



Health Canada
Santé Canada

Your health and
safety... our priority.

Votre santé et votre
sécurité... notre priorité.

Proposed Registration Decision

PRD2010-07

Garlic Oil

(publié aussi en français)

19 March 2010

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. 6604-E2
Ottawa, Ontario
K1A 0K9

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

Canada 

HC Pub: 100131

ISBN: 978-1-100-15354-4 (978-1-100-15355-1)
Catalogue number: H113-9/2010-7E (H113-9/2010-7E-PDF)

© Her Majesty the Queen in Right of Canada, represented by the Minister of Health Canada, 2010

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of the Minister of Public Works and Government Services Canada, Ottawa, Ontario K1A 0S5.

Table of Contents

Overview.....	1
Proposed Registration Decision for Garlic Oil.....	1
What Does Health Canada Consider When Making a Registration Decision?.....	1
Health Considerations	2
Environmental Considerations	4
Value Considerations.....	4
Measures to Minimize Risk.....	4
Next Steps.....	5
Other Information	5
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.....	8
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 Food Residue Exposure Assessment	10
3.3 Residential Risk Assessment	10
3.3.1 Use Description/Use Scenario	10
3.3.2 Applicator Exposure and Risk Assessment	10
3.3.3 Bystander Exposure and Risk Assessment	11
3.3.4 Post-Application Exposure	11
4.0 Impact on the Environment.....	11
4.1 Fate and Behaviour in the Environment	11
4.2 Environmental Risk Characterization.....	11
5.0 Value.....	12
5.1 Effectiveness Against Pests	12
5.1.1 Acceptable Efficacy Claims.....	12
5.2 Sustainability	12
5.2.1 Survey of Alternatives	12
5.2.2 Compatibility with Current Management Practices Including Integrated Pest Management.....	12
5.2.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance	12
6.0 Pest Control Product Policy Considerations.....	12
6.1 Toxic Substances Management Policy Considerations	12
6.1.1 Formulants and Contaminants of Health or Environmental Concern.....	13

7.0	Summary	13
7.1	Human Health and Safety	13
7.2	Environmental Risk	14
7.3	Value	14
7.4	Unsupported Uses	14
8.0	Proposed Regulatory Decision.....	14
	List of Abbreviations	15
	Appendix I Tables and Figures	17
	Table 1 Acute Toxicity of Garlic Oil and Its Associated End-use Product (Comfort Zone).....	17
	References.....	19

Overview

Proposed Registration Decision for Garlic Oil

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 Garlic Oil FCC 8170 and Comfort Zone, containing the technical grade active ingredient garlic oil, to repel mosquitoes outdoors.

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 Garlic Oil FC 8170 and Comfort Zone.

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 Pesticide 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 garlic oil, 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 garlic oil, 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 Garlic Oil?

Garlic oil is an extract of garlic (*Allium sativum*). In the end-use product, Comfort Zone, it is formulated to be water-soluble. Garlic contains a high concentration of sulphur compounds, only some of which contribute to its characteristic odour. Garlic is known to be repellent to various insects, however the exact mode of action of this repellency is unknown.

Health Considerations

Can Approved Uses of Garlic Oil Affect Human Health?

Garlic oil is unlikely to affect your health when used according to label directions.

Exposure to garlic oil may occur when handling and applying the end-use product, Comfort Zone, as well as during typical residential activities following application. 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 (e.g., 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.

The technical grade active ingredient, garlic oil, is of slight acute toxicity by the oral route, low acute toxicity by the dermal route, a severe skin irritant, a moderate eye irritant, and a dermal sensitizer. Because garlic is a known mucosal irritant, inhalation of garlic oil mist or vapour may result in throat and respiratory tract irritation. The end-use product, Comfort Zone, is of low acute toxicity by both the oral and dermal route, may be a skin and eye irritant, and a possible dermal sensitizer. Cautionary statements alerting the user to garlic oil's acute toxicity, skin and eye irritation, and dermal sensitization are required on the technical grade active ingredient product label, as well as Comfort Zone being a possible skin and eye irritant, and a dermal sensitizer.

