Proposed Registration Decision PRD2016-04

Clothianidin

(publié aussi en français)

12 February 2016

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6607 D
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

Canada

ISSN: 1925-0878 (print)
1925-0886 (online)

Catalogue number: H113-9/2016-4E (print version)
H113-9/2016-4E-PDF (PDF version)

Table of Contents

Overview 1
Registration Decision for Clothianidin Technical Insecticide 1
What Does Health Canada Consider When Making a Registration Decision? 1
What Is Clothianidin? 2
Health Considerations 2
Environmental Considerations 4
Value Considerations 4
Measures to Minimize Risk 5
Next Steps 5
Other Information 6
Science Evaluation 7
1.0 The Active Ingredient, Its Properties and Uses 7
1.1 Identity of the Active Ingredient 7
1.2 Physical and Chemical Properties of the Active Ingredient and End-Use Product 7
1.3 Directions for Use 9
1.4 Mode of Action 9
2.0 Methods of Analysis 9
2.1 Methods for Analysis of the Active Ingredient 9
2.2 Method for Formulation Analysis 9
3.0 Impact on Human and Animal Health 9
3.1 Toxicology Summary 9
3.2 Occupational and Residential Risk Assessment 11
3.2.1 Toxicological Endpoints 11
3.2.2 Occupational Exposure and Risk 11
3.2.3 Residential Exposure and Risk Assessment 11
4.0 Impact on the Environment 12
4.1 Fate and Behaviour in the Environment 12
4.2 Environmental Risk Characterization 12
4.2.1 Risks to Terrestrial Organisms 12
4.2.2 Risks to Aquatic Organisms 12
5.0 Value 13
5.1 Consideration of Benefits 13
5.2 Acceptable Claims and Effectiveness Against Pests 13
5.3 Non-Safety Adverse Effects 14
5.4 Supported Uses 14
6.0 Pest Control Product Policy Considerations 14
6.1 Toxic Substances Management Policy Considerations 14
6.2 Formulants and Contaminants of Health or Environmental Concern 15

7.0 Summary 15
7.1 Human Health and Safety 15
7.2 Environmental Risk 16
7.3 Value 16
8.0 Regulatory Decision 16
List of Abbreviations 17
Appendix I Tables and Figures 19
Table 1 Toxicity Profile of MaxForce IMPACT Cockroach Bait Gel 19
Table 2 Amended Table Entry for the Reproduction Study with Clothianidin 20
Table 3 Amended Acceptable Daily Intake (ADI) for Clothianidin 20
References 21

Overview

Registration Decision for Clothianidin Technical Insecticide

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 Clothianidin Technical Insecticide and MaxForce IMPACT Cockroach Bait Gel, containing the technical grade active ingredient clothianidin, as an insecticide product which is applied as a major new use for crack and crevice or spot treatment for control of cockroaches both indoors and on the exterior of structures.

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 Clothianidin Technical Insecticide and MaxForce IMPACT Cockroach Bait Gel.

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 acceptable[1] 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 value[2] 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 (for example, children) as well as organisms in the environment. 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 Pesticides and Pest Management portion of Health Canada's website at 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 clothianidin, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on clothianidin, 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 Clothianidin?

Clothianidin is the active ingredient contained in the commercial-class insecticide Maxforce IMPACT Cockroach Bait Gel. Clothianidin is a member of the neonicotinoid group of insecticides, which act on the insect nervous system by exhibiting agonistic activity on the insect's nicotinic acetylcholine receptors. Maxforce IMPACT Cockroach Bait Gel is a ready-to-use 1.0% clothianidin gel-bait insecticide product which is applied as a crack and crevice or spot treatment for control of cockroaches in structures. Environmental exposure from exterior structural use of the cockroach bait products is expected to be low as applications are limited to cracks and crevices or expansion joints around windows and doors, under stairways and other areas adjacent to homes or structures where cockroaches harbour and in areas not easily accessible to children, pets and other non-target organisms. No environmental exposure is expected from interior use of the cockroach bait products.

Health Considerations

Can Approved Uses of Clothianidin Affect Human Health?

Maxforce IMPACT Cockroach Bait Gel is unlikely to affect your health when used according to label directions.

Potential exposure to clothianidin may occur when handling and applying the product or when entering an area that has been treated with the product. When assessing health risks, two key factors are considered: the levels where 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 populations (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

---

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 pesticide-containing products are used according to label directions.

