Proposed Re-evaluation Decision PRVD2013-04

Paclobutrazol

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the plant growth regulator paclobutrazol, 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 paclobutrazol for sale and use in Canada.

An evaluation of available scientific information found that products containing paclobutrazol do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of paclobutrazol uses, label amendments are proposed for all end-use products. No additional data are being requested at this time.

This proposal affects all end-use products containing paclobutrazol registered in Canada. Once the final 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 paclobutrazol and presents the reasons for the proposed re-evaluation decision. It also proposes label amendments 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 paclobutrazol.

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).

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 DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, presents the details of the cyclical re-evaluation approach, which is in line with the requirements of the *Pest Control Products Act*.

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

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

What Is Paclobutrazol

Paclobutrazol is a plant growth regulator that belongs to the triazole group of pesticides. It inhibits the rate of cell division through the inhibition of gibberellin and sterol biosynthesis. In Canada, it is registered for use on greenhouse container-grown ornamental annual bedding plants in cellpacks, and/or plug trays (begonia, celosia, coleus, impatiens, petunia and salvia), and in pots (geraniums, poinsettias, petunias and chrysanthemums) to produce more compact plants and to enhance flowering. Paclobutrazol is applied by growers or commercial applicators as a foliar spray or drench application using hand-held equipment.

Health Considerations

Can Approved Uses of Paclobutrazol Affect Human Health?

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

Potential exposure to paclobutrazol may occur when applying the product or by entering treated sites. Paclobutrazol is not registered for food use in Canada and, based on the registered use pattern, exposure from drinking water is expected to be limited. 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.

Toxicity endpoints established for technical paclobutrazol during the initial registration of products containing this active ingredient continue to meet the standards of modern science and current policy.

Quantitative occupational mixer/loader/applicator and postapplication exposure and risk assessments were recently conducted by the PMRA. These assessments meet the standards of modern science and current policy and adequately encompass the registered use pattern for paclobutrazol. Risks for occupational handlers are not of concern provided mitigation measures are implemented. Risks for postapplication workers are not of concern under current conditions of use.

Residential postapplication dermal exposure could occur through contact with bedding plants and plugs treated by professional applicators. Residential exposure and risk was qualitatively assessed and is not expected to be of concern. No mitigation measures are proposed.

Environmental Considerations

What Happens When Paclobutrazol Is Introduced Into the Environment?

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

Based on the registered use pattern, environmental exposure is expected to be limited and could occur only in the case of improper irrigation water disposal practices or the improper cleaning of spray equipment. Additional environmental advisory label statements are proposed to reduce potential surface water contamination.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of paclobutrazol, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

Revised personal protective equipment for workers

Environment

Additional advisory label statements to reduce potential surface water contamination

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

Next Steps

Before making a final re-evaluation decision on paclobutrazol, 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] 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

Paclobutrazol is a plant growth regulator. It is used to produce more compact plants and to enhance flowering and fruiting. Following application by foliar spray or by drench application onto the soil, paclobutrazol is taken up into the xylem through the leaves, stems, or roots, and translocated to growing sub-apical meristems. Paclobutrazol reduces internodal elongation by inhibiting gibberellin and sterol biosynthesis and hence the rate of cell division. This active ingredient belongs to the triazole group of pesticides.

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

The purpose of this re-evaluation is to review existing information on the active ingredient, paclobutrazol, and the currently registered paclobutrazol technical products and commercial class end-use products, to ensure that previous risk assessments meet the standards of modern science and current policy.

2.0 Paclobutrazol Profile

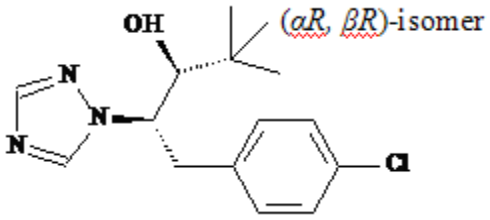
Currently registered products containing paclobutrazol are listed in Appendix I. All current uses are being supported by the registrants and were, therefore, considered in the re-evaluation of paclobutrazol.

