and the use of triforine on roses and ornamentals using groundboom equipment, which were not covered by the RED. Margins of exposure were generated using the USEPA inhalation endpoint in conjunction with Canadian assumptions for unit exposure values, daily treated area and maximum application rates. Canadian potential occupational handler exposure scenario for the use of triforine on these crops can result from the following:

- mixing/loading and/or application of liquids using groundboom spray equipment on lowbush blueberries, cranberries, Saskatoon berries, apple nursery stocks, nonbearing apple trees, or roses and ornamentals;
- mixing/loading and/or application using airblast spray equipment on highbush blueberries, cranberries, Saskatoon berries, stone fruits, apples nursery stocks, or non-bearing apple trees; and
- mixing/loading and/or application using aerial spray equipment on blueberries.

Results indicated that occupational exposures and risks were not of concern. Margins of exposure ranged between 2706 and 84 737.

Based on the risk assessments discussed above, risks of concern are not expected for handlers for the current registered uses of triforine in Canada. As triforine is not registered for use in greenhouses in Canada, the PMRA is requiring that a statement prohibiting such a use be added to the product label. No additional mitigation measures are required by the PMRA with regards to occupational handler exposure. The proposed label amendments are listed in Appendix IV.

3.1.1.2 Postapplication Exposure and Risk

The USEPA considered inhalation postapplication exposure to triforine to be negligible because the dilution factor outdoors is considered infinite. No dermal endpoint of concern was identified by the USEPA. Based on this, a quantitative risk assessment was not conducted for occupational postapplication exposure to triforine.

The label of the end-use product registered in Canada indicates that this product is an eye and skin irritant and currently requires a 48-hour restricted-entry interval. No additional mitigation measure is required by the PMRA with respect to postapplication exposure to triforine.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

There are no domestic class products containing triforine registered in Canada. Based on this, homeowners can be exposed to this active ingredient only when re-entering a treated site (for example, roses and ornamentals in residential settings that were treated by professional applicators).

A dermal endpoint of concern was not identified by the USEPA for triforine. Children were not expected to routinely contact treated plants and engage in mouthing behaviours, therefore, exposure of toddlers via "hand-to-mouth" and "object-to-mouth" activities or through incidental soil ingestion was considered unlikely. The USEPA considered inhalation postapplication exposure to triforine to be negligible because the dilution factor outdoors is considered infinite. Based on this, the USEPA concluded that there were no concerns for residential postapplication exposure to triforine, and a quantitative risk assessment was not conducted. The USEPA required label statements to minimize bystander and pet exposure.

The RED adequately addressed potential exposure scenarios associated with the Canadian residential uses of triforine; thus, the conclusions derived from the RED are considered applicable to the Canadian uses of triforine on outdoor roses and ornamentals. Based on this, the PMRA requires additional label statements to minimize bystander and domestic animal exposure. The proposed label statements are listed in Appendix IV.

3.1.2.2 Exposure From Food and Drinking Water

Based on the registered use pattern, the USEPA did not expect chronic dietary exposure to triforine to occur. In the United States, all the registered uses of triforine are in residential settings on ornamentals (non-food sites). On this basis, the USEPA's exposure and risk assessment was based solely on exposure through the consumption of drinking water, and risk was assessed on an acute basis only.

Based on the USEPA's review of environmental fate data, triforine is moderately persistent in the environment and moderately mobile in soil. On this basis, it has a potential to leach into groundwater and can be expected to reach surface water through runoff or drift (see Section 3.2.1 for more details). In the RED, the USEPA reported that transformation in soil lead primarily to bound residues and carbon dioxide, but that laboratory studies showed that in some environments, other major degradates were possible. No information was available about fate properties of the degradates at the time of the RED, therefore, the USEPA's assessment considered the parent compound only.

Tier I screening level models FQPA Index Reservoir Screening Tool (FIRST) (surface water) and Screening Concentration in Ground Water (SCI-GROW) (groundwater) were used to quantify the upper bound concentrations for drinking water exposure. Estimated drinking water concentrations (EDWCs) were based on the assumption that the entire watershed had been treated with triforine at the maximum application rate (0.52 kg a.i./ha) with ground spray.