In laboratory animals, the technical grade active ingredient clothianidin was of high acute toxicity via the oral route of exposure. Consequently, the hazard signal words "DANGER POISON" are required on the product label. Clothianidin was of low acute toxicity via the dermal and inhalation routes of exposure, was non-irritating to the eyes and skin, and did not produce an allergic skin reaction.

The end-use product Maxforce IMPACT Cockroach Bait Gel, containing clothianidin, was of low acute toxicity by the oral and dermal routes of exposure, was non-irritating to the eyes and skin, and did not cause an allergic skin reaction. It is not considered to pose an acute inhalation hazard due to its viscous gel formulation. Based on these findings, no acute hazard labelling is required.

Registrant-supplied short, and long term (lifetime) animal toxicity tests, as well as information from the published scientific literature were assessed for the potential of clothianidin to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints used for risk assessment included effects on the nervous system, reduced survival and delayed sexual maturation in the developing young. There was an indication that the young were more sensitive than the adult animal. The risk assessment protects against these and any other potential effects by ensuring that the level of exposure to humans is well below the lowest dose at which these effects occurred in animal tests.

Risks in Residential and Other Non-Occupational Environments

Estimated risk for non-occupational exposure is not of concern when used according to label directions.

The commercial class product, MaxForce IMPACT Cockroach Bait Gel, must only be placed in areas inaccessible to children, pets, and non-target organisms, and must only be applied by individuals holding an appropriate pesticide applicator certificate or license recognized by the provincial/territorial pesticide regulatory agency where the application occurs. Application within food handling establishments is limited to crack and crevice treatment only.

Exposure to individuals residing in treated areas is not expected to result in unacceptable risk when the end-use product is used according to label directions.

Occupational Risks From Handling MaxForce IMPACT Cockroach Bait Gel

Occupational risks are not of concern when MaxForce IMPACT Cockroach Bait Gel is applied with the ready-to-use syringe and used according to the label directions, which include protective measures.

As exposure is considered to be negligible when the product is used according to label directions, a risk assessment was not conducted for individuals handling and re-entering areas treated with MaxForce IMPACT Cockroach Bait Gel.

Pesticide applicators applying MaxForce IMPACT Cockroach Bait Gel can come in direct contact with clothianidin on the skin. Therefore the label will specify that anyone applying MaxForce IMPACT Cockroach Bait Gel must wear a long-sleeved shirt, long pants, socks, shoes and chemical-resistant gloves during application and clean-up activities.

Given the product is to be applied as a crack and crevice and spot treatment in locations which are accessible only to cockroaches, there is little potential for exposure to workers re-entering treated areas.

Environmental Considerations

What Happens When Clothianidin Is Introduced Into the Environment?

When used according to label directions, clothianidin is not expected to pose an unacceptable risk to the environment.

Terrestrial or aquatic environments are not expected to be exposed when clothianidin is used as an interior cockroach bait. When clothianidin is used on exterior structures as a cockroach bait, there is limited potential for terrestrial or aquatic environments to be exposed as applications are limited to cracks and crevices or expansion joints around windows and doors, porches, screens, eaves, sills, patios, garages, under stairways and other areas adjacent to homes or structures where cockroaches harbor and in areas not easily accessible to children, pets and other non-target organisms. As environmental exposure is expected to be limited for cockroach bait applications, the risk to terrestrial and aquatic organisms is expected be negligible.

Value Considerations

What Is the Value of MaxForce IMPACT Cockroach Bait Gel?

Maxforce IMPACT Cockroach Bait Gel has value for controlling cockroaches in structures.

Cockroaches are amongst the most common and difficult to control pests found in structures in Canada, and are both a nuisance pest and a public health concern as they can spread bacteria and pose significant health risk to allergy and asthma sufferers. Maxforce IMPACT Cockroach Bait Gel has value as it incorporates a new bait formulation and provides another active ingredient for control of this pest. Cockroaches are known to have developed resistance to many different

insecticide active ingredients and have been known to develop aversion to baits after repeated exposure to the same formulation. Additional bait formulations and active ingredients are needed for control of cockroaches since cockroaches have developed resistance to many older active ingredients and some registered products or uses are proposed for phase-out.