Paclobutrazol is used on greenhouse container-grown ornamental annual bedding plants in cellpacks, and/or plug trays (begonia, celosia, coleus, impatiens, petunia and salvia) and in pots (geraniums, poinsettias, petunias and chrysanthemums). Paclobutrazol is applied as a foliar spray using hand-held equipment or via drench application. Paclobutrazol can be applied once at the maximum application rate (400 g a.i./ha), or up to 3 times (7–14 days apart) with the total amount applied not exceeding the maximum application rate. Paclobutrazol produces no phytotoxic effects when used as directed on the product labels. End-use products are formulated as liquids (solution and suspension).

3.0 The Technical Grade Active Ingredient, Its Properties and Uses

3.1 Identity

Table 1 Identity of the Technical Grade Active Ingredient

Common name		Paclobutrazol	
Function		Plant Growth Regulator	
Chemical family		Triazole	
Chemical name			
1	**International Union of Pure and Applied Chemistry (IUPAC)**	(2*RS*,3*RS*)-1-(4-chlorophenyl)-4,4-dimethyl-2-(1*H*-1,2,4-triazol-1-yl)pentan-3-ol	
2	**Chemical Abstracts Service (CAS)**	(α*R*,β*R*)-*rel*-β-[(4-chlorophenyl)methyl]-α-(1,1-dimethylethyl)-1*H*-1,2,4-triazole-1-ethanol	
CAS Registry Number		76738-62-0	
Molecular formula		$C_{15}H_{20}ClN_3O$	
Structural formula			
Molecular weight		293.80 amu	
Registration Number		24198	28550
Purity of the technical grade active ingredient		96.9%	99.3%

Based on the manufacturing process used, impurities 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.

3.2 Physical and Chemical Properties

Table 2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 20ºC	0.0017 mPa
Ultraviolet (UV) / visible spectrum	λ_{max} = 222 nm Not expected to absorb at λ >300 nm
Solubility in water at 20ºC	26 mg/L
***n*-Octanol–water partition coefficient**	Log K_{ow} = 3.2
Dissociation constant	Not applicable

4.0 Value

Paclobutrazol is one of a few plant growth regulators registered in Canada for use on container-grown ornamental bedding plants and plugs. It is a valuable tool to ornamental growers for managing plant growth thus producing more desirable compact plants.

5.0 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 paclobutrazol may occur through residential exposure, 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).

5.1 Toxicological Summary

In toxicokinetic studies, paclobutrazol administered orally was rapidly absorbed, metabolized and excreted, with no indication of tissue storage. In acute studies, technical paclobutrazol demonstrated slight to moderate acute toxicity by oral, dermal and inhalation routes of exposure, irritation potential to the skin and eye was slight to mild and paclobutrazol was not determined to

be a dermal sensitizer. Paclobutrazol caused reductions in body weight gain and increases in liver lesions in dietary short-term and two-year studies. Paclobutrazol did not demonstrate any evidence of genotoxic or oncogenic potential. In a two-generation reproduction study, paclobutrazol did not affect fertility or reproductive performance at doses which were maternally toxic. Teratogenicity studies in rats and rabbits revealed evidence of teratogenic effects at maternally toxic doses. Table 1 of Appendix II provides an overview of paclobutrazol toxicology endpoints used in human health risk assessments by the PMRA.

5.2 PCPA 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 pre- and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

Furthermore, as the worker population could include pregnant women, it is necessary to afford adequate protection of the foetus who may be exposed via its mother. Consequently, an additional uncertainty factor may be applied to worker exposure scenarios if available data identify concerns for potential effects on the young or if appropriate data are not available to adequately address the concerns.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database for paclobutrazol contains developmental toxicity studies in rats and rabbits and a two-generation reproductive toxicity study in rats. No data gaps were identified in the original toxicology review for technical paclobutrazol. No evidence of increased susceptibility was observed in offspring in the available two-generation reproductive toxicity study conducted with rats.

