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Proposed Registration Decision

Prohexadione Calcium

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Overview

Proposed Registration Decision for Prohexadione Calcium

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the [Pest Control Products Act](#) and Regulations, is proposing full registration for the sale and use of Prohexadione Calcium Technical Plant Growth Regulator and Apogee Plant Growth Regulator, containing the technical grade active ingredient prohexadione calcium, for use in apple orchards to reduce vegetative growth and to allow a balance between canopy development and fruit production.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Prohexadione Calcium Technical Plant Growth Regulator and Apogee Plant Growth Regulator.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable¹ if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value² when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.healthcanada.gc.ca/pmra.

¹ "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

² "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on prohexadione calcium, the PMRA will consider all comments received from the public in response to this consultation document³. The PMRA will then publish a Registration Decision⁴ on Prohexadione Calcium Technical Plant Growth Regulator and Apogee Plant Growth Regulator, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

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

What Is Prohexadione Calcium?

Prohexadione calcium is the active ingredient in the end-use product Apogee Plant Growth Regulator. Apogee Plant Growth Regulator is used in apple orchards to reduce vegetative growth and to allow a balance between canopy development and fruit production.

Prohexadione calcium is a plant growth regulator which blocks certain stages of the biosynthesis of gibberellin in plants. Gibberellin is the natural plant hormone that regulates cell elongation in shoots. Therefore, blocking the production of gibberellin will reduce vegetative shoot growth. The blocking of gibberellin production typically lasts for 2–5 weeks per application in the growing season and does not affect vegetative growth the following year.

Health Considerations

Can Approved Uses of Prohexadione Calcium Affect Human Health?

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

Exposure to prohexadione calcium may occur through diet (food and water) or when handling or applying the product. When assessing health risks, two key factors are considered: 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 (e.g. children and nursing mothers).

³ “Consultation statement” as required by subsection 28(2) of the *Pest Control Products Act*.

⁴ “Decision statement” as required by subsection 28(5) of the *Pest Control Products Act*.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when using prohexadione calcium products according to the label directions.

The technical grade active ingredient prohexadione calcium was considered to be of low acute toxicity, non-irritating to skin, minimally irritating to eyes and not a skin sensitizer. The end-use product Apogee Plant Growth Regulator was also of low acute toxicity, minimally irritating to skin and eyes and not a skin sensitizer. Therefore, no label statements are required on the labels of Prohexadione Calcium Technical Plant Growth Regulator or Apogee Plant Growth Regulator. The first health effects in animals given daily doses of prohexadione calcium over long periods of time included effects on the kidneys of dogs. Body-weight effects were observed at higher doses in rodents. When prohexadione calcium was given to pregnant animals, there were no effects on the developing fetus at doses that were toxic to the mother. No effects on reproduction were seen at doses that were toxic to adult animals. Prohexadione calcium did not cause cancer in animals and was not genotoxic. There were also no indications that prohexadione calcium caused damage to the nervous system of adult animals. The risk assessment is conducted to ensure that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests. Only those uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Residues in Water and Food

Dietary risks from food and water are not of concern

Aggregate dietary intake estimates (food plus water) revealed that the general population and children, the subpopulation which would ingest the most prohexadione calcium relative to body weight, are expected to be exposed to less than 14.2% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from exposure to prohexadione calcium residues is not of concern for any of the population sub-groups.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established under the authority of the *Food and Drugs Act* through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Confirmatory residue trials conducted in North American Free Trade Agreement geographical representative regions, using the end-use product containing prohexadione calcium on apples, were acceptable and will not impact the MRLs. The proposed MRLs for this active ingredient can be found in EMRL2008-02.

Occupational Risks From Handling Apogee Plant Growth Regulator

Occupational risks are not of concern when Apogee Plant Growth Regulator is used according to the label directions, which include protective measures.