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 on the label of MaxForce IMPACT Cockroach Bait Gel to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

To avoid direct applicator contact with clothianidin, the commercial applicators of MaxForce IMPACT Cockroach Bait Gel must wear a long-sleeved shirt, long pants, socks, shoes and chemical-resistant gloves during application and clean-up activities.

Postapplication exposure to clothianidin following application of the commercial class product, MaxForce IMPACT Cockroach Bait Gel, is minimized by limiting application to crack and crevice and spot treatments in areas inaccessible to children and only crack and crevice application in food handling establishments.

Environment

When used according to label directions, clothianidin is not expected to pose an unacceptable risk to the environment.

Next Steps

Before making a final registration decision on clothianidin, the PMRA will consider any 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 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

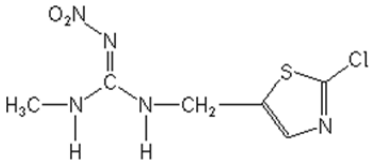
When the PMRA makes its registration decision, it will publish a Registration Decision on clothianidin (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the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

Science Evaluation

Clothianidin Technical Insecticide

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Clothianidin
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	(*E*)-N-[(2-chloro-1,3-thiazol-5-yl)methyl]-*N*′-methyl-*N*″-nitroguanidine OR (*E*)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine
2. Chemical Abstracts Service (CAS)	[C(*E*)]-*N*-[(2-chloro-5-thiazolyl)methyl]-*N*′-methyl-*N*″-nitroguanidine
CAS number	210880-92-5
Molecular formula	$C_6H_8ClN_5O_2S$
Molecular weight	249.68
Structural formula	
Purity of the active ingredient	97.5%

1.2 Physical and Chemical Properties of the Active Ingredient and End-Use Product

Technical Product—Clothianidin Technical Insecticide

Property	Result
Colour and physical state	Clear, colourless solid
Odour	Odourless
Melting range	176.8°C
Boiling point or range	Not applicable
Density	1.61 g/mL

Property	Result
Vapour pressure	1.3×10^{-10} Pa at 25°C 3.8×10^{-11} Pa at 20°C (extrapolated)
Henry's law constant	9.8×10^{-16} atm m^3/mole at 25°C 2.9×10^{-16} atm m^3/mole at 20°C
Ultraviolet (UV)-visible spectrum	λ_{max} = 265.5 nm in acidic and neutral solution. λ_{max} = 246.0 nm in basic solution
Solubility in water at 20°C	0.327 g/L
Solubility in organic solvents at 20°C	Solvent — Solubility (mg/L) heptane — < 0.00104 xylene — 0.0128 dichloromethane — 1.32 methanol — 6.26 octanol — 0.938 acetone — 15.2 ethyl acetate — 2.03
n–Octanol-water partition coefficient (K_{ow})	K_{ow} = 5 log K_{ow} = 0.7
Dissociation constant (pK_a)	11.09
Stability (temperature, metal)	Stable for 12 months at 25°C and 6 months at 40°C

End-Use Product—Maxforce IMPACT Cockroach Bait Gel

Property	Result
Colour	Creamy white with light blue flecks
Odour	Slightly musty, weak cereal
Physical state	Gel
Formulation type	PA (paste)
Guarantee	1.0 %
Container material and description	Plastic containers 25 g to bulk.
Density	1.16-1.20 g/mL
pH of 10% dispersion in water	5.0-6.5
Oxidizing or reducing action	The product is considered to have no oxidizing or reducing action.
Storage stability	The product is stable when stored for 2 weeks at 54°C.
Corrosion characteristics	No changes in the integrity or dimensions of the container were observed following storage at 54°C for 2 weeks.
Explodability	The product is not potentially explosive.

1.3 Directions for Use

Maxforce IMPACT Cockroach Bait Gel is a ready-to-use 1.0% clothianidin gel-bait insecticide product which is applied as crack and crevice or spot treatment both indoors and on the exterior of structures. To control cockroaches, the product is applied at a rate of 0.75 to 1.5 grams of bait per 1.0 m^2 for light-to-moderate infestations, and 1.5 to 3.0 grams of bait per 1.0 m^2 for severe or heavy infestations. The product may be re-applied as required if monitoring indicates that pest populations persist.