With respect to identified concerns relevant to the assessment of risk to infants and children, developmental effects were observed in rat and rabbit teratology studies. The rat developmental lowest observed effect level (LOEL) was set at 250 mg/kg bw/day based on cleft palate, with a NOEL of 100 mg/kg bw/day. The rabbit developmental LOEL was set at 125 mg/kg bw/day based on vertebral defects, with a no observed effect level (NOEL) of 75 mg/kg bw/day.

Risk characterization for all paclobutrazol exposure scenarios was based on a 28-day oral study in rats (NOEL of 2.5 mg/kg bw/day). Because the developmental effects were observed at much higher doses, the selected endpoint and target margin of exposure (MOE) of 100 are expected to be protective of potential developmental effects. No additional uncertainty factor is required for the protection of infants and children when using the 28-day oral study for risk assessment.

5.3 Dermal Absorption

The dermal absorption factor for use in paclobutrazol risk assessments was determined to be 19.3%, based on an in vivo dermal absorption study conducted in rats.

5.4 Occupational Exposure

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a 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, but mitigation measures to reduce risk would be required.

Workers can be exposed to paclobutrazol through mixing, loading or applying the plant growth regulator or when entering a treated site to conduct activities such as scouting and/or handling treated crops.

5.4.1 Mixer/Loader/Applicator Exposure and Risk

Workers can be exposed to paclobutrazol through mixing and loading, and when applying the dilute mixture via drench application or using hand-held spray equipment. Turnover for greenhouse ornamentals depends on the species grown, but also on production systems. Some facilities may, for example, specialize in a few species, whereas others may grow a variety of plants simultaneously or in sequence. Based on the above, and on the paclobutrazol use pattern (i.e., 1–3 applications per production cycle), there is potential for short- (<30 days) to long-term (>6 months) exposure to paclobutrazol for mixers, loaders and applicators.

A mixer/loader/applicator risk assessment was recently conducted by the PMRA. Daily exposure estimates for mixing/loading/applying were calculated based on the following assumptions:

- Unit exposure data for mixing, loading and/or applying a liquid (open pour) using backpack sprayer or low pressure handwand and wearing chemical-resistant coveralls over a long-sleeved shirt and long pants, and chemical-resistant gloves (PHED)
- Area treated per day of 1 ha
- Maximum application rate of 400 g a.i./ha
- 19.3% dermal absorption, 100% inhalation absorption (default)

Using the short-/immediate-term and long-term toxicological endpoints, the re-evaluation determined that combined dermal and inhalation MOEs ranged from 965 to 2,443 (target MOE = 100). On this basis, short- to long-term risks for workers mixing/loading and applying paclobutrazol are not of concern.

The risk assessment conducted by the PMRA encompasses the registered use pattern for paclobutrazol and continues to meet the standards of modern science and current policy. Based on the risk assessment, personal protective equipment consisting of chemical-resistant coveralls over a long-sleeved shirt and long plants, and chemical-resistant gloves is proposed when handling paclobutrazol. Current labels also require a NIOSH-approved respirator, however, based on the risk assessment, a respirator is not required for the protection of workers. The PMRA is proposing that this requirement be removed from end-use product labels.

5.4.2 Postapplication Exposure and Risk

Postapplication occupational risk assessments consider dermal exposure to workers entering treated agricultural sites to conduct agronomic activities involving foliar contact (for example, scouting). Based on the currently registered use pattern, a single application at the maximum approved rate or multiple applications (up to three) resulting in a total rate not exceeding the single maximum application rate, are allowed for each crop cycle in the greenhouse. Considering that a particular greenhouse operation can grow multiple crop cycles throughout the year, worker exposure duration could range from short- to long-term. Even though a worker may be exposed to paclobutrazol residues over a longer period of time, the daily exposure dose is expected to remain constant since no accumulation of paclobutrazol residues is anticipated (i.e., mature treated crops will be removed from the greenhouse and new plants will be introduced).