The workers who mix, load or apply Apogee Plant Growth Regulator to apples as well as entering treated orchards can come in direct contact with Apogee Plant Growth Regulator residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying Apogee Plant Growth Regulator must wear long sleeved shirts, long pants and chemical-resistant gloves. The label also requires that workers do not enter treated orchards for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk to these individuals are not of concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Prohexadione Calcium Is Introduced Into the Environment?

Prohexadione calcium is introduced into the environment when used as a plant growth regulator in apple orchards. Prohexadione calcium is non-persistent to slightly persistent in the terrestrial environment with the aerobic biotransformation in soil being the principal route of dissipation. Hydrolysis is an important route of transformation only in acidic pH conditions, with despropionyl as the only major transformation product detected. Phototransformation on soil surfaces or in water is not an important route of transformation in the environment. Prohexadione calcium is assumed to be stable to aerobic aquatic biotransformation and moderately persistent in anaerobic aquatic systems. The major transformation product despropionyl, is expected to be persistent under these conditions.

Laboratory and field studies indicated that prohexadione calcium has low to moderate mobility in soils. The rapid aerobic soil biotransformation will reduce the overall leaching potential of this compound.

The *n*-octanol-water partition coefficient of prohexadione calcium indicates that bioaccumulation in biological organisms is not likely to occur.

Prohexadione calcium will pose a negligible risk to terrestrial and aquatic organisms. No environmental restrictions on the application of prohexadione calcium (maximum Canadian rate of 1485 g a.i./ha), are required for protection of non-target organisms.

Value Considerations

What Is the Value of Apogee Plant Growth Regulator?

Apogee Plant Growth Regulator is used in apple orchards to reduce vegetative growth and to allow a balance between canopy development and fruit production. The reduction of vegetative growth will suppress fire blight of shoots (shoot blight), resulting in reduced incidence and severity of the disease on shoots and leaves. Apogee Plant Growth Regulator may cause a tree to retain more fruit; therefore, thinning programs may be more aggressive.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Apogee Plant Growth Regulator to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

As there is a concern with users coming into direct contact with Apogee Plant Growth Regulator on the skin or through inhalation of spray mists, anyone mixing/loading and applying Apogee Plant Growth Regulator must wear long sleeved shirts, long pants and chemical-resistant gloves. In addition, standard label statements to protect against drift during application were added to the label.

Environment

In the original risk assessment of prohexadione calcium presented in the REG2006-07, Prohexadione Calcium, a risk had been identified for aquatic vascular plants and the mitigative measure proposed, was a label statement pertaining to buffer zones for the protection of aquatic organisms.

The PMRA environmental risk assessment methodologies, including buffer zone calculations, have been recently updated. Therefore, an updated risk assessment was conducted for prohexadione calcium and, as a result, no risk was identified above the level of concern.

The label statement pertaining to the aquatic buffer zone is no longer required and must be removed from the Apogee Plant Growth Regulator label.

No additional risk-reduction measures are required on the label.

Next Steps

Before making a final registration decision on prohexadion calcium, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on prohexadione calcium (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Prohexadione Calcium

1.0 The Active Ingredient, Its Properties and Uses

A detailed assessment of the chemistry database for Prohexadione Calcium Technical Plant Growth Regulator and Apogee Plant Growth Regulator are presented in REG2006-07: Prohexadione Calcium. No chemistry data were required as a condition of registration, therefore, no amendments to the previous chemistry assessment were necessary.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

A detailed assessment of the methods for analysis of prohexadione calcium is presented in REG2006-07: Prohexadione Calcium. No methods for analysis data were required as a condition of registration, therefore, no amendments to the previous assessment were necessary.

2.2 Method for Formulation Analysis

A detailed assessment of the methods for formulation analysis of prohexadione calcium is presented in REG2006-07: Prohexadione Calcium. No formulation analysis data were required as a condition of registration, therefore, no amendments to the previous assessment were necessary.

2.3 Methods for Residue Analysis

2.3.1 Methods for Residue Analysis of Plant and Plant Products

A detailed assessment of the methods for residue analysis of plants and plant products is presented in REG2006-07: Prohexadione Calcium.