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*.

Inhalation, dermal, and ocular exposures are possible when applying the product, particularly to the applicator and bystanders located near the treatment area. Also, entry into a recently sprayed area may result in dermal exposure. Therefore, spray advisory and restricted entry statements are required on the end-use product label to minimize applicator and bystander exposures.

The data requirements for short-term toxicity, prenatal developmental toxicity, and genotoxicity were waived by the PMRA based on the long history of safe consumption of garlic as a whole foodstuff and garlic oil in natural health products.

Residues in Water and Food

Dietary risks from food and water are not of concern.

The proposed use pattern for Comfort Zone is for non-food situations. Garlic oil readily degrades in the environment, so any inadvertent exposure of garlic oil to food, feed, or water from drift or direct contact is not expected to result in any dietary risk.

Risks From Handling Garlic Oil

Risks are not of concern when Comfort Zone is used according to label directions, which include protective measures.

Domestic users handling and applying Comfort Zone to areas that attract mosquitoes, such as plants, shrubs, turf, and under decks, can come in direct contact with garlic oil on the skin and in the eyes. Following the precautionary label statements aimed at minimizing exposure to the product will ensure domestic users are appropriately protected. Potential for inhalation of garlic oil while handling and applying the end-use product is anticipated to be negligible if users observe the precautionary label statements.

Accidental bystander exposure is possible from spray drift, but exposure is expected to be negligible if the precautionary label statements are observed by the applicator.

Post-application exposure is possible in individuals who immediately enter freshly treated areas. The transfer of garlic oil from turf or foliar application to an individual who is not sensitive to garlic will not pose a health concern.

Environmental Considerations

What Happens When Garlic Oil, as part of the End-Use Product Comfort Zone, Is Introduced Into the Environment?

Garlic oil is not expected to pose significant environmental risk when used according to label directions.

Garlic oil is expected to degrade rapidly in the environment. Garlic oil is a naturally occurring compound, and is considered non-toxic from an environmental perspective because it acts as a repellent. Environmental exposure is expected to be minimal when used according to the label directions.

Value Considerations

What Is the Value of Comfort Zone?

Comfort Zone is an insect repellent for mosquitoes.

Comfort Zone is a product for domestic use containing 4% Garlic oil for application on grass, plants, shrubs and under decks and porches. The product repels mosquitoes from these areas for up to five days.

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 Comfort Zone to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

The statements, “MAY BE A SKIN AND EYE IRRITANT” and “POTENTIAL SKIN SENSITIZER” have been included on the principal display panel of the label and “Do not swallow”, “Avoid getting on skin and in eyes”, “May cause skin and eye irritation”, “Avoid inhaling/breathing mist or vapours”, and “Potential skin sensitizer” have been included in the PRECAUTIONS section of the secondary display panel of the end-use product label.

Because some individuals may be sensitive or allergic to garlic, the statements, “Apply only when the potential for drift is minimal”, “Individuals who are sensitive or allergic to garlic should avoid handling Comfort Zone” and “Individuals who are sensitive or allergic to garlic should avoid treated areas until dry or until after a heavy rain” have also been included in the PRECAUTIONS section of the secondary display panel of the label.

Next Steps

Before making a final registration decision on garlic oil, 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 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 garlic oil (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

Garlic Oil

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Garlic oil
Function	Insect Repellent
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	Not applicable
2. Chemical Abstracts Service (CAS)	Not applicable
CAS number	8000-78-0
Molecular formula	Not applicable, the product is a complex mixture
Molecular weight	Not applicable, the product is a complex mixture
Structural formula	Not applicable, the product is a complex mixture
Purity of the active ingredient	100% nominal (Limits 97 – 100%)

