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Proposed Registration Decision

PRD2015-20

Codlelure

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Overview

Proposed Registration Decision for Codlelure

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 Bedoukian CM Pheromone and Semios CM, containing the technical grade active ingredient codlelure, which is intended to disrupt codling moth (*Cydia pomonella*) mating and is to be used on apples, pears, and other pome fruits; as well as peaches, prunes, and other stone fruits.

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 Bedoukian CM Pheromone and Semios CM.

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 (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 codlelure, the PMRA will consider any comments received from the public in response to this consultation document.³ The PMRA will then publish a Registration Decision⁴ on codlelure, 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 Codlelure?

Codlelure is a major component of the sex pheromone of the codling moth and is the active ingredient in the end-use product Semios CM. This product is formulated for release from automated aerosol dispensers for mating disruption of codling moth in pome and stone fruit orchards. In nature, the sex pheromone is produced by female moths and attracts male moths for mating.

Health Considerations

Can Approved Uses of Codlelure Affect Human Health?

Codlelure is unlikely to affect human health when used according to label directions.

The straight-chain lepidopteran pheromone (SCLP), codlelure, which is used to formulate Semios CM, is unlikely to have a negative effect on human health when the product is used according to label directions. SCLPs are naturally occurring compounds that are produced by many lepidopteran insect species (moths and butterflies) to communicate with other members of the same species.

Exposure to codlelure may occur when handling or applying Semios CM or by entering orchards that are treated with Semios CM. 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 population (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.

In general, SCLPs are non-toxic compounds that are readily metabolized by most living organisms. Toxicity studies on SCLPs have generally indicated no mammalian toxicity. Exposure to people from the use of Semios CM is, therefore, not expected to be of concern.

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*.

Occupational Risks from Handling Semios CM

Occupational risks are not of concern when Semios CM is used according to the proposed label directions, which include protective measures.

Semios CM is to be applied by commercial applicators who will affix dispensers in the upper third of the tree canopy in orchards.

Occupational exposure to individuals handling Semios CM is not expected to result in unacceptable risk when the product is used according to label directions. Precautionary statements (for example, wearing of personal protective equipment) and hygiene statements on the label aimed at mitigating exposure are considered adequate to protect individuals from any unnecessary risk due to occupational exposure.

Residential and Bystander Exposure and Risk

As the application of Semios CM involves only authorized personnel, bystander exposure is expected to be minimal and not of concern when the end-use product is used according to the label directions. Residential exposure is also likely to be minimal when the label directions are followed for Semios CM.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Semios CM is formulated as an aerosol that is automatically dispensed in the upper canopy of orchards with the nozzle pointed away from foliage and fruit. The maximum application rate of Semios CM is 277 g of active ingredient per hectare per year. The PMRA has determined that because codlure is classified as an SCLP and has a maximum application rate that is below the allowable safe limit of 375 g of active ingredient per hectare per year established for SCLPs, a maximum residue limit does not need to be specified for it under the *Pest Control Products Act*. Refer to Regulatory Proposal PRO2002-02, *Guidelines for the Research and Registration of Pest Control Products Containing Pheromones and Other Semiochemicals* for specific details regarding the safe limit of active ingredient per hectare per year established for SCLPs.

No risk due to exposure from drinking water is anticipated as codlure is unlikely to enter drinking water sources.

Environmental Considerations

What Happens When Codlure Is Introduced Into the Environment?

Bedoukian CM Pheromone contains the technical grade active ingredient codlure. Codlure, when used in Semios CM aerosol canisters, enters the environment through vaporization into air by release from automated aerosol “puff-emitting” dispensers in orchards (apples, pears, and other pome fruits; peaches, prunes, and other stone fruits).

The active ingredient is an SCLP, which is a well-defined group of chemicals that are naturally-produced and are known to dissipate rapidly in the environment and, thus, pose minimal risk. Through this use pattern, and because of the inherent nature of SCLPs, limited environmental exposure is expected.

Value Considerations

What Is the Value of Semios CM?

