Proposed Registration Decision PRD2017-16

Eucalyptus Oil, Pine Needle Oil, Oil of Geranium, Lemon Oil and Camphor Oil, and Citrobug Insect Repellent for Dogs and Horses

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Overview

Proposed Registration Decision for Eucalyptus Oil, Pine Needle Oil, Oil of Geranium, Lemon Oil and Camphor 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 Citrobug Formula HE-5000 Essential Oils and Citrobug Insect Repellent for Dogs and Horses, containing the technical grade active ingredients (TGAI) eucalyptus oil, pine needle oil, oil of geranium, lemon oil and camphor oil. These active ingredients are used to formulate this insect repellent for application to the coat of dogs and horses which repels mosquitoes, face flies, horn flies, house flies, and stable flies.

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 Citrobug Formula HE-5000 Essential Oils and Citrobug Insect Repellent for Dogs and Horses.

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.

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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."

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 the Canada.ca website at https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management.html.

Before making a final registration decision on eucalyptus oil, pine needle oil, oil of geranium, lemon oil and camphor oil and Citrobug Insect Repellent for Dogs and Horses, 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 eucalyptus oil, pine needle oil, oil of geranium, lemon oil and camphor oil and Citrobug Insect Repellent for Dogs and Horses, 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 Citrobug Formula HE-5000 Essential Oils?

Citrobug Formula HE-5000 Essential Oils is a mix of eucalyptus oil, pine needle oil, oil of geranium, lemon oil and camphor oil. Citrobug Formula HR-5000 Essential Oils is used to formulate Citrobug Insect Repellent for Dogs and Horses, an insect repellent for application to the coat of dogs and horses which repels mosquitoes, face flies, horn flies, house flies, and stable flies. The mode of action by which this mix of essential oils repels insects is not known.

Health Considerations

Can Approved Uses of Citrobug Formula HE-5000 Essential Oils Affect Human Health?

Products containing eucalyptus oil, pine needle oil, oil of geranium, lemon oil and camphor oil are unlikely to affect your health, or the health of your pets, when used according to label directions.

Potential exposure to Citrobug Formula HE-5000 Essential Oils may occur when handling and applying Citrobug Insect Repellent for Dogs and Horses to dogs and horses. 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. In the case of Citrobug Insect Repellent for Dogs and Horses, the levels to which companion animals (pets) may be exposed must also be considered. The levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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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 products are used according to label directions.

In laboratory animals, Citrobug Formula HE-5000 Essential Oils was of low acute toxicity by the oral and dermal routes of exposure. Based on scientific literature available on the active ingredient oils, Citrobug Formula HE-5000 Essential Oils is expected to be irritating to the skin, eyes and lungs, and be a potential skin sensitizer.

Short- and long-term (lifetime) animal toxicity studies used by Health Canada to assess the potential of active ingredients to cause neurotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, genetic damage, and various other effects were not required for Citrobug Formula HE-5000 Essential Oils. The active ingredients each have a history of use as medicinal or non-medicinal ingredients in natural health products in Canada with leave-on skin type uses similar to the proposed end-use product, Citrobug Insect Repellent for Dogs and Horses. Each also has as a history of use in products administered orally, and in cosmetics and other consumer products in North America as well as flavouring agents in food.

The end-use product, Citrobug Insect Repellent for Dogs and Horses, is expected to be of low acute toxicity to humans and pets via the oral, dermal and inhalation routes of exposure, and non-irritating to the eyes and skin. It is also considered to be a potential skin sensitizer since several active ingredients, and some of their chemical components, are known to be potential skin sensitizers.

Residues in Water and Food

Dietary risks from food and drinking water are not of concern.

As there are no food uses for Citrobug Insect Repellent for Dogs and Horses, there is no concern for dietary exposure. Similarly, dietary exposure from drinking water is also expected to be negligible and thus, dietary risks from food and drinking water are of no concern.

Occupational Risks From Handling the End-Use Product Citrobug Insect Repellent for Dogs and Horses

Occupational risks are not of concern for Citrobug Insect Repellent for Dogs and Horses.

Since Citrobug Insect Repellent for Dogs and Horses is a domestic product, occupational risks are not applicable.

Risks in Residential and Other Non-Occupational Environments

Estimated risk for non-occupational exposure is not of concern when Citrobug Insect Repellent for Dogs and Horses is used according to the label directions.