Two applications, with an application interval of 7 days, were assumed in this assessment. The reported EDWCs for annual average (from surface or ground water sources) were less than 1 ppb. Since the EDWC were based on conservative assumptions, and given the low acute oral toxicity of triforine, the USEPA considered that there was no concern for exposure from drinking water.

The PMRA searched the available Canadian water monitoring data, however, no data are available for triforine.

The USEPA's drinking water assessment is relevant to the Canadian use of triforine on outdoor roses and ornamentals, and conclusions derived from the RED apply to Canada. No additional mitigation measure is required by the PMRA with respect to exposure to triforine through drinking water from the use of triforine on outdoor roses and ornamentals.

The USEPA's assessment, however, does not encompass the Canadian food uses. Dietary exposure and risk from the consumption of food and water will be assessed by the PMRA in the future to determine the acceptability for continued registration of the registered food uses of triforine in Canada. Results from this risk assessment will be communicated in a separate document.

3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to triforine (namely, from food, water and residential exposures). Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures. Short- and intermediate-term aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

There are no domestic class products containing triforine registered in Canada. Based on this, homeowners can be exposed to this active ingredient only when re-entering a treated site, or through dietary exposure.

Aggregate exposure to triforine from ornamental uses was considered in the RED. The USEPA concluded that because there were no concerns from residential postapplication exposure or dietary exposure through drinking water, aggregate exposure to triforine from ornamentals uses is not expected to be of concern.

In Canada, triforine is also registered for use on food crops (blueberries, cranberries, Saskatoon berries and stone fruits); therefore, the Canadian potential aggregate exposure scenarios were not adequately addressed by the USEPA's aggregate risk assessment.

An aggregate exposure and risk assessment will be conducted by the PMRA in the future to determine the acceptability for continued registration of the registered food uses of triforine in Canada. Results from this risk assessment will be communicated in a separate document.

3.1.3 Cumulative Effects

The USEPA has not determined whether triforine has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that triforine does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Fate Characteristics

Triforine was found to be moderately persistent and mobile in soil, and to have the potential to reach aquatic environments by runoff, leaching or spray drift. Triforine was found to degrade rapidly in aquatic environments, and exposure in those environments was expected to be to the degradates rather than the parent compound. Data on physical/chemical properties, toxicity or environmental fate of the degradates were not available at the time of the RED; therefore, triforine was assumed to be stable to hydrolysis, and degradates were assumed to be of equal toxicity to the parent compound. Data for aquatic metabolism was not available at the time of the RED, so a conservative value was derived from the aerobic soil metabolism half-life, and used in assessments. Volatilisation and bioconcentration were not expected to be important fate processes.

3.2.2 Environmental Risk Assessment

To assess the ecological risk of triforine to both terrestrial and aquatic non-target plants and animals, the USEPA calculated risk quotients (RQs) based on appropriate toxicity endpoints and expected environmental concentrations (EECs) and compared the resulting RQs to corresponding levels of concern (LOCs).

Risk assessments for pollinators and beneficial insects were not performed because triforine was found to be practically non-toxic to honey bees. As a result, the potential for triforine to have adverse effects on insects was expected to be low.

In the USEPA's assessment, the calculation of expected environmental concentration was based on one ground spray application at a rate of 0.52 kg a.i./ha, and/or 20 weekly applications at the same rate. The USEPA determined the following:

- Chronic RQs exceeded the LOC for birds feeding on short grass, tall grass and broafleaf forage and small insects, and for small mammals feeding on short grass. The USEPA considered, however that chronic risks may have been overestimated.

Acute and chronic risks assessments were not performed for estuarine/marine fish and invertebrates, and chronic risk was not assessed for freshwater fish and invertebrates, due to lack of data. Based on the available acute data for freshwater animals, risks of concern were not expected for aquatic animals. Risk assessments were not conducted for terrestrial and aquatic vascular plants due to a lack of data; however, information from the open literature and incident data suggest that triforine may cause phytotoxic effects on non-target plants.