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

Technical Product—Garlic Oil FC 8170

Property	Result
Colour and physical state	Clear yellow to orange liquid
Odour	Pungent garlic aroma
Melting range	Not applicable
Boiling point or range	Not available
Density	1.05-1.095 g/mL
Vapour pressure at 20°C	Not available
Henry's law constant at 20°C	
Ultraviolet (UV)-visible spectrum	Not expected to absorb above $\lambda = 300$ nm

Property	Result
Solubility in water at 20°C	Insoluble
Solubility in organic solvents at 20°C (g/100 mL)	Soluble in most organic solvents
<i>n</i> -Octanol-water partition coefficient (K_{ow})	Not available
Dissociation constant (pK_a)	Not applicable
Stability (temperature, metal)	Not available

End-Use Product—Comfort Zone

Property	Result
Colour	Light yellow to amber
Odour	Pungent
Physical state	Liquid
Formulation type	Solution
Guarantee	Garlic oil.....4.0%
Container material and description	32oz. 28-400R 55.00 Gm. HDPE Premier Pistol Grip Sprayer Oval
Density	0.9-1.0 g/mL
pH of 1% dispersion in water	Not available
Oxidizing or reducing action	Not available
Storage stability	Stable when stored at ambient temperature in sealed container
Corrosion characteristics	Non corrosive
Explodability	Product does not contain explosive components

1.3 Directions for Use

Shake well before using. For best results, spray in early morning or early evening. Spray until run-off. Use in areas that attract mosquitoes such as grass, plants, shrubs and under decks and porches. The repelling effect of Comfort Zone lasts up to 5 days. Re-apply after heavy rain or if mosquitoes continue to be a problem.

1.4 Mode of Action

Garlic oil contains a high concentration of sulphur compounds, only some of which contribute to its characteristic odour. Garlic is known to be repellent to various insects, however, the exact mode of action of this repellency is unknown. It is postulated to be the result of one or more of the numerous chemical compounds found in garlic oil.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The product is 100% garlic oil (a complex mixture) and therefore no analytical method is required.

2.2 Method for Formulation Analysis

The product is 4.0% garlic oil (a complex mixture) and therefore no analytical method is required.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of data available in the literature on the toxicology of garlic oil was conducted by the PMRA. The scientific quality of the data is acceptable and the database is sufficiently complete to define the majority of the toxic effects that may result from exposure to garlic oil when it is applied as a pest control product.

Available information from the scientific literature addressed the acute oral toxicity of garlic oil, and the acute dermal toxicity, primary skin irritation, primary eye irritation and dermal sensitization of diallyl disulfide, which comprises 45–60 % of garlic oil, and diallyl sulfide, which comprises approximately 10 % of garlic oil. The information summarized in Table 1 (see Appendix I) was used to assess the toxicological effects of both the technical grade active ingredient (garlic oil) and the end-use product, (Comfort Zone). The end-use product contains no formulants of toxicological concern.

Garlic oil is of slight acute toxicity by the oral route in rats and, based on the acute dermal toxicity of both diallyl sulfide and diallyl disulfide in rats, is expected to be of low acute toxicity by the dermal route. Garlic oil, a mucosal irritant, will result in irritation when inhaled. Comfort Zone is expected to be of low acute toxicity by both the oral and dermal routes.

Diallyl disulfide is moderately irritating to the eyes of rabbits and both diallyl sulfide and diallyl disulfide are severely irritating to the skin of rabbits. Published case studies on the dermal effects of garlic oil in humans (skin ulcerations, severe erythema, and edema) reflect the findings for dermal irritation of the diallyl sulfide compounds. Based on these findings, garlic oil is expected to be a severe skin irritant and a moderate eye irritant. Diallyl disulfide and by extension, garlic oil, is also a dermal sensitizer in guinea pigs. It is expected that Comfort Zone may be a skin and eye irritant, as well as a possible dermal sensitizer.

The mutagenicity of garlic has been reported in bacteria, but, based on the long history of safe consumption of garlic and the low potential for exposure of individuals to Comfort Zone, short-term toxicity, prenatal developmental toxicity, and genotoxicity data requirements for garlic oil were waived.