Health risks to individuals applying the product to their pets, and individuals coming in contact with pets who have been treated with the product are not of concern when the product is used according to label directions. Precautionary statements on the label inform users to apply the product in a well ventilated area (preferably outdoors). Hygiene statements on the label also instruct individuals applying the product to wash their hands with soap and water after application. These instructions will protect against unnecessary risk due to exposure.

Health risks to dogs and horses which are directly exposed to Citrobug Insect Repellent for Dogs and Horses are also not of concern when the product is used according to label directions. Precautionary statements on the label inform users that certain sub-populations may be more sensitive to the essential oil mixture. For this reason, Citrobug Insect Repellent for Dogs and Horses will not be used on animals less than 12 weeks old. The label also states that a veterinarian must be consulted before using the product on sick, old, pregnant, or nursing animals or on animals receiving medication or being treated with another pesticide. If signs of irritation or rash appear, the label informs users to discontinue use on the animal.

Environmental Considerations

An environmental assessment was not required for this application.

Value Considerations

What Is the Value of Citrobug Insect Repellent for Dogs and Horses?

Citrobug Insect Repellent for Dogs and Horses has value as it repels the nuisance pests mosquitoes, face flies, horn flies, house flies, and stable flies. Mosquitoes may also carry diseases which affect dogs and horses.

Mosquitoes can vector diseases, including heartworm in dogs and eastern equine encephalitis, western equine encephalitis, and West Nile virus in horses. Citrobug Insect Repellent for Dogs and Horses provides a new mode of action to repel mosquitoes, face flies, horn flies, house flies, and stable flies from dogs and horses for two hours.

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 Citrobug Formula HE-5000 Essential Oils and the associated end-use product to address the potential risks identified in this assessment are provided below.

Key Risk-Reduction Measures

Human Health

To reduce the potential for exposure for individuals applying Citrobug Insect Repellent for Dogs and Horses to companion animals, the product must be applied in a well-ventilated area, preferably outdoors, and users must wash their hands with soap and water after applications.

To protect dogs and horses from unnecessary risk due to exposure, the label informs users to avoid contact with the animal's eyes, mouth, face and sensitive skin areas when applying the product. The label also warns users that Citrobug Insect Repellent for Dogs and Horses may cause skin reactions in sensitive animals. For this reason, the product must not be used on animals less than 12 weeks old, and the label requires that users consult a veterinarian before using the product on sick, old, pregnant, or nursing animals or on animals receiving medication or being treated with another pesticide. The label also informs users to discontinue use on an animal if signs of irritation or rash appear.

Next Steps

Before making a final registration decision on eucalyptus oil, pine needle oil, oil of geranium, lemon oil and camphor oil and Citrobug Insect Repellent for Dogs and Horses, 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 eucalyptus oil, pine needle oil, oil of geranium, lemon oil and camphor 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

Eucalyptus Oil, Pine Needle Oil, Oil of Geranium, Lemon Oil and Camphor Oil

1.0 The Active Ingredient, Its Properties and Uses

Common Name: Mixture of lemon, eucalyptus, pine needle, geranium and camphor oils

IUPAC Chemical Name: N/A

CAS Chemical Name: N/A

1.1 Identity of the Active Ingredient

Citrobug Formula HE-5000 Essential Oils has the following properties:

Property	Result
Colour and physical state	Yellow liquid
Nominal concentration	Lemon Oil…….23.11% Eucalyptus Oil……..…...23.13% Pine Needle Oil……23.11% Oil of Geranium……..23.11% Camphor Oil……..7.54%
Odour	Eucalyptus lemon oil odour
Density	0.886 g/mL at 20°C
Vapour pressure	N/A
pH	4.12
Solubility in water	Insoluble
n-Octanol/water partition coefficient	N/A

The chemistry requirements for Citrobug Formula HE-5000 Essential Oils and Citrobug Insect Repellent for Dogs and Horses have been fulfilled.

1.2 Directions for Use

For use on dogs and horses. Repels mosquitoes, horn flies, face flies, house flies, and stable flies for 2 hours. Apply a thin layer of the product on the entire body of the dog or horse, spraying from about 30 cm (1 foot) away so that the coat doesn't get oily. Avoid the animal's eyes, mouth and sensitive skin areas. Reapply after 2 hours only if the exposure to pests continues. Do not exceed 2 applications per day.