A postapplication risk assessment was recently conducted by the PMRA for the expansion of the paclobutrazol use pattern to include greenhouse poinsettia and chrysanthemum plugs. Dermal exposure estimates for workers entering treated sites to conduct various activities were calculated assuming default dislodgeable foliar residue (DFR) values (estimated based on the maximum approved rate of 60 g a.i./ha for poinsettias and 400 g a.i./ha for chrysanthemums and assuming 20% residue deposition on the day of application with 0% daily dissipation in greenhouses), a transfer coefficient (TC) of 400 cm^2/hr based on data submitted by the Agricultural Re-Entry Task Force, an average worker body weight of 70 kg, and an 8 hour work day. The Day 0 DFR is equivalent to multiple applications totalling the same rate due to assumed 0% dissipation in greenhouses.

The re-evaluation determined that dermal MOEs above 354 (target MOE of 100) calculated using short- to intermediate- and long-term endpoints indicate that the dermal risk for workers conducting postapplication activities in greenhouses is not of concern.

There is a restricted-entry interval of 12 hours on the label of all paclobutrazol end-use products. No further mitigation is proposed.

5.5 Non-occupational Exposure

5.5.1 Residential Exposure and Risk

While paclobutrazol is registered for commercial use on container-grown ornamental bedding plants and plugs only, residential postapplication dermal exposure could occur through contact with bedding plants and plugs treated by professional applicators in private or commercial greenhouses.

The potential for residential exposure was expected to be significantly less than exposure estimates for workers, which was not of concern. Therefore, a quantitative exposure risk assessment was not conducted.

5.5.2 Residue Limits in Food Commodities

Paclobutrazol is not registered for food use in Canada. There are no maximum residue limits established for paclobutrazol in Canada or by the Codex Alimentarius Commission. There are no paclobutrazol tolerances established in the United States.

5.5.3 Dietary Exposure and Risk

Paclobutrazol is not registered for food use in Canada and therefore no dietary risk assessment is required. Based on the registered use pattern of paclobutrazol, a quantitative drinking water exposure and risk assessment has not been conducted by the PMRA. Since paclobutrazol is for use on container-grown greenhouse bedding plants and plugs only, runoff and leaching of residues into sources of drinking water is expected to be limited, and therefore there is no expectation of exposure from drinking water.

5.5.4 Aggregate Exposure and Risk

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

An aggregate exposure assessment was not conducted because paclobutrazol is not registered for food uses in Canada, exposure from drinking water is expected to be limited based on the use pattern, and residential exposure is expected to be minimal.

5.6 Cumulative Exposure and Risk

A common mechanism of action has not been found for paclobutrazol and other pesticide products, nor is this active ingredient considered to produce a metabolite common to other pesticide active ingredients. Therefore, a cumulative risk assessment is not required.

6.0 Environment

6.1 Environmental Fate

An environmental evaluation of paclobutrazol was conducted by the PMRA for the original registration. Paclobutrazol was determined to be soluble in water, which indicated a potential for mobility in soil. Based on paclobutrazol's dissociation constant, the acidic chemical was expected to be mobile at environmentally relevant pHs. Adsorption coefficients in nine soils indicated that paclobutrazol would be of low to high mobility in soil, depending on the organic carbon content and texture of the soil. Data from a soil thick-layer descending chromatography study indicated that paclobutrazol would be of low mobility in fine-textured soil, but would be of moderate mobility in coarse-textured soil. Based on its vapour pressure and Henry Law's Constant, paclobutrazol was expected to be relatively non-volatile. Paclobutrazol was determined to be stable to hydrolysis at environmentally relevant pHs. In a phototransformation study,

paclobutrazol was reported to be stable to photolysis on soil. Paclobutrazol was found to be moderately persistent to persistent in soil.