3.2 Food Residue Exposure Assessment

A food residue exposure assessment was not required for the non-food/feed uses of the end-use product, Comfort Zone.

3.3 Residential Risk Assessment

3.3.1 Use Description/Use Scenario

The proposed domestic use of Comfort Zone is as an area insect repellent spray using a handheld trigger pump. Exposure was based on a daily maximum rate of application of a one litre bottle of Comfort Zone, covering a 25 m² area, and incidental contact with treated objects and areas, such as foliage, turf, and standing water. The applicator will handle a maximum of 40.0-44.4 g a.i. per day and the number of applications per year is unlimited. According to the product label, reapplication is recommended after a heavy rain or after 5-7 days of application.

3.3.2 Applicator Exposure and Risk Assessment

Exposure to Comfort Zone is expected to be short-term in duration and predominantly by both the inhalation and dermal routes. Accidental ingestion, and ocular exposure of the end-use product are also possible during application, but are likely to only be minor routes of exposure. Although a margin of exposure could not be estimated based on the toxicological information available, exposure to the end-use product, when label instructions and precautions are observed, is not expected to pose a health concern.

Using the Pesticide Handler Exposure Database (PHED), the PMRA estimated that the applicator will be dermally exposed to 3.63 mg garlic oil/L when wearing maximum protective cover (i.e., chemical resistant coveralls and gloves) and 21.21 mg of garlic oil /L when wearing minimal protective cover (i.e., short pants, short sleeve shirt, and no gloves). Inhalation exposure during the application of Comfort Zone is expected to range from 59-66 mg garlic oil/day for light activities to 94-105 mg garlic oil/day during moderate activities. The American Conference of Governmental Industrial Hygienists (ACGIH) calculated an occupational exposure Threshold Limit Value–Time Weighted Average (TLV-TWA) of 0.5 ppm (0.03 mg/L) for diallyl disulfide,

based on the irritation and lacrimation properties of the compound, which translates into 128.4-152.4 mg garlic oil/day (for male and female adults weighing 69-74 kg). The TLV–TWA of a compound is a level to which it is believed a worker can be exposed day after day for a working lifetime without adverse health effects on the basis of a 8h/day, 40h/week work schedule. Given that Comfort Zone will be at most applied on a weekly basis for approximately five months of the year and garlic oil maximally contains 60% diallyl disulfide, inhalation of the product is expected to be below the diallyl disulfide TLV–TWA for domestic applicators adhering to the label instructions.

The risk due to dermal and inhalation exposure of the applicator to garlic oil is anticipated to be negligible if the precautionary label statements are observed. Individuals with garlic sensitivities should not handle Comfort Zone.

3.3.3 Bystander Exposure and Risk Assessment

Bystanders are likely to walk in and out of a treated area. This transient exposure is not expected to pose a health risk for individuals who are not sensitive to garlic. Individuals who are sensitive to garlic should avoid treated areas until dry or until after a heavy rainfall.

Accidental bystander exposure is possible from spray drift, the extent to which may be limited with appropriate label statements warning against application on days where the wind is sufficient to cause drift.

These mitigative measures are expected to minimize the potential for exposure of bystanders to Comfort Zone when applied in outdoor domestic settings.

3.3.4 Post-Application Exposure

Post-application activities are expected to be typical of a residential setting, thus, post-application exposure to adults and children is likely. Individuals with sensitivities to garlic should avoid recently treated areas until dry or until after a heavy rain.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Garlic oil is a naturally occurring substance and rapid degradation in the environment is expected to occur through normal biological, physical, and chemical processes.

4.2 Environmental Risk Characterization

Based on limited exposure, the chemical's natural occurrence and the likelihood for relatively rapid transformation under environmental conditions, the proposed use of garlic oil is not expected to pose a significant risk to the environment under the proposed use pattern.