The requested residue trial information has been submitted to the PMRA and has been found to be acceptable. The evaluation of this information is presented below.

A gas chromatography with mass selective detector (GC-MSD) method (D9601) was developed for the analysis of prohexadione calcium in peanut RAC (nutmeat and hay) and peanut processed fractions (meal and refined oil) for data gathering and enforcement purposes. Residues of prohexadione calcium are extracted from the peanut matrices by using acetonitrile: 1.5M H₂SO₄ (9:1, v/v). Aliquots of the extracts are purified by mini-Isolute ENV column. The eluant is methylated with MeOH/ H₂SO₄ and refluxed for 30 minutes. Residues of prohexadione calcium are measured as prohexadione methyl ester at m/z 226. A molecular weight correction factor of 1.107 was used to report residues as prohexadione calcium. The method fulfilled the

requirements with regards to specificity, accuracy and precision at the method limit of quantitation of 0.05 ppm reported for peanut commodities. Acceptable recoveries (70–120%) of prohexadione calcium were obtained in peanut matrices. Extraction efficiency data demonstrated that the enforcement method can account for incurred residues of prohexadione calcium in peanut nutmeat with an accountability of 102%. A similar method (D9608) was developed and previously reviewed (REG2006-07: Prohexadione Calcium) for the determination of prohexadione calcium in pome fruits and animal commodities. The extraction efficiency and independent laboratory validation conducted for method D9601 using peanut nutmeat can be extended to method D9608, due to the similarity of the methods.

An LC-MS/MS method (564/0) was also developed for the determination of the residues of prohexadione calcium (as the free acid) in/on apples for the confirmatory residue trials. Briefly, residues of prohexadione calcium were extracted with acetonitrile: 2M H₂SO₄ solution (9:1, v/v) and cleaned-up on a ENV+™ column eluted with acetonitrile:methanol:formic acid (95:5:1, v/v/v). MS/MS detection in the positive ionization mode was used to monitor ion transitions from m/z 213 → 157 for prohexadione. A molecular weight conversion factor (1.179) was used to express prohexadione as parent prohexadione calcium equivalents. The limit of detection (LOD) and the validated limit of quantitation (LOQ) for residues of prohexadione calcium in/on apple fruit were 0.002 and 0.01 ppm, respectively. This method fulfilled the requirements with regards to specificity, accuracy and precision at the method LOQ. Acceptable recoveries (70–120%) of prohexadione calcium were obtained in apple commodities.

3.0 Impact on Human and Animal Health

A detailed assessment of the toxicology database for Prohexadione Calcium Technical Plant Growth Regulator and Apogee Plant Growth Regulator are presented in REG2006-07: Prohexadione Calcium. No toxicology data were required as a condition of registration, therefore, no amendments to the previous toxicology assessment were necessary.

4.0 Impact on the Environment

A detailed assessment of the environmental impact of prohexadione calcium is presented in REG2006-07: Prohexadione Calcium.

4.1 Fate and Behaviour in the Environment

A detailed assessment of the fate and behaviour of prohexadione calcium are presented in REG2006-07: Prohexadione Calcium.

4.2 Effects on Non-Target Species

4.2.1 Effects on Terrestrial Organisms

A detailed assessment of the effects of prohexadione calcium on terrestrial organisms is presented in REG2006-07: Prohexadione Calcium.

The requested information on the toxicity of prohexadione calcium on beneficial arthropods has been submitted to the PMRA and has been found to be acceptable. The evaluation of these data is presented below.

Five studies on the toxicity of prohexadione calcium to one parasitic and four predatory arthropods were provided. Prohexadione calcium demonstrated low toxicity to beneficial arthropods. The predatory mite (*Typhlodromus pyri*) was tested at concentrations up to 750 g a.i./ha with no significant effects on mortality; other arthropods were tested at concentrations up to 500 g ai./ha. The risk assessment for arthropods was conducted using the LR₅₀ value of > 500 g a.i./ha

4.2.2 Effects on Aquatic Organisms

A detailed assessment of the effects of prohexadione calcium on aquatic organisms is presented in REG2006-07: Prohexadione Calcium.