1.3 Mode of Action

The mode of action by which Citrobug Formula HE-5000 Essential Oils (mix of eucalyptus oil, pine needle oil, oil of geranium, lemon oil and camphor oil) repels insects is not known.

2.0 Impact on Human and Animal Health

2.1 Toxicology Summary

Citrobug Formula HE-5000 Essential Oils, is currently registered as a TGAI in two registered personal insect repellents. Citrobug Insect Repellent for Dogs and Horses is intended for use on dogs and horses, and represents a new use for the active ingredient.

The PMRA previously conducted a detailed review of the toxicological database for Citrobug Formula HE-5000 Essential Oils. The database is complete consisting of acute toxicity studies submitted for the original versions of the TGAI and publicly available toxicity information for each of the essential oils in Citrobug Formula HE-5000 Essential Oils. The data requirements for short-term toxicity, prenatal developmental toxicity, and genotoxicity were waived by the PMRA based on the fact that the active ingredients have a history of use as medicinal or non-medicinal ingredients in natural health products in Canada with "leave-on" the skin type use patterns similar to the end-use product, as well as a history of use in products administered orally, and in cosmetics and other consumer products in North America, and as flavouring agents (for example, in baked goods, candy, etc.).

The scientific quality of the data was acceptable and the database is considered sufficiently complete to characterize the toxicity of Citrobug Formula HE-5000 Essential Oils and associated end-use product, and to support the use expansion of the TGAI to dogs and horses.

Citrobug Formula HE-5000 Essential Oils is of low acute oral and dermal toxicity. Although no skin sensitization study was submitted, based on published information, several of the essential oils and some of their components are potential skin sensitizers. A query of incident reports from databases in Canada and the United States show incidents of eye, skin, and respiratory tract irritation in workers exposed to pine oil, and of eye, skin and respiratory tract irritation in residential settings following exposure to areas treated with pesticides containing, pine oil, d-limonene or linalool. Incidents of eye irritation were also reported from exposure to eucalyptus oil. Based on all the available toxicological information, the essential oils in Citrobug Insect Repellent for Dogs and Horses are considered potential skin, eye, mucous membrane, and respiratory tract irritants. In the absence of submitted studies, Citrobug Formula HE-5000 Essential Oils is considered to be a moderate skin and eye irritant, and to be potentially irritating

to the respiratory tract. The TGAI label will include hazard statements for skin and eye irritation and precautionary statements indicating that it may cause skin reactions in sensitive individuals, and instructions to avoid contact with eyes and skin, and inhalation of vapours.

The end-use product, Citrobug Insect Repellent for Dogs and Horses, is considered to be of low acute oral and dermal toxicity, and non-irritating to the eyes and skin. Since the product is a volatile mixture that is applied in well-ventilated areas or outdoors, the constituents of the mixture will partially evaporate when it is sprayed onto animals, which will minimize inhalation exposure for the user. Thus, the concentration of the active ingredients from inhalation exposure will be low. Consequently, toxicity to pets from acute inhalation exposure will be low. Since reports from the published literature indicate that several of the active ingredients in the end-use product, and some of their components, are potential skin sensitizers, Citrobug Insect Repellent for Dogs and Horses may cause skin reactions on sensitive animals. Precautionary statements will be included on the secondary display panel of the end-use product label to warn users to avoid contact with the animal's eyes, mouth, and sensitive skin areas. The end-use product label will also warn users that Citrobug Insect Repellent for Dogs and Horses may cause skin reactions in sensitive animals, and to discontinue use if signs of irritation or rash appear.

Incident reports

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the Pesticides and Pest Management portion of the Canada.ca website. Incidents from Canada and the United States were searched and reviewed for the active ingredients, lemon oil, eucalyptus oil, pine needle oil, oil of geranium and camphor oil.

As of 7 July 2017, there were no incidents in the database for the active ingredients lemon oil, eucalyptus oil, pine needle soil, oil of geranium and camphor oil. There were, however, nine domestic animal incidents in the database for the active d-limonene (LMN), which is a major component of lemon oil.