6.2 Environmental Exposure and Risk Assessment

The most recent qualitative environmental exposure assessment conducted by the PMRA was in 2010, for the expansion of the paclobutrazol use pattern to include greenhouse poinsettia and chrysanthemum plugs. The assessment concluded that, although some greenhouses have plants "bedded" in outdoor settings where environmental exposure may be of concern, environmental exposure for the proposed use was considered limited, as the plants are grown in containers. Environmental exposure could potentially occur in the case of improper irrigation water disposal practices or the improper cleaning of spray equipment. It was concluded that this risk scenario could be mitigated by advisory environmental label statements. The paclobutrazol use pattern (i.e., use on container-grown greenhouse bedding plants and plugs only) is encompassed by the 2010 assessment and continues to meet the standards of modern science and current policy. On this basis, similar environmental label statements are proposed for all paclobutrazol end-use product labels.

6.3 Overall Conclusions and Mitigation Measures

Based on the above and on current PMRA general practices, the following label statements are proposed for all paclobutrazol end-use product labels:

> **DO NOT** contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
>
> **DO NOT** allow effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other waters.

7.0 Pest Control Product Policy Considerations

7.1 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, i.e., persistent (in air, soil, water and/or sediment), bioaccumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the re-evaluation process, paclobutrazol 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. In order for paclobutrazol to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met. The PMRA has reached the following conclusion:

- Persistence. Paclobutrazol was found to be moderately persistent to persistent in soil (half-life in aerobic soils ranging from 1.5 month to over 1 year at 20-25ºC). Given that TSMP Track 1 criterion is a half-life in soil or water ≥182 days or in sediment >365 days it is concluded that paclobutrazol does meet the criteria for persistence.
- Bioaccumulation. Bioconcentration factors (BCFs) for paclobutrazol of up to 248-fold were found for paclobutrazol, which is below the TSMP Track 1 criterion (BCF ≥ 5,000). Furthermore, the log K_{ow} of 3.2 for paclobutrazol is below the TSMP Track 1 criterion (log K_{ow} ≥ 5). On this basis, it is concluded that paclobutrazol does not meet the criteria for bioaccumulation.
- Paclobutrazol does not meet all Track 1 criteria and therefore is not considered a Track 1 substance.

7.2 Contaminants and Formulants of Health or Environmental Concern

During the re-evaluation of paclobutrazol, 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*[3]. 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 reached the following conclusion:

- Technical grade paclobutrazol 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.

During the review process, the potential presence of impurities known to have, or suspected to have, health and/or environmental implications are assessed in accordance with DIR98-04[4].

[3] *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

[4] DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*.

8.0 Incident Reports

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame.

As of 2 October 2013, no reports of incidents have been reported to the PMRA for paclobutrazol.

9.0 Organisation for Economic Co-operation and Development Status of Paclobutrazol

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 34 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

Paclobutrazol is currently approved for use in several OECD countries, including the United States, Australia and certain European Union member states. No decision by an OECD member country to prohibit all uses of paclobutrazol for health or environmental reasons has been identified.

10.0 Proposed Re-evaluation Decision

The PMRA has determined that products containing paclobutrazol for sale and use in Canada are acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use products must be amended to include the label statements listed in Appendix III. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. No additional data are being requested at this time.

11.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, 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 United States Environmental Protection Agency documents for the registration review of paclobutrazol are available at www.regulations.gov (Docket ID: EPA-HQ-OPP-2006-0109).

List of Abbreviations

µg	microgram
ADI	acceptable daily intake
a.i.	active ingredient
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetre(s)
DACO	data code
g	gram(s)
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
LOEL	lowest observed effect level
m^2	metre(s) squared
m^3	metre(s) cubed
mg	milligram(s)
mm Hg	millimetre mercury
MOE	margin of exposure
nm	nanometre
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
PCPA	*Pest Control Products Act*
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
p*K*a	-log10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
PRVD	Proposed Re-evaluation Decision
RfD	reference dose
RVD	Re-evaluation Decision
TSMP	Toxic Substances Management Policy
UV	ultraviolet