4.2.3 Risk Assessment

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

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (e.g. direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value ($RQ = \text{exposure}/\text{toxicity}$), and the risk quotient is then compared to the level of concern (LOC = 1; but LOC = 2 for beneficial arthropods only). If the screening level risk quotient is below the level of concern, the risk is considered negligible and

no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

Estimated environmental concentrations and risk quotients were recalculated for all organisms, as the PMRA risk assessment methods have been updated since the initial review of prohexadione calcium. The updated values are found in Tables 3 and 4. As a result of the updated risk assessment for prohexadione calcium, no level of concern (LOC) was exceeded at the screening level, indicating negligible risk of prohexadione calcium to non-target terrestrial and aquatic organisms. Based on these results, no mitigative measures are required and the aquatic buffer zones currently required on the Apogee Plant Growth Regulator label are no longer required.

5.0 Value

A detailed assessment of the value of Apogee Plant Growth Regulator is presented in REG2006-07: Prohexadione Calcium. No value data were required as a condition of registration, therefore, no amendments to the previous value assessment were necessary.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's Toxic Substances Management Policy, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework, to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, prohexadione calcium was assessed in accordance with the PMRA Regulatory Directive DIR99-03, The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy. Substances associated with the use of prohexadione calcium were also considered, including transformation products formed in the environment, microcontaminants in the technical product and the end-use product Apogee Plant Growth Regulator.

Based on an assessment of the complete data package, the PMRA has reached the conclusion that these products do not meet TSMP Track 1 criteria. The end-use product does not contain any USEPA or the PMRA List 1 or 2 formulators. Refer to REG2006-07: Prohexadione Calcium for more details.

7.0 Summary

7.1 Human Health and Safety

Occupational risks are not of concern when Apogee Plant Growth Regulator is used according to the proposed label directions, which include protective measures. For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and children, the subpopulation which would ingest the most prohexadione calcium relative to body weight, are expected to be exposed to less than 14.2% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from exposure to prohexadione calcium residues is not of concern for any of the population subgroups.

7.2 Environmental Risk

Prohexadione calcium is introduced into the environment when used as a plant growth regulator in apple orchards. Prohexadione calcium will pose a negligible risk to terrestrial organisms and most aquatic organisms. No environmental restrictions on the application of prohexadione calcium (maximum Canadian rate of 1485 g a.i./ha) are required for protection of non-target terrestrial and aquatic organisms.

7.3 Value

Apogee Plant Growth Regulator, which contains prohexadione calcium is used in apple orchards to reduce vegetative growth and to allow a balance between canopy development and fruit production. The reduction of vegetative growth will suppress fire blight of shoots (shoot blight), resulting in reduced incidence and severity of the disease on shoots and leaves. Apogee Plant Growth Regulator may cause a tree to retain more fruit, therefore, thinning programs may be more aggressive.

8.0 Proposed Regulatory Decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the [Pest Control Products Act](#) and Regulations, is proposing full registration for the sale and use of Prohexadione Calcium Technical Plant Growth Regulator and Apogee Plant Growth Regulator, containing the technical grade active ingredient prohexadione calcium, for use in apple orchards to reduce vegetative growth and to allow a balance between canopy development and fruit production. An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

a.i.	active ingredient
EC ₂₅	effective concentration on 25% of the population
EC ₅₀	effective concentration on 50% of the population
EEC	expected environmental concentrations
EPA	Environmental Protection Agency
FDA	<i>Food and Drugs Act</i>
g	gram
ha	hectare(s)
kg	kilogram
L	litre
LC ₅₀	lethal concentration 50%
LD ₅₀	lethal dose 50%
LOC	level of concern
LOD	limit of detection
LOQ	limit of quantitation
LR ₅₀	lethal rate 50%
mg	milligram
MRL	maximum residue limit
MS	mass spectrometry
NAFTA	North America Free Trade Agreement
NOEC	no observed effect concentration
NOEL	no observed effect level
PCPAS	<i>Pest Control Products Act</i>
PMRA	Pest Management Regulatory Agency
ppm	parts per million
RQ	risk quotient
T _{1/2}	half-life
TSMP	Toxic Substances Management Policy