1.4 Mode of Action

The active ingredient clothianidin is an insecticide that acts on the insect nervous system, exhibiting agonistic activity on the insect nicotinic acetylcholine receptor, causing death of the insect. Clothianidin has activity both through contact and by ingestion.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods previously provided for the analysis of the active ingredient and the impurities in Clothianidin Technical Insecticide have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The method provided for the analysis of clothianidin in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for clothianidin was conducted previously in 2003 and is summarized in Regulatory Note REG2004-06 (revision), *Clothianidin Poncho 600 Seed Treatment Insecticide*. An updated review was conducted in 2010 and is summarized in the Evaluation Report for submission number 2007-6020.[5] The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to clothianidin.

In short-term and chronic studies on laboratory animals, toxicity was manifested as effects on body weight and food consumption. In addition, effects were seen on the liver, kidneys, reproductive organs, gastrointestinal tract and the immune system. Although genotoxicity was

[5] http://pr-rp.hc-sc.gc.ca/pi-ip/adoc-ddoc-eng.php?p_app_id=2007-6020

noted in several in vitro assays, in vivo genotoxicity assays were negative and there was no evidence of carcinogenicity in rats or mice. Developmental toxicity, in the form of absent lung lobe and delayed sternal ossification in the rabbit fetus, was observed at a dose level which also caused toxicity in maternal animals. In the reproductive toxicity study, effects in the offspring (decreased thymus weight and reduced body weight gain in both sexes as well as delayed sexual maturation in males) were seen at a maternally non-toxic dose and a serious endpoint (stillbirth) was identified. In the developmental neurotoxicity (DNT) study, signs of potential neurotoxicity (decreased motor activity and auditory startle response) were observed in young animals in the absence of maternal toxicity. There was no evidence of toxic effects on the developing immune system.

In acute toxicity testing, the end-use product Maxforce IMPACT Cockroach Bait Gel was found to be of low acute toxicity in rats via the oral and dermal routes of exposure. It was non-irritating to the eyes and skin of rabbits, and was not a skin sensitizer when tested in the local lymph node assay (LLNA) in mice. Based on its viscous gel formulation, the end-use product is not considered to pose an acute inhalation hazard.

Results of the toxicology studies conducted on laboratory animals with clothianidin can be found in REG2004-06 (revision), *Clothianidin Poncho 600 Seed Treatment Insecticide* and in the Evaluation Report for submission number 2007-6020. However, corrections to the reporting of the offspring NOAEL and LOAEL in the rat reproductive toxicity study in these documents are required (see below). There was a typographical error in the reporting of the offspring LOAEL in the determination of the Acceptable Daily Intake (ADI), which was stated to be 10 mg/kg bw/day. Additionally, the offspring NOAEL and LOAEL should have been expressed as the dose administered to parental females, as opposed to that given to parental males. Accordingly, the offspring NOAEL and LOAEL values are 11.5 mg/kg bw/day and 36.8 mg/kg bw/day, respectively. Since the offspring NOAEL formed the basis for the ADI, the ADI should be reported as 0.04 mg/kg bw/day as opposed to 0.03 mg/kg bw/day. Furthermore, in REG2004-06 (revision), the increased incidence of stillbirths noted in the rat reproductive toxicity study was reported as an offspring effect while it is more appropriately considered a reproductive effect. Thus, the reproductive NOAEL and LOAEL in females are 11.5 mg/kg bw/day and 36.8 mg/kg bw/day, respectively.

The corrected table entries for the reproduction study and the ADI, as well as the results of the toxicology studies conducted on laboratory animals with the end-use product, are summarized in Appendix I, Tables 1–3 of this document.

Due to the expected negligible exposure from the use of Maxforce IMPACT Cockroach Bait Gel, and the fact that there are no food uses associated with the product, toxicological endpoints for clothianidin are not outlined further in this document.

Incident Reports

Incidents were searched and reviewed for clothianidin. As of 19 November 2015, a total of seven human and six domestic animal incidents involving clothianidin have been reported to the PMRA. All of these incidents involved other active ingredients in addition to clothianidin, and

were related to commercial or agricultural class insecticides used to treat seeds. One child and several animals accidentally ingested clothianidin products. All subjects experienced gastrointestinal symptoms. The incident data did not impact the current assessment.

3.2 Occupational and Residential Risk Assessment

3.2.1 Toxicological Endpoints

Repeat dermal, inhalation or incidental oral exposure is not expected based on the use location and the application method for either the applicator or for people re-entering treated rooms.