Semios CM controls codling moth by mating disruption in pome and stone fruit orchards.

Semios CM dispensers are placed in pome or stone fruit orchards and release the pheromone, codlelure, into the atmosphere. This release of pheromone interferes with the ability of male codling moths to find mates, thus reducing the number of larvae that damage pome and stone fruit. Semios CM can be used as part of an integrated pest management program for codling moth by both conventional and organic producers and is compatible with other management strategies. In conventional orchards, the use of pheromone-based mating disruption can reduce the need for application of conventional pest control products. Resistance to pheromone-based mating disruption is unlikely to develop.

Semios CM is dispensed by a new technology for releasing codling moth pheromone for mating disruption. It is a liquid formulation which is released by automatic dispensers as an aerosol spray. Other registered products for mating disruption of codling moth are solid dispensers. In comparison to the solid dispensers, far fewer Semios CM dispensers are required per unit area, which may result in time and labour savings during installation. Semios CM dispensers also release pheromone only during the period of time when the moths are active, in contrast to the solid dispensers which release pheromone continuously. They also release the same amount of pheromone throughout the season for season-long consistency in application rate, even at the end of the growing season when rates from solid dispensers tend to decline as their supply of pheromone becomes depleted.

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.

Key Risk-Reduction Measures

Human Health

The key risk-reduction measures being proposed on the label of the technical product (Bedoukian CM Pheromone) and end-use product (Semios CM) to address the potential risks identified in this assessment are as follows.

The signal words “DANGER – SKIN IRRITANT” are required on the principal display panels of the labels for both Bedoukian CM Pheromone and Semios CM. The signal words “WARNING – EYE IRRITANT” are required on the principal display panel of the Semios CM label and the signal words “CAUTION – EYE IRRITANT” are required on the principal display panel of the Bedoukian CM Pheromone label.

Standard hazard and precautionary statements are also required on the end-use product labels to inform workers of the irritation potential of the active ingredient to the skin and eyes. Workers handling containers of Semios CM will be required to wear standard personal protective equipment including chemical resistant gloves, coveralls, goggles or face shield, long-sleeved shirt, shoes, and socks.

A restricted-entry interval is not required for Semios CM.

Next Steps

Before making a final registration decision on codlure, 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 codlure (based on the Science Evaluation section 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

Codlure

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Codlure
Function	Pheromone
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	(8E,10E)-dodeca-8,10-dien-1-ol
2. Chemical Abstracts Service (CAS)	(8E,10E)-8,10-dodecadien-1-ol
CAS number	33956-49-9
Molecular formula	C ₁₂ H ₂₂ O
Molecular weight	182.13
Structural formula	
Purity of the active ingredient	94%

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

Technical Product – Bedoukian CM Pheromone

Property	Result
Colour and physical state	White to pale yellow solid
Odour	Waxy, fatty odour
Melting point	26.98 °C
Boiling point	282.81 °C
Density	0.87 g/mL
Vapour pressure at 20 °C	0.00035 mmHg
Ultraviolet (UV)-visible spectrum	$\lambda_{\text{max}} = 227 \text{ nm}$
Solubility in water at 20 °C	34.15 mg/L
Solubility in organic solvents at 20 °C	Insoluble at 1% in non-polar solvents, fully soluble in polar solvents
<i>n</i> -Octanol-water partition coefficient (K_{ow})	$\log Kow = 4.34$
Dissociation constant (pK_a)	N/A
Stability (temperature, metal)	A slight visible change in the colour of the material was observed in room temperature samples with iron acetate. Discoloration was observed in nearly all of the elevated temperature samples. The purity measurements on some samples changed slightly at both room temperature and at 54 °C by the end of the 14 day test period.