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte(s)	Method Type	LOQ		Reference
Plant (peanut matrices)	D9601	Prohexadione calcium analyzed as prohexadione methyl ester; prohexadione calcium equivalents calculated by multiplying a molecular weight correction factor of 1.107.	Data gathering and Enforcement: GC-MSD	0.05 ppm	Peanuts and peanut processed fractions	1525280 923900
Plant (apples)	564/0	Prohexadione followed by molecular weight conversion factor (1.179) to express as prohexadione calcium equivalents	Data gathering for confirmatory trials on apples LC-MS/MS	0.01 ppm	Apple fruit	1525282 1525291
Plant (pome fruits)	D9608	Prohexadione calcium analyzed as prohexadione methyl ester; prohexadione calcium equivalents calculated by multiplying a molecular weight correction factor of 1.107.	Data gathering for apples and apple commodities and enforcement method	0.05 ppm	Apple commodities	627278

Table 2 Integrated Food Residue Chemistry Summary

CROP FIELD TRIALS ON APPLES							PMRA # 1525297			
Field trial data have been generated for prohexadione calcium (BAS 125 W) on apples. A total of eight apple field trials were conducted in North American Free Trade Agreement representative growing region 1 (New York, three trials; Nova Scotia, one trial) and region 5 (Michigan, two trials; Wisconsin and Ontario, one trial each) during the 2007 growing season. At each test location, one untreated control plot (Treatment 1) and one treated plot (Treatment 2) were established. The treated plot received four foliar applications of prohexadione calcium (27.5% WG formulation of Apogee plant growth regulator) at 0.39–0.57 kg a.i./ha, with a 13 to 15 day retreatment interval, for a total rate of 1.60–1.81 kg a.i./ha/season (1.1–fold label use rate). The four sprays were made to fruiting apple trees at 87–88, 73–74, 58–61, and 44–46 days prior to mature harvest with ground equipment (airblast sprayers). All applications were made using water (453–656 L/ha) as the carrier, Agral 90 non-ionic surfactant as an adjuvant, and ammonium sulfate (AMS). Apples (treated and untreated) were harvested 44 to 46 days after the last application (DALA). At one site (Region 5), apple fruit samples were harvested 10, 25, 35 and 55 DALA to examine residue decline. The residues from the confirmatory trials will be covered by the established MRL of 3 ppm.										
Commodity	Total Applic. Rate (kg a.i./ha)	PHI (days)	Residue Levels (ppm)							
			n	Minimum	Maximum	HAFT*	Median (STMdR)	Mean (STMR)	Standard Deviation	
Prohexadione Calcium										
Apple fruit	1.60–1.81	44–46	16	< 0.01	0.62	0.60	0.075	0.16	0.047	
Prohexadione calcium residue decline (region 5)										
Apple fruit	1.61	10	2	0.30	0.34	0.32	—	0.32	—	
Apple fruit	1.61	25	2	0.17	0.17	0.17	—	0.17	—	
Apple fruit	1.61	35	2	0.08	0.11	0.095	—	0.095	—	
Apple fruit	1.61	46	2	0.05	0.06	0.055	—	0.055	—	
Apple fruit	1.61	55	2	0.05	0.05	0.05	—	0.05	—	
*Highest Average Field Trial										

Table 3 Risk (Updated) Assessment for Non-Target Terrestrial Organisms Exposed to Prohexadione Calcium (Based on the Current Canadian Label Rate)