3.2.1.1 Dermal Absorption

Given a quantitative risk assessment was not calculated for dermal exposure scenarios, a dermal absorption value was not required.

3.2.2 Occupational Exposure and Risk

3.2.2.1 Applicator Exposure and Risk Assessment

Commercial applicator exposure is considered to be negligible as the product is housed in a ready-to-use syringe.

3.2.2.2 Postapplication Worker Exposure and Risk

Workers re-entering treated areas will have less exposure than that of the applicator, which is considered negligible.

3.2.3 Residential Exposure and Risk Assessment

3.2.3.1 Handler Exposure and Risk

The assessment of residential exposure and risk is not required for commercial class products.

3.2.3.2 Postapplication Exposure and Risk

The United States Environmental Protection Agency 2012 Residential standard operation procedure states that postapplication risk assessments for dermal, inhalation or oral exposures are not required for paste/gel products used as baits.

Inhalation exposure is expected to be minimal because clothianidin has a very low vapour pressure (1.3×10^{-10} Pa at 25ºC) and meets North American Free Trade Agreement criteria for a non-volatile product used indoors (1×10^{-5} kPa at 20-30^{o}C).

Postapplication dermal and incidental oral exposures are not expected to occur because of label statements limiting applications to areas inaccessible to children.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

The fate and behaviour of clothianidin in the terrestrial and aquatic environment is summarized in Regulatory Note REG2004-06 (revision), *Clothianidin Poncho 600 Seed Treatment Insecticide* and in Registration Decision RD2013-14 *Clutch 50 WDG, Arena 50 WDG and Clothianidin Insecticides.*

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. The use of clothianidin as a cockroach bait represents a much lower environmental exposure potential in comparison to current use applications of clothianidin in seed treatment and foliar use products. Environmental exposure from use of the cockroach bait products on exterior structures is expected to be low as applications are limited to cracks and crevices or expansion joints around windows and doors, porches, screens, eaves, sills, patios, garages, under stairways and other areas adjacent to homes or structures where cockroaches harbor and in areas not easily accessible to children, pets and other non-target organisms. As environmental exposure to clothianidin is expected to be limited from cockroach bait applications, the risk to terrestrial and aquatic organisms is expected be negligible. No environmental exposure is expected from interior use of the cockroach bait products.

4.2.1 Risks to Terrestrial Organisms

The use of Maxforce IMPACT Cockroach Bait Gel is limited to interior use and to use on exterior structures in cracks and crevices or expansion joints around windows and doors, porches, screens, eaves, sills, patios, garages, under stairways and other areas adjacent to homes or structures where cockroaches harbor and in areas not easily accessible to children, pets and other non-target organisms. Therefore access to clothianidin by terrestrial organisms is expected to be very limited and the risk to terrestrial organisms is expected to be negligible.

4.2.2 Risks to Aquatic Organisms

Clothianidin is not expected to enter the aquatic environment when used as a cockroach bait, therefore the risk to aquatic organisms is expected to be negligible.

5.0 Value

5.1 Consideration of Benefits

Maxforce IMPACT Cockroach Bait Gel has value as it controls cockroaches, which are amongst the most common and difficult to control pests found in structures in Canada. Cockroaches are a serious nuisance and public health pest as they can spread bacteria, and can pose a significant health risk to allergy and asthma sufferers. Cockroaches are active year round and can be found in all types of structures in all types of conditions, ranging from the cleanest conditions to the most unsanitary.

Maxforce IMPACT Cockroach Bait Gel also has value as it incorporates a new bait formulation. Cockroaches have been known to develop aversion to baits after repeated exposure to the same formulation. Baits are widely used in the management of cockroaches, and a new formulation will provide users with an alternate bait to rotate with registered bait formulations. This will reduce the chance for bait aversion to develop and can also help overcome current problems of bait aversion in certain strains of cockroaches.

Maxforce IMPACT Cockroach Bait Gel has value as it provides another alternative active ingredient for control of this pest, and is compatible with standard cockroach control programs and methods. Cockroaches have developed resistance to many different insecticide active ingredients. This product does not provide a new mode of action for use against cockroaches. However, it does have value as it is a different mode of action from most registered cockroach products, provides an additional active ingredient, and is a new bait formulation.