Appendix I Registered Products Containing Paclobutrazol as of 2 October 2013

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
24198	Technical	Syngenta Canada Inc.	Paclobutrazol Technical	Solid	96.9%
28550	Technical	Fine Agrochemicals Limited	Paclobutrazol Technical Plant Growth Regulator	Dust	99.3%
25678	Manufacturing Concentrate	Syngenta Canada Inc.	Bonzi Plant Growth Regulator Manufacturing Concentrate	Suspension	4 g/L
25453	Commercial	Syngenta Canada Inc.	Bonzi Plant Growth Regulator	Suspension	4 g/L
28400	Commercial	Fine Agrochemicals Limited	Piccolo Plant Growth Regulator	Solution	4 g/L

Appendix II Toxicological Endpoints for Paclobutrazol Health Risk Assessments

Exposure Scenario	Dose (mg/kg bw/day)	Study	Safety Factor or Target MOE
Short- and intermediate-term dermal	NOEL = 2.5	28-day range-finding rat dietary study. Based on lowered food consumption, increased cholesterol levels, increased absolute and relative liver weights and higher incidence of non-neoplastic lesions in liver and hepatocellular hypertrophy.	100
	Dermal absorption factor is 19.3%, based on a rat in vivo dermal absorption study.		
Short- and intermediate-term inhalation	NOEL = 2.5	28-day range-finding rat dietary study. Based on lowered food consumption, increased cholesterol levels, increased absolute and relative liver weights and higher incidence of non-neoplastic lesions in liver and hepatocellular hypertrophy.	100
Cancer (oral, dermal, inhalation)	No evidence of oncogenicity.		
Long-term dermal and inhalation	NOEL = 2.5	Two-year rat dietary study. Based on decreased bodyweight gain and increased incidence of liver lesions.	100

Note: NOEL = no observed effect level ; target MOE = margin of exposure.

Appendix III Label Amendments for End-Use Products Containing Paclobutrazol

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. 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 commercial 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**.

> Wear chemical-resistant coveralls over a long-sleeved shirt and long pants, and chemical-resistant gloves during mixing, loading, application, clean-up and repair activities.

II) It is recommended that the current label requirement for applicators to wear a NIOSH-approved respirator during application be removed from end-use product labels.

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

> **DO NOT** contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
>
> **DO NOT** allow effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other waters.

References

Chemistry

A. Studies/Information Submitted By The Registrant (Unpublished)

PMRA Document Number	Reference
1241949	Paclobutrazol Technical: Chemical and Physical Properties, DACO: 2.14.1, 2.14.10, 2.14.11, 2.14.12, 2.14.13, 2.14.14, 2.14.2, 2.14.3, 2.14.4, 2.14.5, 2.14.6, 2.14.7, 2.14.8, 2.14.9
1848523	PAZ-SYY-1 Chemistry - Active Ingredient, Chemical and Physical Properties, Manufacturing Method, Specification, Quality Control Method, Analytical Data and Methodology, The Determination of Paclobutrazol in Technical and Formulated Materials by Capillary Gas Chromatography, DACO: 2.1, 2.10, 2.11, 2.12, 2.13, 2.14, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9
1346259	Summary of Chemical and Physical Properties, DACO: 2.14.1, 2.14.10, 2.14.11, 2.14.12, 2.14.13, 2.14.14, 2.14.2, 2.14.3, 2.14.4, 2.14.5, 2.14.6, 2.14.7, 2.14.8, 2.14.9, 2.16
1346261	(Pure Grade) Physico-Chemical Properties, DACO: 2.14.4
1346250	Description of Starting Materials, DACO: 2.11.2
1346251	Detailed Production Process Description: Product Identity and Composition, Description of Beginning Materials, Production Process, Discussion of Formation of Impurities, and Certified Limits, DACO: 2.11.3
1241937	Paclobutrazol Technical – TGAI Starting Materials, DACO: 2.11.2
1241938	Manufacturing Process – Paclobutrazol (PP333), DACO: 2.11.3
1241947	Detailed Analysis of Technical Materials Representative of Large Scale Product, DACO: 2.13.3
1346257	Analysis of Five Batches of Technical Paclobutrazol. Final Report (Amendment 2), DACO: 2.13.3