All nine incidents occurred in the USA. Death was reported in six cats and four dogs. Most incidents involved one USA product, a flea and tick shampoo containing d-limonene at 5%. Three other incidents were associated with a spot-on product that contained permethrin, pyriproxyfen and d-limonene. Exposure scenarios reported in incidents include cats treated with a product for use on dogs, cats coming in physical contact with treated dogs, as well as applying a product to animals younger than the age specified on the product label. Based on the reported exposure scenarios, no additional mitigation measures are being proposed.

2.2 Occupational and Residential Risk Assessment

2.2.1 Use Description

Citrobug Insect Repellent for Dogs and Horses is a ready-to-use domestic product that will be applied by individuals in a residential setting to dogs and horses as an insect repellent.

Citrobug Insect Repellent for Dogs and Horses is applied in well-ventilated areas (preferably outdoors) as a light spray. The animal's body will be covered in a light spray of Citrobug Insect Repellent for Dogs and Horses, with no additional massaging or rubbing into the fur. A maximum of two applications are permitted per day. The product will be used intermittently on dogs and horses during the biting insect season (generally May to August).

Application to the animal's eyes, mouth and sensitive skin areas should be avoided. The product will not be used on animals less than 12 weeks old, and users are required to consult a veterinarian before using the product on sick, old, pregnant, or nursing animals or on animals receiving medication or being treated with another pesticide. Precautionary statements on the product label warn users that Citrobug Insect Repellent for Dogs and Horses may cause skin reactions in sensitive animals, and that use should be discontinued if signs of irritation or rash appear.

2.2.1.1 Dermal Absorption

The carrier oils in Citrobug Insect Repellent for Dogs and Horses do not have any permeation-enhancing properties which would increase absorption. However, based on the inherent lipophilic nature of the constituents in the active ingredients, and the oil-based nature of the formulation, dermal absorption is expected.

Citrobug Insect Repellent for Dogs and Horses is applied as light spray onto the animal's fur with no additional rubbing in. Small volatile essential oil constituents will partially evaporate when the product is sprayed and the majority of the spray will land on the animal's hair coat. The back and neck area of the animals will be sprayed, as well as the legs and abdomen. Therefore, while dermal exposure is expected, dogs and horses are not considered to be more sensitive to Citrobug Insect Repellent for Dogs and Horses than humans. In addition, to further protect dogs and horses from unnecessary risk due to exposure, the label informs users to avoid contact with the animal's eyes, mouth, face and sensitive skin areas when applying the product. Precautionary statements on the product's label regarding skin sensitization are also intended to protect companion animals from any unnecessary risk due to exposure.

2.2.2 Occupational Exposure and Risk Assessment

2.2.2.1 Mixer/loader/applicator Exposure and Risk

Mixer/loader/applicator exposure is not applicable as Citrobug Insect Repellent for Dogs and Horses is a ready-to-use domestic product.

2.2.2.2 Postapplication Exposure and Risk

Citrobug Insect Repellent for Dogs and Horses is a ready-to-use domestic product. Postapplication exposure is addressed under Residential Exposure and Risk Assessment.

2.2.3 Residential Exposure and Risk Assessment

2.2.3.1 Handler Exposure and Risk

Residential exposure will occur in handlers (adults) who are applying the product onto dogs and horses. This exposure is characterized as acute from occasional use and intermediate from prolonged seasonal use. Since the TGAI is already registered for use as a personal insect repellent, the increase in exposure for individuals applying the product to companion animals is low.

The product is applied as a light spray onto the hair coat of animals, without rubbing in. Consequently, dermal exposure for handlers is low. Since the essential oils in Citrobug Insect Repellent for Dogs and Horses are a mixture of volatile, organic constituents, the concentration of the active ingredients in the product, upon application, will be low. Consequently, inhalation exposure for handlers is also low. Inhalation exposure will be highest for individuals who are applying the product to horses, where much more of the product is used to cover the larger animal. Applications to horses are also more likely to be carried out in a barn, rather than outdoors where there is better ventilation.

Exposure to individuals applying Citrobug Insect Repellent for Dogs and Horses will not present a health risk of concern based on the low toxicity profile of the active ingredients and the expectation that label directions are followed.