Registered control products for cockroaches include dusts, powders, sprays, fumigants, and baits, and are formulated with a wide variety of active ingredients, including both older and newer chemistries. The majority of products registered for use against cockroaches are non-bait products which contain pyrethriods or pyrethrins. Currently registered cockroach bait products contain the active ingredients silicon dioxide, imidacloprid, abamectin, boron (present as boric acid or disodium octaborate tetrahydrate) or hydramethylnon. Additional bait formulations and active ingredients are needed for control of cockroaches since cockroaches have developed resistance to many older active ingredients and some registered products or uses are proposed for phase-out.

5.2 Acceptable Claims and Effectiveness Against Pests

In support of label claims for use of Maxforce IMPACT Cockroach Bait Gel against cockroaches, value information, which included nine laboratory trials, one small-scale trial, and four large-scale operational trials, was submitted for review. These studies support a general claim for control of cockroaches as data were submitted on Oriental, German, and American cockroaches. The value information supports an application rate of 0.75 to 1.5 g of bait per 1.0 m^2 for light-to-moderate infestations and up to 3.0 g of bait per 1.0 m^2 for severe or heavy infestations, applied as a crack and crevice or spot treatment. The submitted information demonstrated that the lower application rate was effective under light infestations.

The higher application rate under severe or heavy infestations is supported in areas with a higher infestation rate as more bait would be consumed by a larger cockroach population. If monitoring indicates that pest populations persist, bait placements may be replenished when consumed according to the remaining level of infestation.

5.3 Non-Safety Adverse Effects

Non-safety adverse effects are not expected from use of these products.

5.4 Supported Uses

The reviewed value information supports the use of Maxforce IMPACT Cockroach Bait Gel as a crack and crevice or spot treatment for control of cockroaches in structures at an application rate of 0.75 to 1.5 g of bait per 1.0 m^2 for light-to-moderate infestations and up to 3.0 g of bait per 1.0 m^2 for severe or heavy infestations.

6.0 Pest Control Product Policy Considerations

6.1 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: persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*.]

Clothianidin and its transformation products have previously been assessed in accordance with the PMRA Regulatory Directive DIR99-03[6] and evaluated against the Track 1 criteria during the environmental assessment of seed treatment uses. Refer to Regulatory Note REG2004-06 (revision)*, Clothianidin Poncho 600 Seed Treatment Insecticide* for details.

The PMRA has reached the following conclusions:

- Clothianidin does not meet all Track 1 criteria, and is not considered a Track 1 substance.
- Clothianidin does not form any transformation products that meet all Track 1 criteria.

[6] DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[7] The list is used as described in the PMRA Notice of Intent NOI2005-01[8] and is based on existing policies and regulations including DIR99-03 and DIR2006-02,[9] 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 conclusions:

Technical grade clothianidin and the end-use product Maxforce IMPACT Cockroach Bait Gel do not contain any formulants or 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.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for clothianidin is adequate to define the majority of toxic effects that may result from exposure. In short-term and chronic studies on laboratory animals, generalized toxicity manifested as effects on body weight and food consumption. In addition, effects were seen in liver, kidneys, reproductive organs, gastrointestinal tract and the immune system. Although genotoxicity was noted in several in vitro assays, there was no evidence of genotoxicity in several in vivo assays nor was there evidence of carcinogenicity in rats or mice. Developmental toxicity in the rabbit fetus was observed at a dose level which also caused effects in maternal animals. In the reproductive toxicity study, effects in the offspring were seen at a maternally non-toxic dose and a serious endpoint (stillbirth) was identified. In the developmental neurotoxicity study, signs of potential neurotoxicity (decreased motor activity and auditory startle response) were observed in young animals in the absence of maternal toxicity. There was no evidence of toxic effects in the developing immune system of offspring. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

---

7 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) 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, SI/2008-67 (2008-06-25) 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.*

8 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* under the *New Pest Control Products Act*.

9 DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

Exposure to clothianidin by applicators handling MaxForce IMPACT Cockroach Bait Gel and workers re-entering treated areas is expected to be negligible. The personal protective equipment on the product label, which is adequate to protect workers, includes wearing a long-sleeved shirt, long pants, socks, shoes and chemical-resistant gloves during application and clean-up activities.

Residential exposure is not expected to result in unacceptable risk when MaxForce IMPACT Cockroach Bait Gel is applied in areas inaccessible to children.