Based on concerns for risks to birds, mammals, as well as aquatic and terrestrial plants, the USEPA required mitigation measures to reduce ecological exposure, including limiting the maximum number of applications on roses and ornamentals, and additional label statements. Terrestrial and aquatic plant toxicity data was also required by the USEPA.

The aerial application of triforine on blueberries registered in Canada was not encompassed by the USEPA's assessment, and the Canadian maximum application rate (0.57 kg a.i./ha) is slightly higher than the rate used in the RED assessments. However, assumptions used in the USEPA's assessment were conservative (for example, 20 weekly applications at the maximum rate) and most likely overestimate exposure to triforine in Canada. On this basis, the USEPA's conclusion are considered relevant to the Canadian situation. The PMRA is proposing the requirement of the following mitigation measures:

- adding advisory statements, and statements regarding runoff and contamination of groundwater on the product label
- limiting the number of applications per year on roses and ornamentals to 3

In addition, the PMRA has calculated aquatic buffer zones using the toxicity data provided in the RED and is proposing a requirement to minimize spray drift to non-target species during applications. The proposed label amendments are listed in Appendix IV. Inputs to buffer zone models are described in Appendix V. Terrestrial buffer zones were not calculated by the PMRA because toxicity data were not available for terrestrial plants. In order to address terrestrial plant data deficiencies to assess the risks of triforine to sensitive terrestrial habitats, and for calculation of terrestrial buffer zones and confirmation of aquatic buffer zones, the PMRA is proposing that the following data be requested:

- DACO 9.8.4: Terrestrial vascular plants
- DACO 9.8.5: Aquatic vascular plants

3.3 Pest Control Product Policy Considerations

3.3.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances (those that meet all four criteria outlined in the policy, namely, CEPA-toxic or equivalent, predominantly anthropogenic, persistent and bioaccumulative.

During the re-evaluation process, triforine 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,* and evaluated against the Track 1 criteria for persistence and bioaccumulation. In order for triforine or its transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met.

The PMRA concluded that triforine does not meet the Track 1 criterion for persistence in soil, as its half-life values in soil (23–56 days) are below the Track 1 criterion of 182 days. Triforine does not meet the Track 1 criterion for persistence in air because volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on its vapour pressure (6.0×10^{-4} mm Hg) and Henry's Law constant (2.5 Pa m^3 mol^{-1}). Given that its octanol-water partition coefficient (log K_{ow} of 2.2) is below the Track 1 criterion of 5, triforine does not meet the criterion for bioaccumulation. Given that triforine does not meet all Track 1 criteria, it is not considered a Track 1 substance.

3.3.2 Contaminants and Formulants of Health or Environmental Concern

During the re-evaluation of triforine, contaminants in the technical are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*. The list is used as described in the PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including: DIR99-03; and DIR2006-02, and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has concluded that technical grade triforine does not contain any contaminants of health or environmental concern identified in the *Canada Gazette*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

4.0 Incident reports

Starting 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.

Available information from the PMRA database indicates that one report of an incident related to the use of triforine was submitted to the PMRA in 2008. This incident occurred in the United States and involved the death of a domestic animal. The causality of this incident could not be established by the PMRA since the incident did not occur in Canada and involved exposure to at least three active ingredients.

5.0 International Status of Triforine

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 30 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies. They compare experiences, share information and analyses, seek answers to common problems, and work to co-ordinate domestic and international policies to allow for consistency in practices across nations.

Based on the current available information on the status of triforine in other countries, this chemical is registered for use in New Zealand on food crops, roses and ornamentals. Triforine is also registered for use in Australia on food crops, roses and ornamentals.

Triforine was not supported by the manufacturers when reviewed as part of the European Commission Programme (Regulation 2002/2076) and, as a result, has been withdrawn from Annex I to Council Directive 91/414/EEC, which harmonizes the regulation of plant protection products in the European community.