2.2.3.2 Postapplication and Bystander Exposure and Risk

Since Citrobug Insect Repellent for Dogs and Horses is used on companion animals in a domestic setting, there is potential for postapplication exposure to adults, children and toddlers who may handle companion animals after they have been sprayed. The primary route of exposure would be through the dermal route. However, for toddlers, one additional exposure scenario was identified: non-dietary oral exposure resulting from potential transfer of residues from the skin to the mouth from hand-to-mouth activities.

Since the TGAI is already registered for use in personal insect repellents, the increase in exposure from postapplication exposure to companion animals is low.

Residential postapplication exposure to Citrobug Insect Repellent for Dogs and Horses will not present a health risk of concern based on the toxicity profile of the active ingredients and the expectation that label directions are followed.

Dogs and horses will be directly exposed when sprayed with Citrobug Insect Repellent for Dogs and Horses. This exposure is characterized as acute from occasional use, and intermediate from prolonged seasonal use, and occurs predominantly via the dermal and inhalation route of exposure.

Inhalation exposure to pets will be low since Citrobug Insect Repellent for Dogs and Horses is sprayed in well-ventilated areas, and the formulation is a volatile mixture. Dermal exposure for companion animals to Citrobug Insect Repellent for Dogs and Horses is considered as the primary route of exposure to dogs and horses since the product is applied directly onto the animal. The majority of the spray will land on the animal's hair coat and the product is not massaged into the skin. Precautionary statements on the label are adequate to protect companion animals from the potential for dermal sensitization, and the product will not be used on sensitive sub-populations of animals. Therefore, exposure to dogs and horses from Citrobug Insect Repellent for Dogs and Horses will not present a health risk of concern based on the toxicity profile of the active ingredients and when used according to the label directions.

2.3 Dietary Exposure and Risk Assessment

2.3.1 Food

As there are no food uses for Citrobug Insect Repellent for Dogs and Horses, there is no concern from dietary exposure.

2.3.2 Drinking Water

Exposure to residues of lemon oil, eucalyptus oil, pine needle oil, oil of geranium and camphor oil in drinking water from the use of Citrobug Insect Repellent for Dogs and Horses as an insect repellent for dogs and horses is expected to be negligible and will not pose a health risk of concern.

2.3.3 Acute and Chronic Dietary Risks for Sensitive Subpopulations

Calculations of acute reference doses (ARfDs) and acceptable daily intakes (ADIs) are not required for lemon oil, eucalyptus oil, pine needle oil, oil of geranium and camphor oil.

Based on all the available information and hazard data, these essential oils are considered to be of low toxicity. As a result, there is no need to apply uncertainty factors to account for intra- and interspecies variability or have a margin of exposure given that a threshold for potential effects is not required.

2.3.4 Aggregate Exposure and Risk

The use pattern of Citrobug Insect Repellent for Dogs and Horses is limited to use on pets to repel biting insects and thus, exposure from the diet (food and water) is considered to be negligible, if any. In turn, there is reasonable certainty that no harm will result from aggregate exposure of residues of lemon oil, eucalyptus oil, pine needle oil, oil of geranium and camphor oil to the general Canadian population, including infants and children, when the end-use product is used as labelled.

2.3.5 Cumulative Exposure and Risk

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. While all essential oil-based pest control products are comprised of chemically-similar constituent ingredients, it is often not possible to fully identify and characterize the constituent(s) responsible for toxicity, thus confounding a determination of whether the constituents share a common mechanism of action. Notwithstanding the above, the potential risks from cumulative exposure of Citrobug Insect Repellent for Dogs and Horses with other pest control products with similar constituents are not of concern given the low toxicity profile of the active ingredients and the proposed limited use pattern on pets (dogs and horses).

3.0 Impact on the Environment

An environmental assessment was not required for this application.

4.0 Value

4.1 Consideration of Benefits

Mosquitoes are a nuisance pest to dogs and horses, and can vector various diseases including heartworm in dogs and eastern equine encephalitis, western equine encephalitis, and West Nile virus in horses. While horn flies and face flies are primary pests of cattle, they are also pests of horses, and can be a particular nuisance in areas close to cattle. House flies are a nuisance pest and stable flies bite both horses and dogs. Alternative products available for application to horses and dogs for use against mosquitoes, horn flies, face flies, house flies, and stable flies are limited to products formulated with pyrethroids and/or pyrethrins (various topically-applied products for use on horses; spot on products and one spray-on product for use on dogs). Citrobug Insect Repellent for Dogs and Horses provides a new mode of action to repel these pests from dogs and horses.