End-Use Product – Semios CM

Property	Result
Colour	Clear pale yellow
Odour	Waxy odour
Physical state	Aerosol
Formulation type	Pressurized product
Guarantee	18.05%
Container material and description	Metered aerosol dispensing apparatus made from steel (with reservoir at the valve). 154–614 g
Density	0.80–0.83 g/mL
pH of 1% dispersion in water	N/A
Oxidizing or reducing action	N/A
Storage stability	The product was shown to be stable when stored for 12 months at room temperature in commercial packaging.
Corrosion characteristics	Not corrosive to the container material.
Explodability	The product in the container is not explosive, but the containers should not be exposed to temperatures above 50°C as the content is under pressure and may explode if heated.

1.3 Directions for Use

Semios CM controls codling moth by mating disruption. The product is emitted from automated dispensers as an aerosol of 40 mg product every 15 minutes for up to 12 hours per day for up to 160 days. Dispensers are placed in pome and stone fruit orchards at 2.5 dispensers/ha and up to 5 dispensers/ha at the orchard edge facing the prevailing wind. Automated dispensers allow for Semios CM to be released only when codling moths are flying (dusk to dawn when temperatures are above 10°C). While the maximum application rate of Semios CM is 277 g a.i./ha/year, no more than 375 g a.i./ha are to be applied per year.

1.4 Mode of Action

The precise mode of action of mating disruption is not yet well understood. For example, it may be behavioural, with males being attracted to pheromone dispensers rather than to females; it may be physiological, with the insect nervous system becoming habituated and ceasing to respond to the continuous presence of pheromone in the atmosphere; or it may involve more than one mechanism. The end result is that males fail to find females for mating and, therefore, the females cannot lay fertile eggs so that the subsequent larval population is low enough that fruit damage is maintained below economic thresholds.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and impurities in the technical product have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the end-use product has been assessed to be acceptable for use as an enforcement analytical method.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

In general, SCLPs have been well-characterized as having non-toxic modes of action with known low mammalian toxicity and no evidence of mutagenicity or other long term effects. With an established history of exposure to humans and the environment with no known adverse effects other than mating disruption within the targeted lepidopteran insect population, it is generally accepted that SCLP-containing products will pose minimal risk to human health. Therefore, reduced toxicological data requirements have been established by PMRA for SCLPs and all are judged to be toxicologically equivalent. The applicant submitted scientific rationales to waive toxicity testing of the technical grade active ingredient (Bedoukian CM Pheromone) and the end-use product (Semios CM) based on arguments of toxicological equivalence of codlelure to other SCLPs and the hazard profiles of the formulants in the end-use product, which were determined to be acceptable.

Available acute toxicity data on various SCLPs indicate low oral toxicity ($LD_{50} > 5000$ mg/kg; practically nontoxic), low dermal toxicity ($LD_{50} > 2000$ mg/kg; practically nontoxic), low inhalation toxicity (LC_{50} generally > 5 mg/L; practically nontoxic), and no evidence of mutagenicity (Ames Salmonella assay). Although limited in number, available short-term toxicity studies also indicate SCLPs pose no long-term health concerns in mammals. A 90-day feeding study in the rat was conducted at doses up to 1 g/kg of a commercial blend of branched acetates with an aliphatic chain length between C10 and C14. The results indicated no significant signs of toxicity other than those expected from longer-term exposure to high doses of a hydrocarbon, namely, histopathologic evidence of nephropathy in males and increased liver and kidney weights in both sexes. A developmental toxicity study in the rat involving inhalation exposure to unbranched, primary alcohols with chain length C8 to C10 indicated no detectable developmental toxicity.

SCLPs are readily metabolized by enzyme systems present in most living organisms and should, therefore, present no risk to individuals with normal physiology. SCLPs, like other long-chain fatty acid molecules, are metabolized either by β -oxidation or by forming complexes with glucuronide and excreted by the kidneys.

In a published primary skin irritation study, 0.5 mL of undiluted SCLP ((Z)-7-dodecen-1-ol) was administered onto the skin of six albino rabbits. The mean primary irritation score for (Z)-7-dodecen-1-ol was 8.0/8.0 because it caused superficial burns on the test animal and was, therefore, categorized as extremely irritating to the skin. Because codlelure is structurally similar to (Z)-7-dodecen-1-ol, the PMRA has determined that it, too, is likely to be an extreme skin irritant. Furthermore, since codlelure comprises 18.05% of the end-use product, Semios CM is also expected to be extremely irritating to the skin.