Triforine is scheduled for re-evaluation by the Food and Agriculture Organization of the United Nations and the World Health Organization (FAO/WHO) in 2013.

In 2008, the United States assessed uses of triforine on roses and ornamental plants and concluded that using triforine as a pesticide does not result in unreasonable adverse effects to human health or the environment, provided the risk-reduction measures recommended in its RED document were implemented.

6.0 Proposed Re-evaluation Decision

The PMRA has determined that the use of triforine on outdoor roses and ornamentals is acceptable for continued registration. The PMRA has also determined that the currently registered food uses, which include blueberries, cranberries, Saskatoon berries, stone fruits, apple nursery stocks and non-bearing apple trees, do not pose risks of concern to occupational handlers, or to the environment, when used according to label directions. As a condition of the continued registration of products containing triforine, new risk-reduction measures must be included on the labels of all products. These measures are required to further protect human health and the environment. The labels of Canadian end-use product must be amended to include the label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrant of the technical grade active ingredient is required to submit data as a condition of continued registration under Section 12 of the *Pest Control Products Act*. Appendix I lists the proposed data requirements.

A dietary risk assessment, including a consideration of aggregate exposure will be conducted by the PMRA in the future and will be communicated in a separate document. It should be noted that the registration status of triforine and its end-use products registered in Canada might change as a result of the outcome of these risk assessments.

7.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, *Pest Management Regulatory Agency Re-evaluation Program,* and DACO tables can be found on the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800 267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document for triforine (Docket ID. 2008-0196) is available on the USEPA Pesticide Registration Status page at www.regulations.gov.

Information on the European Commission's Annex I of Directive 91/414/EEC is available at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32002R2076:EN:HTML.

The Australian Pesticides and Veterinary Medecines Authority's report on the review of triforine is available at http://www.apvma.gov.au/products/review/docs/triforine_report.pdf.

Information on the FAO/WHO re-evaluation schedule is available at: http://www.fao.org/.

List of Abbreviations

ADI	acceptable daily intake
a.i.	active ingredient
atm	atmosphere(s)
bw	body weight
CAS	Chemical Abstracts Service
DACO	data code
EDWC	estimated drinking water concentration
EEC	expected environmental concentration [also estimated environmental concentration]
FIRST	FQPA Index Reservoir Screening Tool
FQPA	*Food Quality Protection Act*
g	gram(s)
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LOAEL	lowest observed adverse effect level
LOC	level of concern
m^3	metre(s) cubed
mg	milligram(s)
mm Hg	millimetre mercury
MOE	margin of exposure
nm	nanometre
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PCPA	*Pest Control Products Act*
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
ppm	parts per million
RED	Reregistration Eligibility Decision
RQ	risk quotient
SCI-GROW	Screening Concentration in Ground Water
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency

Appendix I Additional Data Requirements

The following data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrant of triforine is required to provide these data or an acceptable scientific rationale to the PMRA for confirmation of aquatic buffer zones and calculation of terrestrial buffer zones within the timeline specified in the decision letter the PMRA will send.

- DACO 9.8.4: Terrestrial Vascular Plants - Seedling Emergence (USEPA OPPTS 850.4100 guideline) and Vegetative Vigour (USEPA OPPTS 850.4150 guideline).

- DACO 9.8.5: Aquatic Vascular Plants (USEPA OPPTS 850.4400 guideline)

These studies must be conducted according to the appropriate Office of Prevention, Pesticides and Toxic Substances (OPPTS) guidelines indicated.