Toxicology

A. Studies/Information Submitted By The Registrant (Unpublished)

PMRA Document Number	Reference
1148783	Paclobutrazol: An Evaluation In The Mouse Micronucleus Test (CTL/P/3216;4b.3/9;Sm0484), DACO: 4.5.4
1227766	Paclobutrazol : A Sub-Acute Cytogenetic Study In The Rat (CTL/P/926), DACO: 4.5.4
1231117	PP333: 6 Week Oral Dosing Study In Dogs (CTL/P/767), DACO: 4.3.1
1231122	Paclobutyrazol: 104 Week (Dietary Administration) Combined Toxicity & Carcinogenicity Study In The Rat With A 52 Week Interim Kill (5055-72/273), DACO: 4.4.2
1231127	PP333: Acute Oral;, Dermal & Intraperitoneal Toxicity (CTL/P748), DACO: 4.2.1,4.2.2
1231128	Paclobutrazol: Acute Dermal Toxicity (CTL/P/1173), DACO: 4.2.2
1231129	Paclobutrazol: 4-Hour Acute Inhalation Toxicity Studty In The Rat (CTL/P/2072), DACO: 4.2.3
1231130	PP333: Skin Irritation, Eye Irritation, & Skin Sensitisation (CTL/P/741), DACO: 4.2.4,4.2.5,4.2.6
1231134	Paclobutrazol: Teratogenicity Study In The Rat (CTL/P/842), DACO: 4.5.2
1231135	Paclobutrazol: Teratogenicity Study In The Rat Individual Animal Data Supplement Appendices A To E (CTL/P/842s), DACO: 4.5.2
1231136	Paclobutrazol: Second Teratogenicity Study In The Rat (CTL/P/997), DACO: 4.5.2
1231137	Paclobutrazol: Second Teratogenicity Study In The Rat (CTL/P/997S), DACO: 4.5.2
1231138	Paclobutrazol: 104 Week Oral (Dietary Administration) Combined Toxicity & Carcinogenicity Study In The Mouse With A 52 Week Interim Kill (5014-72/274), DACO: 4.4.1,4.4.2

1231140 Paclobutrazol: 1 Year Oral Dosing Study In Dogs (CTL/P/958), DACO: 4.3.1

1231141 Paclobutrazol: 1 Year Oral Dosing Study In Dogs Individual Animal Data Supplement (CTL/P/9585), DACO: 4.3.1

1231142 Paclobutrazol: Two Generation Reproduction Study In Rats (CTL/P/1496), DACO: 4.5.1

1231143 Paclobutrazol: Two Generation Reproduction Study In Rats Individual Animal Data Supplement (CTL/P/14965), DACO: 4.5.1

1232549 Paclobutrazol: Second Teratogencity Study In The Rat (CTL/P/997S), DACO: 4.5.2

1232551 PP333: Assessment Of Mutagenic Potential In The Mouse Lymphoma Mutation Asssay (730415), DACO: 4.5.4

1232554 Paclobutrazol: Dominant Lethal Study In The Mouse (CTL/P/922), DACO: 4.5.4

1232555 Paclobutrazol: Dominant Lethal Study In The Mouse. Individual Animal Data (CTL/P/922S), DACO: 4.5.4

1232557 Paclobutrazol: Assessment For The Induction Of Unscheduled Dna Synthesis In Rat Heptacoytes In Vivo (CTL/P/1608), DACO: 4.5.4

1232560 Paclobutrazol: Excretion & Tissue Retention Of A Single Oral Dose (10 Mg/Kg) In The Rat (CTL/P/870), DACO: 6.4

1232562 Paclobutrazol: Whole Body Autoradiography Study In The Rat Following A Single Oral Dose (250 Mg/Kg) (CTL/P/1035), DACO: 6.4

1232564 (14C) - Paclobutrazol: Excretion & Tissue Retention Of A Single Oral Dose (5 Mg/Kg) In The Rat (3456-72/267), DACO: 6.4