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

One acceptable efficacy trial in which the product was applied to four representative sites was submitted in support of Comfort Zone. Three sites were located on a golf course and the fourth site was a treed cottage lot with shrubs located beside a river. It was observed that application of Comfort Zone according to label directions resulted in much lower mosquito trap counts in treated areas compared to control areas, for up to five days. Therefore, from a value and sustainability perspective, the claim that the product repels mosquitoes can be accepted for up to five days.

5.2 Sustainability

5.2.1 Survey of Alternatives

Alternative mosquito area repellents for domestic outdoor use (i.e., in residential outdoor areas) include mosquito coils and heat-powered lanterns containing allethrin.

5.2.2 Compatibility with Current Management Practices Including Integrated Pest Management

Comfort Zone is compatible with other methods used to repel mosquitoes in residential outdoor areas.

5.2.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

As the mode of action of Comfort Zone is as an insect repellent, rather than an insecticide, it is not expected to exert selection pressure that would lead to the development of resistance.

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, i.e., 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, garlic oil and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03⁵ and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Garlic oil does not meet the Track 1 criteria and will not form any transformation products, which meet the Track 1 criteria. Garlic oil is a naturally occurring substance and is not expected to be persistent or bioaccumulative in the environment.

6.1.1 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use product are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*⁶. The list is used as described in the PMRA Notice of Intent NOI2005-01⁷ and is based on existing policies and regulations including: DIR99-03; and DIR2006-02⁸, 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 garlic oil and the end-use product, Comfort Zone, 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 DIR2006-02⁹.

7.0 Summary

7.1 Human Health and Safety

The available toxicological information on garlic oil is adequate to identify the majority of toxic effects that may result from human and companion animal exposure to the active ingredient. Moderate eye and severe skin irritation, dermal sensitization, and slight acute oral toxicity were observed in laboratory animals. No other toxicologically significant effects were reported in available information on garlic oil.

⁵ DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

⁶ *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.*

⁷ NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

⁸ DIR2006-02, PMRA Formulants Policy.

⁹ DIR2006-02, PMRA Formulants Policy.

The precautionary statements on the product labels are adequate to protect applicators and bystanders. The product label will instruct domestic users to not apply Comfort Zone if the wind is sufficient to cause drifting of the spray away from treated areas. When applied according to the label directions, application of the product is not expected to result in applicators being exposed to concentrations of garlic oil that would be of concern. Furthermore, allowing Comfort Zone to dry after each application will ensure that bystanders and pets are unlikely to come in contact with garlic oil at concentrations that would be of concern.

Because Comfort Zone is not to be applied to food or feed, the establishment of a maximum residue limit was not required for garlic oil.

Individuals who are sensitive or allergic to garlic are advised to avoid handling Comfort Zone, as well entering recently treated areas.

7.2 Environmental Risk

Based on limited exposure, the chemical's natural occurrence and the likelihood for relatively rapid transformation under environmental conditions, the proposed use of garlic oil is not expected to pose a significant risk to the environment.

7.3 Value

The data submitted to register Comfort Zone are adequate to support its use as an outdoor mosquito repellent, when used according to the directions provided on the label.

7.4 Unsupported Uses

The proposed use on standing water was not supported, as data were not provided and the use directions provided were inappropriate for use on standing water.

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 Garlic Oil FC 8170 and Comfort Zone, containing the technical grade active ingredient garlic oil, to repel mosquitoes outdoors.

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
bw	body weight
ACGIH	American Conference of Governmental Industrial Hygienists
g	gram(s)
IUPAC	International Union of Pure and Applied Chemistry
h	hour(s)
kg	kilogram(s)
K_{ow}	<i>n</i> -octanol–water partition coefficient
L	litre(s)
LD50	lethal dose to 50% (a dose causing 50% mortality in the test population)
m ²	metre(s) squared
mg	milligram(s)
mL	millilitre(s)
nm	nanometre
PHED	Pesticide Handler Exposure Database
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
TLV	threshold limit value
TWA	time weighted average
TSMP	Toxic Substances Management Policy