7.2 Environmental Risk

The use of clothianidin in the cockroach bait product Maxforce IMPACT Cockroach Bait Gel is expected to result in limited environmental exposure and therefore the risk to terrestrial and aquatic non-target organisms is expected to be negligible.

7.3 Value

Maxforce IMPACT Cockroach Bait Gel has value as it controls cockroaches when applied as a crack and crevice or spot treatment at an application rate of 0.75 to 1.5 g of bait per 1.0 m^2 for light-to-moderate infestations and up to 3.0 g of bait per 1.0 m^2 for severe or heavy infestations. Maxforce IMPACT Cockroach Bait Gel is compatible with standard cockroach control programs and methods. Cockroaches are a common and difficult to control pest found in structures, and are both a nuisance pest and a public health concern as they can spread bacteria and pose significant health risk to allergy and asthma sufferers. Maxforce IMPACT Cockroach Bait Gel also has value as it incorporates a new bait formulation and provides another active ingredient for control of this pest. Cockroaches are known to have developed resistance to many different insecticide active ingredients and have been known to develop aversion to baits after repeated exposure to the same formulation. Additional bait formulations and active ingredients are needed for control of cockroaches since cockroaches have developed resistance to many older active ingredients and some registered products or uses are proposed for phase-out.

8.0 Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Clothianidin Technical Insecticide and MaxForce IMPACT Cockroach Bait Gel, containing the technical grade active ingredient clothianidin, for crack and crevice or spot treatment for control of cockroaches both indoors and on the exterior of structures.

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

♂	male
♀	female
λ	wavelength
µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
ARfD	acute reference dose
atm	atmosphere
bw	body weight
°C	Celsius
CAS	Chemical Abstracts Service
cm	centimetres
DF	dry flowable
DNA	deoxyribonucleic acid
DNT	developmental neurotoxicity
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{75}	dissipation time 75% (the dose required to observe a 75% decline in concentration)
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
ER_{25}	effective rate for 25% of the population
F1	first generation
F2	second generation
g	gram
ha	hectare(s)
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation

LR_{50}	lethal rate 50%
m	metre
mg	milligram
mL	millilitre
MAS	maximum average score
MIS	maximum irritation score
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
NAFTA	North American Free Trade Agreement
N/A	not applicable
Nm	nanometre
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
P	parental generation
PBI	plantback interval
PCPA	*Pest Control Product Act*
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
RSD	relative standard deviation
SC	soluble concentrate
SOP	standard operating procedure
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 1 Toxicity Profile of MaxForce IMPACT Cockroach Bait Gel

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons)

Study Type/Animal/PMRA #	Study Results
Acute oral toxicity Sprague-Dawley rats PMRA #2367000	LD_{50} > 5000 mg/kg bw Low toxicity
Acute dermal toxicity Sprague-Dawley rats PMRA #2367002	LD_{50} > 5000 mg/kg bw Low toxicity
Acute inhalation toxicity Waiver PMRA #2367003	Based on the formulation type (viscous gel), the identity of the ingredients within the product, and the fact that the active ingredient has been demonstrated to be of low acute inhalation toxicity in the rat, the end-use product is not considered to pose an acute inhalation hazard
Eye irritation New Zealand white rabbits PMRA #2367005	MAS = 0, MIS = 4 (at 1 hour) Non-irritating
Skin irritation New Zealand white rabbits PMRA #2367005	All scores were 0 Non-irritating
Skin sensitization (LLNA) CBA/J mice PMRA #2367006	Non-sensitizer

Table 2 Amended Table Entry for the Reproduction Study with Clothianidin

Study Type / Animal / PMRA #	Study Results
Two-generation reproduction (dietary) Sprague-Dawley Rat PMRA 1194613, 1194614, 1194616	Parental NOAEL = 31.2/36.8 mg/kg bw/day in ♂/♀ Parental LOAEL = 163/189 mg/kg bw/day in ♂/♀ Effects at the LOAEL: Decreased body weight and body weight gain, decreased food conversion efficiency, and decreased thymus weight in P and F1 ♂ and ♀. Offspring NOAEL = 11.5 mg/kg bw/day Offspring LOAEL = 36.8 mg/kg bw/day Effects at the LOAEL: Decreased body weight gain and decreased thymus weight in F1 ♂ and ♀, delayed sexual maturation in F1 ♂. Reproductive NOAEL (♀) = 11.5 mg/kg bw/day Reproductive LOAEL (♀) = 36.8 mg/kg bw/day Effects at the LOAEL: Increased incidence of stillbirths in F1 and F2 litters. Reproductive NOAEL (♂) = 31.2 mg/kg bw/day Reproductive LOAEL (♂) = 163 mg/kg bw/day Effects at the LOAEL: Decreased percentage of progressively motile sperm in P and F1 ♂, decreased percentage of motile sperm in F1 ♂, increased percentage of sperm with detached heads in P and F1 ♂.