In a published primary eye irritation study, 0.1 mL of undiluted SCLP ((Z)-7-dodecen-1-ol) was instilled into the conjunctival sac of the right eye of six New Zealand White rabbits. Irritation was scored by the method of Draize. Since the time where the score equals zero exceeds 72 hours, (Z)-7-dodecen-1-ol is categorized as a mild eye irritant. Because codlure is structurally similar to (Z)-7-dodecen-1-ol, it is also expected to be a mild eye irritant. However, Semios CM is expected to be moderately irritating to the eye based on the ocular irritancy of certain formulant ingredients contained in the end-use product.

Based on all of the available data for SCLPs, there is no evidence of increased susceptibility of infants and children in comparison to adults that may result from exposure to SCLPs. Furthermore, there is no evidence that SCLPs have a potential to disrupt endocrine activity in humans.

Incident Reports

Since 26 April 2007, registrants have been required by law to report incidents to the PMRA, including adverse effects to Canadian health or the environment. Incidents were searched and reviewed for the active ingredient codlure. As of 17 March 2015, no incident reports involving codlure had been submitted to the PMRA.

3.2 Occupational and Bystander Exposure and Risk Assessment

3.2.1 Dermal Absorption

Due to the rapid volatility of codlure, dermal absorption from the application of Semios CM is expected to be minimal.

3.2.2 Use Description

Semios CM is to be emitted by automated (battery-powered) aerosol dispensers every 15 minutes over a 12 hour period spanning dusk to dawn. The dispensers are to be equipped with radio transceivers to allow them to be controlled remotely. Dispensers are to be placed in the top third of the orchard canopy and evenly spaced so that there are 2.5 dispensers per hectare. The density will be increased to five dispensers per hectare at the edge of the orchard that is facing the prevailing winds. Optimal application begins at or just before codling moth first flight which is determined by degree-day models and presence of codling moths in pheromone traps and will continue until the end of moth flight of the last seasonal moth generation or until harvest, whichever comes first. The aerosol containers will range from 154 g (27.79 g of active ingredient)/canister to 614 g (110.83 g of active ingredient)/canister representing 3,850 to 15,350 emissions, respectively. Each emission will contain 7.22 mg of active ingredient. Assuming a standard rate of application, canisters will have enough pheromone for 80 days (154 g canister) to 320 days (614 g canister). The maximum full season (160 days) application for 2.5 dispensers per hectare is 138.5 g of active ingredient/ha; when five dispensers per hectare are used, the maximum full season application is 277 g of active ingredient/ha.

3.2.3 Mixer, Loader and Applicator Exposure and Risk Assessment

Occupational exposure to Semios CM is expected to be mainly via the dermal route, and to a lesser extent by inhalation, during handling and placement of the dispensers in application sites.

Mixing is not required, but the pressurized canisters containing Semios CM require installation in automated dispenser units. Since the end-use product is expected to be corrosive to the skin and moderately irritating to the eyes, precautionary statements on the product label require the user to wear chemical resistant gloves, coveralls, goggles or face shield, long-sleeved shirt, shoes and socks, and to not allow product to get in eyes or on skin, avoid inhaling/breathing vapour or spray mist and to wash hands with soap and water after use. Since inhalation exposure is not expected to be a concern due to the low acute inhalation toxicity of SCLPs to humans, a respirator is not required for use during handling or installation of the canisters.

Clean-up activity is limited to collecting the dispensers and removing the canisters at the end of the use season. Repair activities consist of locating a malfunctioning dispenser and either replacing it or visually diagnosing a potential problem. Dispensers do not emit aerosol during the daytime when such work is likely to occur; however, the label includes the precautionary statement 'Ensure dispensing control is set to off on user interface when setting up, repairing or removing dispensers' to minimize unintended exposure.