Appendix II Registered Products Containing Triforine as of 12 March 2010

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
20333	Technical	Summit Agro (USA) Corporation	Technical Active Ingredient Funginex (Triforine)	Solid	99.15
27686	Commercial	Summit Agro (USA) Corporation	Funginex DC Fungicide	Emulsifiable concentrate	19

Appendix III Toxicological Endpoints used by the USEPA for Triforine Health Risk Assessments

Exposure Scenario (route and period of exposure)	Dose	Study	Target MOE [a]
All Dietary Scenarios	The USEPA did not expect any risk from this exposure scenario since no hazard was identified in any toxicity study. Based on the U.S. use pattern for triforine, acute and chronic dietary exposure was not anticipated by the USEPA.		
Incidental Oral Short- (1–30 days) and Intermediate-Term (1–6 months)	Based on the U.S. use pattern for triforine, incidental oral exposure was not anticipated by the USEPA.		
Dermal Short- (1-30 days) and Intermediate-Term (1–6 months)	The USEPA did not expect any risk from this exposure scenario since no hazard was identified in a 21-day dermal toxicity study conducted at the limit dose.		
Inhalation Short- (1–30 days) and Intermediate-Term (1–6 months)	NOAEL = 23 mg/kg bw /day (oral considered equivalent to inhalation)	Subchronic/chronic oral toxicity in the dog LOAEL = 120 mg/kg bw/day, based on decreased RBC, hematocrit, hemoglobin values, increased spleen weight, and siderosis in the liver, spleen and bone marrow.	100[b]
Cancer (oral, dermal, inhalation)	Classification: "Suggestive Evidence of Carcinogenicity, but not sufficient to assess human carcinogenic potential" based on two adequate rodent carcinogenicity studies. Quantification of human carcinogenic risk was not required by the USEPA for triforine.		

[a] Target MOE refers to desired margin of exposure for occupational or residential assessments.

[b] 10× uncertainty factor for interspecies extrapolation ; 10× uncertainty factor for intraspecies variability

NOAEL = No observed adverse effect level ; LOAEL = Lowest observed adverse effect level

Appendix IV Label Amendments for Products Containing Triforine

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

I) The following statements must be included in a section entitled **PRECAUTIONS**.

When the product is used in a residential setting:

DO NOT apply this product in a way that will contact any person or pet, either directly or through drift. Keep people and pets out of the area during application.

DO NOT allow pets to enter the treated area until the product has dried.

II) The following statements must be included in a section entitled **DIRECTIONS FOR USE**.

DO NOT use in greenhouses.

DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

The maximum number of applications per year allowed on roses and ornamentals is 3.

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground.

Airblast application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

Aerial application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 16 km/h at flying height at the site of application. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length **MUST NOT** exceed 65% of the wing- or rotorspan.

Buffer zones:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

Method of application	Crop		Buffer Zones (metres) Required for the Protection of Aquatic Habitat at Water Depths of:	
			Less than 1 m	Greater than 1 m
Field sprayer	Lowbush blueberries, cranberries, apple nursery stocks and nonbearing apple trees		1	0
Airblast	Cranberries, highbush blueberries, apple nursery stocks and nonbearing apple trees		1	0
Aerial	Highbush and lowbush blueberries	Fixed wing	1	0
		Rotary wing	1	0

III) The following statements must be included in a section entitled **ENVIRONMENTAL HAZARDS**.

TOXIC to aquatic organisms, birds and small wild mammals. Observe buffer zones specified under **DIRECTIONS FOR USE**.

To minimize surface water contamination when used on cranberries, all effluent water must be impounded and released only when levels of the active ingredient are < 1100 µg a.i./L.

The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (e.g., sandy soil) and/or the depth to the water table is shallow.

To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.

Avoid application when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

Appendix V Inputs to Buffer Zone Models

Table 1 Ground Use Data (from Canadian labels)