Organism	Exposure	Endpoint value	EEC	RQ	Risk Greater Than LOC ¹
Invertebrates					
Earthworm	14-day Acute	½ LC ₅₀ : > 500 mg a.i./kg dw soil	0.397 mg a.i./kg dw soil	0.001	No
Bee	48-hour Oral	LD ₅₀ : > 100 µg a.i./bee, equivalent to 112 kg a.i./ha	1.0268 kg a.i./ha	0.009	No
	48-hour Contact	LD ₅₀ : > 100 µg a.i./bee, equivalent to 112 kg a.i./ha	1.0268 kg a.i./ha	0.009	No
<i>Aphidius rhopalosiphi</i>	48-hour Contact	LR ₅₀ : > 500 g a.i./ha	1026.8 g a.i./ha	2.054	No ²
<i>Typhlodromus Pyri</i>	10-week Contact	LR ₅₀ : > 750 g a.i./ha	1026.8 g a.i./ha	1.369	No
<i>Chrysoperla carnea</i>	14-day Contact	LR ₅₀ : > 500 g a.i./ha	1026.8 g a.i./ha	2.054	No ²
<i>Pardosa</i> spp.	14-day Contact	LR ₅₀ : > 500 g a.i./ha	894.3 g a.i./ha	1.789	No
<i>Aleochara bilineata</i>	37-day Contact	LR ₅₀ : > 500 g a.i./ha	894.3 g a.i./ha	1.789	No
Birds					
Bobwhite quail	Acute Oral	LD ₅₀ : > 2000 mg a.i./kg bw	179.77 mg a.i./kg dw, equivalent to 19.09 mg a.i./kg bw	0.010	No
	8-day Dietary	NOEC: 5200 mg a.i./kg dw	179.77 mg a.i./kg dw	0.035	No
	22-week Reproduction	NOEC: 1000 mg a.i./kg dw	179.77 mg a.i./kg dw	0.180	No
Mallard Duck	8-day Dietary	NOEC: 5200 mg a.i./kg dw	34.73 mg a.i./kg dw	0.007	No
	23-week Reproduction	NOEC: 1000 mg a.i./kg dw	34.73 mg a.i./kg dw	0.035	No
Mammals					
Rat	Acute oral	NOEL: 5000 mg a.i./kg bw	518.02 mg a.i./kg dw, equivalent to 88.80 mg a.i./kg bw	0.018	No
	90-day Dietary	NOEL: 1000 mg a.i./kg diet	518.02 mg a.i./kg dw	0.518	No
	Reproduction	Reproductive NOEL: 50000 mg a.i./kg diet	518.02 mg a.i./kg dw	0.010	No

Organism	Exposure	Endpoint value	EEC	RQ	Risk Greater Than LOC ¹
Rabbit	Developmental	Maternal (premature deliveries) NOEL : 3333 mg a.i./kg diet (converted from 100 mg a.i./kg bw/d)	774.57 mg a.i./kg dw	0.232	No
Vascular Plants					
Vascular plant	Seedling emergence	EC ₂₅ : >1905 g a.i./ha	391.71 g a.i./ha	0.206	No
	Vegetative vigour	EC ₂₅ : >1905 g a.i./ha	391.71 g a.i./ha	0.206	No
¹ For terrestrial organisms, the level of concern (LOC) is 2 for arthropods, and 1 for all other organisms. ² Rounded to 2.0, therefore the risk was not exceeded.					

Table 4 Risk (Updated) Assessment for Non-Target Aquatic Organisms Exposed to Prohexadione Calcium (Based on the Current Canadian Label Rate).