3.2.4 Post-Application Exposure and Risk

Minimal post-application exposure is expected when the end-use product is used according to label directions and applied overnight by an automated dispenser system. Between applications, workers performing routine daily activities such as scouting for insects and disease, harvesting, pruning, and other maintenance practices are expected to come in contact with treated foliage, fruit, tree limbs, etc., but exposure to codlure on such surfaces is expected to be negligible due to the volatile nature of the active ingredient. Workers performing these activities should also be able to avoid direct contact with the dispensers. Inhalation exposure to codlure is expected to be comparable or less than pheromone levels occurring naturally during codling moth outbreaks and, therefore, not of concern. A restricted-entry interval is not required for Semios CM.

3.2.5 Residential and Bystander Exposure and Risk

Due to the placement of the dispensers in orchard canopies, the timing of the applications (overnight), the volatility and rapid degradability of the components of Semios CM, and the rate of application of active ingredient being comparable to (or less than) natural background levels, bystander and residential exposure to codlure is expected to be negligible and not of concern.

3.3 Food Residue Exposure Assessment

3.3.1 Food and Drinking Water

Semios CM is formulated as an aerosol that is automatically dispensed in the upper canopy of orchards with the nozzle pointed away from foliage and fruit. The maximum application rate of Semios CM is 277 g of active ingredient/ha/year. Therefore, the use of Semios CM formulated with codlure is not expected to result in unacceptable dietary risks when the product is used according to label directions. In addition, no risk due to exposure from drinking water is anticipated as the active ingredient is volatile and thus unlikely to enter surface or underground sources of drinking water.

3.3.2 Maximum Residue Limits

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine that the consumption of the maximum amount of residues that are expected to remain on food products, when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally established as a Maximum Residue Limit (MRL) under the *Pest Control Products Act* for the purposes of adulteration provision of the *Food and Drugs Act*. Health Canada sets science-based MRLs to ensure the food Canadians eat is safe.

Given the full season application rate for Semios CM is 138.5–277 g a.i./ha/year, which is below the allowable limit of 375 g of active ingredient/ha/year established as safe for SCLPs, as well as the low acute, short-term and chronic toxicity of SCLPs, the specification of an MRL is not required for codlelure under the *Pest Control Products Act*.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Straight-chained lepidopteran pheromones consist of unbranched aliphatic compounds. Degradation and dissipation in the environment is rapid, primarily through oxidative processes with enzymes found ubiquitously in nature. Therefore, when codlelure is released into the environment, the active ingredient is expected to degrade rapidly. Codlelure, when used in Semios CM aerosol canisters, enters the environment through vaporization into air by release from automated aerosol “puff-emitting” dispensers in orchards (apples, pears, and other pome fruits; peaches, prunes, and other stone fruits). Dispensers are hung in the upper third of the tree canopy with the nozzle pointing away from foliage and fruit at an average density of 2.5 dispensers per hectare. The chemical is, therefore, expected to remain as a vapour and degrade rapidly, and is not expected to partition to water, soil, or to non-target organism food materials.

4.2 Environmental Risk Characterization and Effects on Non-Target Species

A risk assessment was not conducted for Bedoukian CM Pheromone. Environmental exposure is expected to be minimal for this type of pheromone dispenser. At the default dispensing rate of 7.22 mg a.i. per 40 mg puff, 1 puff per 15 minutes over the maximum of 12 hours per day, and approximately 160 days of use per season, the total maximum rate of application is 138.5 g a.i./ha per season. This rate is considered to be comparable to naturally occurring emissions of pheromones that could occur during a potential infestation. It is, therefore, not expected to have an impact on non-target organisms and no environmental toxicity data were required (see Regulatory Proposal PRO2002-02 – *Guidelines for the Research and Registration of Pest Control Products Containing Pheromones and Other Semiochemicals*). Further to this, arthropod semiochemicals are inherently different from conventional pesticides in their non-toxic, target-specific mode of action and natural occurrence. They are generally effective at very low rates, comparable to levels that occur naturally.