Crop	Formulation Type	Method of Application	Number of Application	Maximum Application Rate (g a.i./ha)	Minimum Application Interval (days)
Lowbush blueberries	Emulsifiable concentrate	Field (medium)	4	570	1st - 2nd appl.: 10 2nd - 3rd appl.: 20 3rd - 4th appl.: 10
Highbush blueberries	Emulsifiable concentrate	Airblast (early)	4	570	1st - 2nd appl.: 10 2nd - 3rd appl.: 20 3rd - 4th appl.: 10
Highbush blueberries	Emulsifiable concentrate	Airblast (late)	4	570	1st - 2nd appl.: 10 2nd - 3rd appl.: 20 3rd - 4th appl.: 10
Cranberries	Emulsifiable concentrate	Field (medium)	4	570	1st - 2nd appl.: 10 2nd - 3rd appl.: 30 3rd - 4th appl.: 10
Cranberries	Emulsifiable concentrate	Airblast (early)	4	570	1st - 2nd appl.: 10 2nd - 3rd appl.: 30 3rd - 4th appl.: 10
Cranberries	Emulsifiable concentrate	Airblast (late)	4	570	1st - 2nd appl.: 10 2nd - 3rd appl.: 30 3rd - 4th appl.: 10
Saskatoon berries	Emulsifiable concentrate	Field (medium)	1	570	–
Saskatoon berries	Emulsifiable concentrate	Airblast (early)	1	570	–
Saskatoon berries	Emulsifiable concentrate	Airblast (late)	1	570	–
Peaches, cherries, plums, prunes	Emulsifiable concentrate	Airblast (early)	3	475	5
Peaches, cherries, plums, prunes	Emulsifiable concentrate	Airblast (late)	3	475	5
Apple nursery stocks and non-bearing apple trees	Emulsifiable concentrate	Field (medium)	5	475	1st - 2nd appl.: 7 2nd - 3rd appl.: 7 3rd - 4th appl.: 10 4th - 5th appl.: 14
Apple nursery stocks and non-bearing apple trees	Emulsifiable concentrate	Airblast (early)	5	475	1st - 2nd appl.: 7 2nd - 3rd appl.: 7 3rd - 4th appl.: 10 4th - 5th appl.: 14

Crop	Formulation Type	Method of Application	Number of Application	Maximum Application Rate (g a.i./ha)	Minimum Application Interval (days)
Apple nursery stocks and non-bearing apple trees	Emulsifiable concentrate	Airblast (late)	5	475	1st - 2nd appl.: 7 2nd - 3rd appl.: 7 3rd - 4th appl.: 10 4th - 5th appl.: 14
Roses and ornamentals	Emulsifiable concentrate	Field medium	3	190	7

Table 2 Model Input Data for Aquatic and Terrestrial Buffer Zones (from 2008 RED)

Half-life for aquatic buffer zones	Aerobic water	123.8 days
Most sensitive fish endpoint for amphibian species risk assessment	Rainbow trout	1/10 LC_{50} = 1.1 mg a.i./L
Most sensitive freshwater species	Rainbow trout	1/10 LC_{50} = 1.1 mg a.i./L
Most sensitive estuarine/marine species	Rainbow trout	1/10 LC_{50} = 1.1 mg a.i./L
Half-life for terrestrial buffer zones	Aerobic soil	61.9 days
Most sensitive terrestrial plant species	No toxicity data available for terrestrial plants; terrestrial buffer zones can not be calculated.	

Table 3 Aerial Use Data (from Canadian Labels)

Crop	Formulation Type	Registration No.	Number of Applications	Rate of Application (g a.i./h)	Minimum Application Interval (days)
Blueberries	Emulsifiable concentrate	27686	4	570	1st - 2nd appl.: 10 2nd - 3rd appl.: 20 3rd - 4th appl.: 10

Table 4 Product Information for Aerial Use

Parameter	Value
Registration No. 27686	
Aircraft type	Fixed or rotary wing
ASAE spray quality	Crop (medium)
Carrier	Water
Product guarantee (g a.i./L)	190
Specific gravity of end-use product (g/L)	1.071
Minimum spray volume (L/ha)	50
Water content of product (%)	0
Wind speed (km/h)	16
Temperature (°C)	25
Relative humidity (%)	50

References

Studies considered in the Chemistry Assessment

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1301014	1998, Triforine (AC 902194) Technical Material: Description of the Materials Used to Produce the Product and of the Production Process Conform EPA Product Properties Test Guidelines OPPTS 830.1600 and OPPTS 830-1620, CFS 1998-045, MRID: n/a, DACO: 2.11.1