1232565 (14C) - Paclobutrazol: Excretion & Tissue Retention Of A Single Oral Dose (250mg/Kg) In The Rat (3268-72/268), DACO: 6.4

1232566 (14C) - Paclobutrazol: Bioaccumulation Of Repeated Oral Doses (5mg/Kg/Day) In The Rat (3743-72/269), DACO: 6.4

1232567 (14C) - Paclobutrazol: Absorption, Excretion & Tissue Retention Of A Single Oral Dose (5mg/Kg) In The Dog (3494-72/270), DACO: 6.4

1232568 Paclobutrazol: Biotransformation In The Rat (CT/P/1036 Revised), DACO: 6.4

1232576 Paclobutrazol: Teratogenicity Study In The Rabbit (CTL/P/861), DACO: 4.5.2

1232588 Paclobutrazol: Teratogenicity Study In The Rabbit Individual Animal Data Supplement Appendices A To E (CTL/P/861S), DACO: 4.5.2

1232601 Paclobutrazol: Second Teratogenicity Study In Rabbit (CTL/P/1460), DACO: 4.5.2

1232612 Paclobutrazol: Second Teratogenicity Study In Rabbit Individual Animal Data Supplement (CTL/P/14605), DACO: 4.5.2

1232637 PP333: An Evaluation In The Salmonella/Microsome Mutagenicity Assay (CTL/P/722), DACO: 4.5.4

1232853 Paclobutrazol: Two Generation Reproduction Study In Rats (CTL/P/1496), DACO: 4.5.1

1232864 First Supplement To Paclobutrazol: Two Generation Reproduction Study In Rats (CTL/P/1496), DACO: 4.5.1

1232873 Paclobutrazol: Two Generation Reproduction Study In Rats - Individual Animal Data Supplement (CTL/P/1496S), DACO: 4.5.1

1232874 Paclobutrazol: Two Generation Reproduction Study In Rats - Individual Animal Data Supplement (CTL/P/1496S), DACO: 4.5.1

Occupational and Non-occupational

A. Studies/Information Submitted By The Registrant (Unpublished)

PMRA Document Number **Reference**

1929187 Exposure Summary, DACO: 5.1

1929188 Use Description, DACO: 5.2

1929189 Mixer/Loader/Applicator - Passive Dosimetry Data, DACO: 5.4

1929190 Post-Application - Passive Dosimetry Data, DACO: 5.6

1929191 Dislodgeable Residues, DACO: 5.9

1156475 Paclobutrazol: In Vivo Percutaneous Absorption Study In The Rat (CTL/P/2285;SA19/88;Y00001/097/001;UR0259;3B.3/1)(Confer), DACO: 4.7

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Environment

A. Studies/Information Submitted By The Registrant (Unpublished)

PMRA Document Number	Reference
1232599	PP333: Effects On Earthworms, Lumbricidae Of 2 Annual Field Applications (RJ 0280B), DACO: 9.2.3.1
1232602	PP333: Effects On Soil Microarthorpods Of Two Annual Field Applications (RJ 0283B), DACO: 9.2.7
1232581	PP333; Degredation In Soil (RJ0256BR), DACO: 8.3.2.3
1232582	Paclobutrazol: Degredation In Aerobic & Flooded Soils (RJ0370B), DACO: 8.2.3.1
1232579	PP333: Leaching In Soil (RJ0244B), DACO: 8.2.4.1
1232598	PP333: Acute Oral & Contact Toxicity To Honey Bees (RJ 0278B), DACO: 9.2.4.1
1232578	Paclobutrazol: Adsorption & Desorption Equilibria In Soils (TMJ2377b), DACO: 8.2.4.1
1232573	Paclobutrazol: Photolytic Stability On A Soil Surface (RJ0601B), DACO: 8.2.1
1232571	PP333: Hydrolysis In Water At Ph4, 7 & 9 (RJ0316B), DACO: 8.2.1

B. Additional Information Considered

Published Information

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