Appendix I Tables and Figures

Table 1 Acute Toxicity of Garlic Oil and Its Associated End-use Product (Comfort Zone)

Study Type	Species	Result	Comment	Reference
Acute Toxicity of Garlic Oil (Technical)				
Oral	Rat	LD ₅₀ 1360 mg/kg bw	Slight toxicity	1861165
Dermal	Rat	<u>Diallyl sulfide</u> LD ₅₀ > 5 g/kg bw	Low toxicity	1860536 1860541
		<u>Diallyl disulfide</u> LD ₅₀ (♂) 1826 mg/kg bw		
Inhalation	The data requirement was waived on the basis of available information which did not note any deaths or significant acute effects, other than mucosal irritation and lacrimation, from the inhalation of garlic oil vapour. The ACGIH has listed a TLV–TWA of 0.5 ppm (0.03 mg/L) for diallyl disulfide, a major component of garlic oil, based on the irritation and lacrimation properties of the compound.			1864853
Skin irritation	Rabbit	<u>Diallyl sulfide</u> Irritation and skin ulceration (occluded patch test for 24 hours)	Severe irritation	1860488 1860536 1860541
		<u>Diallyl disulfide</u> Severe erythema (1 hour after exposure)		
Eye irritation	Rabbit	<u>Diallyl disulfide</u> Corneal opacity and conjunctivitis resolved by day 14 of study	Moderate irritation	1860488
Skin sensitization	Guinea Pig	<u>Diallyl disulfide</u> Positive for dermal sensitization	Dermal sensitization	1860536
Acute Toxicity of End-Use Product – Comfort Zone				
Oral	The estimated LD ₅₀ is calculated to be > 2000 mg/kg bw.			
Dermal	Refer to the acute toxicity of garlic oil.			
Inhalation	Refer to the acute toxicity of garlic oil.			
Skin irritation	Based on available information, the end-use product may be a skin irritant.			
Eye irritation	Based on available information, the end-use product may be an eye irritant.			
Skin sensitization	Based on available information, the end-use product is a possible skin sensitizer.			

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

- 1594643 Manufacturing Methods for the TGAI, DACO: 2.11 **CBI**
 1594644 Chemical and Physical Properties for AIC, DACO: 2.14 **CBI**
 1594645 Properties for the TGAI , DACO: 2.14.1 **CBI**
 1594649 Properties for the TGAI, DACO: 2.14.2 **CBI**
 1594651 Properties for the TGAI, DACO: 2.14.3 **CBI**
 1594652 DACO 2.14.6 Chemical and Physical Properties, DACO: 2.14.6 **CBI**
 1594653 Water Solubility (mg/L), DACO: 2.14.7 **CBI**
 1594654 Solvent Solubility (mg/L), DACO: 2.14.8 **CBI**
 1594656 Properties for the TGAI, DACO: 2.15 **CBI**
 1594657 Properties for the TGAI, DACO: 2.16 **CBI**
 1679580 2008, Odour, DACO: 3.5.3 **CBI**
 1679581 2008, Formulation type, DACO: 3.5.4 **CBI**
 1679582 2008, Bottle Specifications, DACO: 3.5.5 **CBI**
 1679583 2008, Density or specific gravity, DACO: 3.5.6 **CBI**
 1679584 2008, pH, DACO: 3.5.7 **CBI**
 1679585 2008, Oxidizing and Reducing, DACO: 3.5.8 **CBI**
 1679586 2008, Viscosity, DACO: 3.5.9 **CBI**
 1679609 2008, Manufacturing methods, DACO: 2.11.1, 2.11.2, 2.11.3, 2.11.4, 2.12, 2.13 **CBI**
 1778107 2008, Certificate of Analysis, DACO: 2.13.2 **CBI**
 1778114 Product Specification Sheet, Ecom Industries Inc. **CBI**
 1594602 Impurities of Toxicological Concern, DACO: 3.4.2 **CBI**
 1594603 Colour, DACO: 3.5.1
 1679579 2008, Physical State, DACO: 3.5.2 **CBI**
 1832111 2009, Formulation Process, DACO: 3.2.2 **CBI**