Therefore, based on the proposed application method (volatilization into air by release from automated aerosol “puff-emitting” dispensers, at a density of 2.5 dispensers per hectare and up to 5 dispensers per hectare at the orchard edge facing the prevailing wind), expected rapid breakdown, and limited potential to partition to water or soil, exposure to non-target aquatic and terrestrial organisms in areas of use will be low. Therefore, the proposed use of codlelure for this use is not expected to pose a concern to non-target organisms.

5.0 Value

5.1 Consideration of Benefits

Semios CM dispensers can be a valuable addition to sustainable pest management in pome and stone fruit orchards. Codling moth is a direct pest of various pome and stone fruits, and pheromone-based mating disruption using Semios CM dispensers can be part of an integrated pest management program for codling moth in both conventional and organic production.

Alternative active ingredients registered for control of codling moth include conventional pest control products such as carbamates, organophosphates, pyrethroids, neonicotinoids, spinosyns, diamides and insect growth regulators. Registered alternatives also include nonconventional active ingredients such as *Bacillus thuringiensis aizawai*, codling moth granuloviruses and kaolin, as well as codling moth pheromone formulated as solid matrix dispensers. In conventional orchards, pheromone-based mating disruption with Semios CM has value in an integrated pest management program because it can reduce the need for application of conventional pest control products. Some of the alternative active ingredients, such as codling moth granulovirus, are only effective under limited environmental parameters (for example, certain temperature and humidity conditions) or may be relatively slow acting so that some fruit damage may occur before larval death (for example, insect growth regulators). In organic production systems, Semios CM can help reduce populations in orchards that rely more on physical and cultural controls, such as orchard sanitation practices.

Another benefit of pheromone-based mating disruption is that development of resistance to the use of pheromones is considered to be unlikely, which is not the case for some of the conventional products. Also, when the use of mating disruption reduces the need for applications of conventional chemicals, selection pressure for possible development of resistance to those chemicals may be reduced.

Codlelure, along with two other pheromone components of codling moth, is also formulated into solid dispensers for mating disruption. These dispensers are also placed in the orchard, but at much higher densities and the pheromone is released continuously. In comparison, far fewer Semios CM dispensers are required per unit area, which may result in time and labour savings during installation. Semios CM dispensers also release pheromone only during the period of time when the moths are active, in contrast to the solid dispensers which release pheromone continuously. They also release the same amount of pheromone throughout the season for season-long consistency in application rate, even at the end of the growing season when rates from solid dispensers tend to decline as their supply of pheromone becomes depleted.

5.2 Effectiveness Against Pests

Two operational efficacy trials testing Semios CM were conducted in British Columbia and Ontario. These trials demonstrated that Semios CM, emitted every 15 minutes during a 12-hour period (5:00PM – 5:00AM) over the growing season, controlled codling moths in pome and stone fruits.

5.3 Non-Safety Adverse Effects

Semios CM caused slight foliage speckling within 0.5-1 metre of the dispenser nozzle and minor fruit russetting within two metres. To mitigate these effects a statement is included on the label instructing the user to place the dispensers in a manner to minimize Semios CM contact with plant tissues.

5.4 Supported Uses

Semios CM controls codling moth in pome and stone fruit orchards by mating disruption and is applied by automated dispensers. These automated dispensers allow the active ingredient to be released only when codling moths are flying (dusk to dawn when temperatures are above 10°C). Each dispenser emits an aerosol of 40 mg product every 15 minutes for up to 12 hours per day for up to 160 days. Dispensers are placed in orchards at 2.5 dispensers/ha and up to 5 dispensers/ha along the orchard edge facing the prevailing wind. No more than 375 g a.i./ha are to be applied per year.

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*].

During the review process, Bedoukian CM Pheromone (the technical grade active ingredient) and Semios CM (the end-use product) containing codlelure were 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. The PMRA has reached the following conclusions:

- Bedoukian CM Pheromone (containing codlelure) does not meet Track 1 criteria as the active ingredient is not highly toxic, and will not form any transformation products which meet the Track 1 criteria. Codlelure is a naturally-produced chemical and is not expected to be persistent in the environment or to bioaccumulate.
- There are also no formulants, contaminants or impurities present in the end-use product that would meet the TSMP Track 1 criteria.