Table 3 Amended Acceptable Daily Intake (ADI) for Clothianidin

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1]
Chronic dietary	Two-generation reproductive toxicity study in rats (dietary)	Offspring NOAEL = 11.5 mg/kg bw/day Decreased body weight gain, increased incidence of stillbirths, delayed sexual maturation in male offspring and decreased thymus weight in offspring of both sexes	300
	ADI = 0.04 mg/kg bw/day		

[1] CAF (composite assessment factor) refers to the total of uncertainty and *Pest Control Product Act* factors for dietary and residential risk assessments

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
2366995	2013, Maxforce Impact Cockroach Gel (Bayer Advances Cockroach Bait Gel) Part 3, DACO: 3.0 CBI
2366996	2013, Product Chemistry of BES0600 Insecticide, DACO: 3.1, 3.1.1, 3.1.2, 3.1.3, 3.2.1, 3.2.2, 3.4.1, 3.5.1, 3.5.11, 3.5.12, 3.5.13, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.5, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
2434698	2014, Maxforce IMPACT Cockroach Bait Gel (containing clothianidin) Sub. No. 2013- 6683; Response to Clarification e-mail, DACO: 3.2.1, 3.4.1, 3.5.1, 3.5.10, 3.5.14, 3.5.2, 3.5.3, 3.5.6, 3.5.7, 3.5.9 CBI
2434700	2013, Certificate of Analysis [CBI REMOVED], DACO: 3.2.1 CBI
2434701	2014, Change in the peak shape of Chlothianidin in the chromatograms within the same sequence, DACO: 3.4.1 CBI
2434703	2012, GLP Physical & Chemical Characterization Study Raw Data Sheet, DACO: 3.5.1, 3.5.2, 3.5.3, 3.5.6, 3.5.7, 3.5.9 CBI
2436777	2014, Maxforce IMPACT Cockroach Bait Gel (containing clothianidin) Sub. No. 2013- 6683; Response to Clarification e-mail , DACO: 3.2.1,3.5.10,3.5.14 CBI
2436778	2014, 100% Composition of [CBI REMOVED] (material number 10198998), DACO: 3.2.1 CBI
2436779	2013, Determination of physico-chemical propoerties and accelerated storage stability test for clothianidin RB 1% in PE Syringe, DACO: 3.5.10,3.5.14 CBI

2.0 Human and Animal Health

PMRA Document Number	Reference
2367000	2013, BES0600 Insecticide Acute Oral Toxicity Up and Down Procedure in Rats, DACO: 4.6.1
2367002	2013, BES0600 Insecticide Acute Dermal Toxicity Study in Rats, DACO: 4.6.2
2367003	2013, Waiver of DACO 4.6.3 Acute Inhalation Requirement, DACO: 4.6.3
2367004	2013, BES0600 Insecticide Primary Eye Irritation Study in Rabbits, DACO: 4.6.4

2367005	2013, BES0600 Insecticide Primary Skin Irritation Study in Rabbits, DACO: 4.6.5
2367006	2013, BES0600 Insecticide Local Lymph Node Assay (LLNA) in Mice, DACO: 4.6.6

3.0 Value

PMRA Document Number	Reference
2366989	2013, Clothianidin Gel-Bait Insecticide (BES0600 Insecticide) for use as a crack and crevice treatment containing 1.0 % w/w clothianidin insecticide for the control of cockroach species indoors and outdoors for the professional market: Maxforce Impact Cockroach Bait Gel and the consumer market: Bayer Advance Cockroach Bait Gel, DACO: 10.1,10.2.1,10.2.2,10.2.3.1, 10.2.3.3,10.3.1,10.3.2
2366992	2013, Laboratory and field studies, DACO: 10.2.3.3
2366993	2013, Product Performance: Laboratory and Field Efficacy Testing for BES0600 Insecticide, DACO: 10.2.3.3