4.2 Effectiveness Against Pests

Value information reviewed in support of the claim that Citrobug Insect Repellent for Dogs and Horses will repel mosquitoes, horn flies, face flies, house flies, and stable flies from dogs and horses consisted of a field trial conducted on flies and a scientific rationale to support the claim for mosquitoes.

The field trial was conducted over two years, and tested the efficacy of Citrobug Insect Repellent for Dogs and Horses when used on cows to repel face, horn, house and stable flies. This trial was sufficient to support the use of Citrobug Insect Repellent for Dogs and Horses on dogs and horses to repel horn flies, face flies, house flies, and stable flies for 2 hours.

The scientific rationale to support the claim for mosquitoes was extrapolation from a currently registered product, which is registered to repel mosquitoes from humans for 2 hours. No difference in repellency is expected whether the product is applied to dogs, horses, or humans. While the field trial did not test the performance of Citrobug Insect Repellent for Dogs and Horses on dogs or horses against mosquitoes, it supported this rationale as it demonstrated that the product has insect repellent properties when applied to animal fur. This rationale was acceptable to support the use of Citrobug Insect Repellent for Dogs and Horses on dogs and horses to repel mosquitoes for 2 hours.

4.3 Non-Safety Adverse Effects

Application of Citrobug Insect Repellent for Dogs and Horses to dog and horse fur may cause the animal's coat to become oily. To minimise this, the product label has directions to spray a thin layer of the product on the animal's coat from 30 cm away.

4.4 Supported Uses

The value information was sufficient to support use of Citrobug Insect Repellent for Dogs and Horses on dogs and horses, with a claim that the product repels mosquitoes, horn flies, face flies, house flies, and stable flies for 2 hours.

5.0 Pest Control Product Policy Considerations

5.1 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*].

Citrobug Formula HE-5000 Essential Oils and the end-use product, Citrobug Insect Repellent for Dogs and Horses were assessed in accordance with the PMRA Regulatory Directive DIR99-03.[5]

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

- Citrobug Formula HE-5000 Essential Oils does not meet the Track 1 criteria as the active ingredient is not considered CEPA-toxic equivalent, i.e. is not entering the environment at levels that would cause risk, 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, Citrobug Insect Repellent for Dogs and Horses that would meet the TSMP Track 1 criteria.

5.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use 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 NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[8] 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:

- Citrobug Formula HE-5000 Essential Oils and Citrobug Insect Repellent for Dogs and Horses do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.
- Citrobug Insect Repellent for Dogs and Horses does contain a petroleum distillate at a concentration >10%. Therefore, the statement, "Note: Product contains a petroleum distillate", will be included on the end-use product label, and the First Aid section will include the standard statements related to swallowing products containing petroleum distillates.

6.0 Summary

6.1 Human Health and Safety

The existing toxicological database for Citrobug Formula HE-5000 Essential Oils (PCP# 31191) and currently registered associated end-use products was determined to be sufficiently complete to permit a decision on the expansion of use to companion animals (dogs and horses).

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6 *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.*

7 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.*

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

Citrobug Formula HE-5000 Essential Oils (technical grade active ingredient) is of low acute oral and dermal toxicity, a moderate skin and eye irritant, and potentially irritating to the respiratory tract. The technical grade active ingredient may also cause skin reactions in sensitive individuals. The hazard and precautions statements included on the technical grade active ingredient label will mitigate concerns.

Citrobug Insect Repellent for Dogs and Horses is of low acute toxicity via the oral, dermal and inhalation route of exposure, and non-irritating to the eyes and skin. It is a potential skin sensitizer. The product is a domestic-class insect repellent that is applied as a light spray onto dogs and horses, to cover the animal's body. The majority of the spray will land on the animal's hair coat. The constituents of the mixture will partially evaporate when the product is sprayed in a well-ventilated area.

For individuals applying the product and for individuals coming in contact with pets that have been sprayed with Citrobug Insect Repellent for Dogs and Horses, dermal and inhalation exposure is low.

For dogs and horses, while inhalation exposure is expected to be low, based on how the product is applied, there will be dermal exposure. However, dogs and horses are not considered to be more sensitive to Citrobug Insect Repellent for Dogs and Horses than humans. In addition, the precautionary statements on the end-use product label with respect to skin sensitization will protect companion animals from any unnecessary risk due to exposure.