Organism	Exposure	Endpoint value	EEC	RQ	Risk greater than LOC ¹ ?
Freshwater Species					
<i>Daphnia magna</i>	48-hour Acute	½ EC ₅₀ : > 45 mg a.i./L	0.186 mg a.i./L	0.004	No
Rainbow trout	96-hour Acute	1/10 LC ₅₀ : > 9.2 mg a.i./L	0.186 mg a.i./L	0.020	No
Bluegill sunfish	96-hour Acute	1/10 LC ₅₀ : > 9.56 mg a.i./L	0.186 mg a.i./L	0.020	No
Amphibians (using Trout data)	96-hour Acute	1/10 LC ₅₀ : > 9.2 mg a.i./L	0.990 mg a.i./L	0.108	No
Freshwater alga (<i>S. capricornutum</i>)	5-day Acute	½ EC ₅₀ : > 0.55 mg a.i./L	0.186 mg a.i./L	0.338	No
Vascular plant (<i>Lemna gibba</i>)	14-day Dissolved	½ EC ₅₀ : > 0.60 mg a.i./L	0.186 mg a.i./L	0.310	No
Marine Species					
Crustacean (<i>M. bahia</i>)	96-hour Acute	½ EC ₅₀ : > 62.5 mg a.i./L	0.186 mg a.i./L	0.003	No
Mollusk (<i>C. virginica</i>)	96-hour Acute	½ EC ₅₀ : > 58.5 mg a.i./L	0.186 mg a.i./L	0.003	No
Fish (sheepshead minnow)	96-hour Acute	1/10 LC ₅₀ : > 12.2 mg a.i./L	0.186 mg a.i./L	0.015	No
Marine alga (<i>S. costatum</i>)	5-day Acute	½ EC ₅₀ : > 0.55 mg a.i./L	0.186 mg a.i./L	0.338	No
¹ For aquatic organisms, the level of concern (LOC) is 1.0					

References

A. List of Studies/Information Submitted by Registrant

1.0 Human and Animal Health

- 627278 1997, Methods for Determination of BAS 125 W and Its Metabolite in Animal Tissues (Liver, Kidney, Fat and Muscle), Milk and Apple Commodities. Reg. Doc. #97/5034, DACO: 7.2.1,7.2.2
- 1525208 1997, Metabolism of 14C BAS 125 W (Prohexadione Calcium) in Peanut, US-SC930242, PR. NO. 93148 NO-M9412, US-44457793, MRID: 44457793, DACO: 6.3
- 1525280 1996, Method for Determination of BAS 125 W (Prohexadione) Residues in Peanut RAC (Nutmeat and Hay), and Peanut Process Fractions (Meal and Refined Oil) by GC-MS, US-95164, US-44457806, MRID: N/A, DACO: 7.2.1
- 1525282 2005, Validation of the analytical method 564/0: Method for the determination of Prohexadione-Ca in plant and animal matrices, 134609, MRID: N/A, DACO: 7.2.1
- 1525291 2005, Independent laboratory validation of BASF method 564/0: Method for the determination of Prohexadione-Ca in plant and animal matrices (BASF Study Code 134612), BAS-0407V, Az. G04-0099, BASF Study Code 134612, MRID: N/A, DACO: 7.2.3
- 1525297 2007, Magnitude of BAS 125 W residues in apple following applications of Apogee, 147287, MRID: N/A, DACO: 7.4.1

2.0 Environment

- 1525213 2000, BAS 125 10 W - Laboratory test on *Pardosa* spp. (Araneae, Lycosidae), EU-000417BO, EU-IPA72321, MRID: N/A, DACO: 9.2.5
- 1525216 2000, BAS 125 10 W - Side effects on the larvae of the green lacewing, *Chrysoperla carnea*, EU-000112BO, EU-IFA69661, MRID: N/a, DACO: 9.2.5
- 1525218 2001, BAS 125 10 W: Laboratory test with *Aleochara bilineata* GYLL. (Coleoptera: Staphylinidae), EU-1031.029.371, MRID: N/A, DACO: 9.2.5
- 1525219 2000, BAS 125 10 W: Toxicity to the predatory mite, *Typhlodromus pyri* SCHEUTEN (Acari, Phytoseiidae) in the laboratory, EU-99011/01-NLTp, MRID: N/A, DACO: 9.2.5
- 1525222 2000, A laboratory test to determine the effects of BAS 125 10 W on the parasitic wasp, *Aphidius rhopalosiphi*, EU-BASF-00-3, MRID: N/A, DACO: 9.2.6