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*⁵. The list is used as described in the PMRA Notice of Intent NOI2005-01⁶ and is based on existing policies and regulations including DIR99-03 and DIR2006-02⁷ 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:

- Bedoukian CM Pheromone and Semios CM do not contain any other formulants or contaminants of environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641-2643: *List of Pest Control Product Formulants of Health or Environmental Concern*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

7.0 Summary

7.1 Human Health and Safety

The technical product (Bedoukian CM Pheromone) and end-use product (Semios CM) containing the active ingredient codlelure, are expected to be of low acute toxicity via the oral, dermal, and inhalation routes. They are not considered to be dermal sensitizers, but Bedoukian CM Pheromone and Semios CM are expected to be extremely irritating to the skin. Bedoukian CM Pheromone is expected to be mildly irritating and Semios CM moderately irritating to the eyes. Bedoukian CM Pheromone and Semios CM are considered to be non-mutagenic.

Occupational exposure to Semios CM is expected to be minimal if the precautionary and hygiene statements and recommended personal protective equipment on the product label, which are intended to minimize worker exposure, are observed. Bystander and post-application exposure is also likely to be minimal and not of concern.

⁵ *Canada Gazette*, Part II, Volume 139, Number 24, SI/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 I 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*.

⁶ Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*.

⁷ Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

Dietary exposure to codlelure from the use of Semios CM is not expected to result in unacceptable dietary risks when the product is used according to label instructions. The Agency did not specify an MRL for codlelure.

7.2 Environmental Risk

The active ingredient, codlelure, is a straight-chained lepidopteran pheromone, a group of chemicals that are naturally-produced and are well known to break down rapidly in the environment. Codlelure enters the environment through volatilization into air when released from fixed automated aerosol “puff-emitting dispensers”. Partitioning to water or soil is not expected to occur and exposure to non-target aquatic and terrestrial organisms in crop areas will be low. Therefore, risk to the environment is expected to be minimal with the use of codlelure in the end-use product Semios CM.

7.3 Value

Sufficient value information was supplied to support the registration of Semios CM to control codling moth by mating disruption in pome and stone fruits. Semios CM has value to pome and stone fruit growers as part of an integrated pest management program in both conventional and organic orchards. Use of Semios CM in conventional orchards may reduce the need for application of conventional pest control products to control codling moth and thereby reduce selection pressure for resistance to those products. With Semios CM, pheromone is released by automatic dispensers only when conditions are suitable for codling moth flight and more consistently over the season than with solid dispensers. In addition, far fewer Semios CM dispensers are required per unit area than the solid dispensers, which may result in time and labour savings during installation.

8.0 Proposed 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 Bedoukian CM Pheromone and Semios CM, containing the technical grade active ingredient codlelure, which is intended to disrupt codling moth (*Cydia pomonella*) mating and is to be used on apples, pears, and other pome fruits; as well as peaches, prunes, and other stone fruits.

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

°C	degrees Celsius
λ	wavelength
a.i.	active ingredient
CAS	Chemical Abstracts Service
CBI	confidential business information
DACO	data code
g	gram(s)
ha	hectare(s)
Hg	mercury
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{ow}	<i>n</i> -octanol-water partition coefficient
L	litre
LC ₅₀	lethal concentration 50%
LD ₅₀	lethal dose 50%
mg	milligram(s)
mL	millilitre
mm	millimetre
MRL	maximum residue limit
nm	nanometre
pH	measure of the acidity or basicity of an aqueous solution
p <i>K</i> _a	dissociation constant
PMRA	Pest Management Regulatory Agency
SCLP	straight-chain lepidopteran pheromone
TSMP	Toxic Substances Management Policy
UV	ultraviolet