Overall, exposure to Citrobug Insect Repellent for Dogs and Horses in individuals applying the product or coming in contact with companion animals and in companion animals themselves will not pose a health risk of concern based on the toxicity profile of the active ingredients and the expectation that the end-use product is used according to label directions.

Impurities and formulants of human health or environmental concern as identified in the *Canada Gazette*, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances and allergens known to cause anaphylactic-type reactions, are not expected to be present in the Citrobug Insect Repellent for Dogs and Horses, nor carried through from the technical grade active ingredient.

As the end-use product contains a petroleum distillate at a concentration >10%, the statement, "Note: Product contains a petroleum distillate", will be included on label, as well as standard First Aid statements related to swallowing products containing petroleum distillates.

6.2 Value

Citrobug Insect Repellent for Dogs and Horses has value as it will provide two hours of repellency and a new mode of action for repelling mosquitoes, which may transmit disease, and horn flies, face flies, house flies, and stable flies, which are nuisance pests, from dogs and horses.

7.0 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 Citrobug Formula HE-5000 Essential Oils and Citrobug Insect Repellent for Dogs and Horses, containing the technical grade active ingredients eucalyptus oil, pine needle oil, oil of geranium, lemon oil and camphor oil. These active ingredients are used to formulate this insect repellent for application to the coat of dogs and horses which repels mosquitoes, face flies, horn flies, house flies, and stable flies.

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

ARfD	acute reference dose
ADI	acceptable daily intakes
°C	degree(s) Celsius
CEPA	*Canadian Environmental Protection Act*
g	gram
LMN	d-limonene
mL	millilitre
N/A	not available
PMRA	Pest Management Regulatory Agency
TGAI	Technical grade active ingredient
TSMP	Toxic Substances Management Policy
USA	United States of America

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

1963126 TABLEAU CODO 0.8 FOR COMMERCIAL PRODUCT 25797, DACO: 2.0,2.14,3.5,4.1,5.1,M12.5.2 CBI
1963128 CHROMATOGRAPHIES DES HUILES ESSENTIELLE, DACO: 2.14,3.4,3.5,M12.5.2 CBI
2030028 chromatographies sur toutes les huiles essentielles, DACO: 2.14 CBI
2030029 CUDO, DACO: 2.0 CBI
2030037 rationale pour le batch data, DACO: 2.13.3 CBI
2030038 rationale sur agent de conservation, DACO: 2.0 CBI
2224118 2.11.2 100169 NOVO JM, DACO: 2.11.2 CBI
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2224122 2.11.2 100630-Novo CM, DACO: 2.11.2 CBI
2224123 2.11.2 103115 Novo SC, DACO: 2.11.2 CBI
2224124 2.11.3 100169-Novo, DACO: 2.11.3 CBI
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2224129 2.11.3 103115-Novo, DACO: 2.11.3 CBI
2224130 2.11.3 103219, 100451-Novo _method of manuf_., DACO: 2.11.3 CBI
2224131 2.13.1, 2.13.4 103219, 100451-Novo (CBI removed)., DACO: 2.13.3,3.2.3,3.4.2 CBI
2224136 2.13.3 Data #3, DACO: 2.13.3 CBI
2224137 2.13.3 Data #4, DACO: 2.13.3 CBI
2247441 MS Citronella oil lot 36875 ANNEXE 4, DACO: 2.13.3 CBI
2247442 MS Geranium oil lot 36718 ANNEXE 3., DACO: 2.13.3 CBI
2247443 MS (CBI removed) Standard ANNEXE 2., DACO: 2.13.3 CBI
2247444 MS Method ANNEXE, DACO: 2.13.1 CBI

2.0 Human and Animal Health

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3.0 Value

2685565 2016, Value Dossier rationale and mode of action, DACO: 10.1
2607795 2016, Exigences CODO Rational, DACO: 10.1, 10.2, 10.2.1, 10.2.2, 10.2.3, 10.2.4, 10.3, 10.5.5, 10.7.1, 10.7.2, 12.5.10, 12.7, 12.7.10
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B. Additional Information Considered

i) Unpublished Information

2766698 2017, Clarification Email DACO 5.2

ii) Published Information

1.0 Human and Animal Health

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