2.0 Human and Animal Health

- 1594606 Summaries, DACO: 5.1
 1594607 Other studies/Data/Reports, DACO: 5.14
 1594658 TOXICOLOGY, DACO: 4.1
 1594661 1992, US EPA, Foreign Reviews, DACO: M12.5
 1763339 2009, Material Safety data Sheet, DACO:
 0.9,2.14.1,2.14.2,2.14.3,2.14.6,2.2,2.3,2.3.1,2.5,2.6,2.7,2.8,2.9
 1854234 DACO 5.2 - New Discussion for Garlic Oil Use Description/Scenario
 (Application and Post Application)., DACO: 5.2

3.0 Value

- 1594610 Value Summaries, DACO: 10.1
- 1594611 Efficacy Studies, Mode of Action, DACO: 10.2
- 1594612 Mode of Action, DACO: 10.2.1
- 1594613 Description of Pest Problem, DACO: 10.2.2
- 1594614 EFFICACY TRIALS, DACO: 10.2.3
- 1594615 Efficacy of An Area Repellent against Mosquitoes, DACO: 10.2.1,10.2.3.3,10.3.1,10.4,10.5
- 1594616 Adverse Effects on Use Site, DACO: 10.3
- 1594617 Survey of Alternatives (chemical and non-chemical), DACO: 10.5.1
- 1679575 2008, Summary, DACO: 10.1
- 1679576 2008, Mode of Action, DACO: 10.2.1
- 1679577 2008, 10.3.1 Summary, DACO: 10.3.1
- 1679595 2008, Efficacy of an Area Repellent against mosquitoes modified, DACO: 10.2.3
- 1807203 1998,html:file://C:\BRCA%20Documents\Corporate%20Documents\Opera tion%20Blackberr... 12/3/2005, Garlic Patent. Mosquito Repelling Technique. US Patent # 5,733,552 Current U.S. Class: 424/754 Intern'l Class:A61K 035/78, DACO: 10.2
- 1807207 1995, MOSQUITO BARRIER Tests of Mosquito Barrier® Garlic Juice, DACO: 10.2

B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

- 1859677 Chapter 8 Garlic Forensic Science and Medicine. Herbal Products: Toxicology and Clinical Pharmacology, Second Edition., DACO: 4.8
- 1860488 RTECS Registry of Toxic Effects of Chemical Substances Allyl disulfide, Canadian Centre for Occupational Health & Safety, DACO: 4.2.1,4.2.2,4.2.4,4.2.5,4.3.1,4.5.4,4.5.5
- 1860536 Fragrance raw materials monographs DIALLYL DISULPHIDE, DACO: 4.2.1,4.2.2,4.2.5,4.2.6,4.5.4,4.5.5
- 1860541 Fragrance raw materials monographs DIALLYL SULPHIDE, DACO: 4.2.1,4.2.2,4.2.5,4.2.6,4.5.4,4.5.5
- 1861150 2003, Rules and Regulation Diallyl Sulfides; Exemption from the Requirement of a Tolerance, Federal Register Vol. 68, No. 131, DACO: 4.8
- 1861165 RTECS Registry of Toxic Effects of Chemical Substances - Garlic Oil, Canadian Centre for Occupational Health and Safety, DACO: 4.2.1,4.3.1
- 1861167 ChemIDplus Advanced Allyl sulfide, United States National Library of Medicine, DACO: 4.2.1
- 1861180 garlic oil china 8000-78-0 allium sativum l. bulb oil, DACO: 4.8

- 1861197 ChemIDplus Advanced Allyl sulfide, U.S. National Library of Medicine, DACO: 4.2.1,4.2.2
- 1861206 ChemIDplus Advanced Diallyl disulfide, U.S. National Library of Medicine, DACO: 4.2.1,4.2.2
- 1864853 2004 TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices., DACO: 4.8