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	References
2399655	2014, Manufacturer/Product Info, DACO: 2.2,2.3,2.3.1,2.4,2.5,2.6,2.7,2.8,2.9
2399657	2014, Process Summary, DACO: 2.11.1 CBI
2399660	2014, Starting Materials, DACO: 2.11.2 CBI
2399662	2014, Process - detailed, DACO: 2.11.3 CBI
2399664	2014, Impurity ID/Discussion, DACO: 2.11.4 CBI
2399666	2014, Certified Limits, DACO: 2.12.1 CBI
2399667	2014, Method Validation, DACO: 2.13.1 CBI
2399668	2014, Confirmation of ID, DACO: 2.13.2
2399671	2014, Batch data, DACO: 2.13.3 CBI
2399673	2014, Phys/chem properties, DACO: 2.14
2399675	2014, UV Spectrum, DACO: 2.14.12
2399676	2014, Stability study, DACO: 2.14.13 CBI
2468063	2014, Detailed process description plus antioxidant addition for Bedoukian CM Pheromone sub # 2014-0861, DACO: 2.11.3 CBI
2499789	2015, Confirmation of identity of impurities for Bedoukian CM Technical Pheromone Sub 2014-0861, DACO: 2.13.2 CBI
2427446	2014, Product Identification, DACO: 3.1
2427447	2013, Product Chemistry: Group A, DACO: 3.2,3.3.1 CBI
2427448	2013, Enforcement analytical method, DACO: 3.4 CBI
2427449	2013, Product Chemistry: Group B, DACO: 3.5 CBI
2427450	2014, Chemical and physical properties (part 2), DACO: 3.5
2490522	2014, Application for Registration of Semios CM - Physical and Chemical Characteristics: Storage Stability and Corrosion Characteristics, DACO: 3.5.10,3.5.14 CBI

2.0 Human and Animal Health

PMRA Document Number	References
2427451	2014, Toxicity data requirements for Semios CM Scientific rationales to fulfill certain toxicity requirements Part 1, DACO: 4.6.1 CBI
2427452	2014, Toxicity data requirements for Semios CM Scientific rationales to fulfill certain toxicity requirements Part 2, DACO: 4.6.2 CBI
2427453	2014, Toxicity data requirements for Semios CM Scientific rationales to fulfill certain toxicity requirements Part 3, DACO: 4.6.3 CBI

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- 2427454 2014, Toxicity data requirements for Semios CM Scientific rationales to fulfill certain toxicity requirements Part 4, DACO: 4.6.4 CBI
- 2427455 2014, Toxicity data requirements for Semios CM Scientific rationales to fulfill certain toxicity requirements Part 5, DACO: 4.6.5 CBI
- 2427456 2014, Toxicity data requirements for Semios CM Scientific rationales to fulfill certain toxicity requirements Part 6, DACO: 4.6.6 CBI
- 2541024 2014, Exposure (Occupational and/or Bystander) Summary for Semios CM Aerosol, DACO: 5.1,5.2
- 2541025 2014, Exposure (Occupational and/or Bystander) Summary for Semios CM Aerosol, DACO: 5.1,5.2 CBI

3.0 Value

- 2539475 2014, Value summary for registration of Semios CM aerosol mating disruption formulation for codling moth (*Cydia pomonella*), DACO: 10.1,10.2,10.3,10.4,10.5 CBI
- 2439476 2014, Value summary for registration of Semios CM aerosol mating disruption formulation for codling moth (*Cydia pomonella*), DACO: 10.1,10.2,10.3,10.4,10.5

B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

- 2501760 Beroza, Morton, et al. 1975. Acute Toxicity Studies with Insect Attractants. *Toxicology and Applied Pharmacology*, 31: 421-429, DACO: 4.6.4, 4.6.5

2.0 Value

Ontario Ministry of Agriculture, Food and Rural Affairs. 2011. Codling moth. <http://www.omafra.gov.on.ca/english/crops/facts/codling.htm>. Accessed 8 July 2014.

Michigan State University Arthropod Pesticide Resistance Database, <http://www.pesticideresistance.org>, Accessed 9 March 2015.