Proposed Re-evaluation Decision PRVD2021-14

p-Menthane-3,8-diol and Its Associated End-use Products

Consultation Document

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Table of Contents

Proposed Re-evaluation Decision for p-menthane-3,8-diol and associated end-use products

Under the authority of the *Pest Control Products Act,* all registered pesticides must be re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they continue to meet current health and environmental standards and continue to have value. The re-evaluation considers data and information from pesticide manufacturers, published scientific reports and other regulatory agencies. Health Canada applies internationally accepted risk assessment methods as well as current risk management approaches and policies.

p-Menthane-3,8-diol is a synthetic analogue of a compound derived from the lemon eucalyptus plant. Products containing p-menthane-3,8-diol are applied as personal insect repellents to repel mosquitoes, biting midges, blackflies and ticks. Currently registered products containing p-menthane-3,8-diol can be found in the Pesticide Label Search and in Appendix I.

This document presents the proposed re-evaluation decision for p-menthane-3,8-diol, as well as the science evaluation on which the proposed decision is based. All products containing p-menthane-3,8-diol that are registered in Canada are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period,[1] during which the public (including the pesticide manufacturers and stakeholders) may submit written comments and additional information to PMRA Publications. The final re-evaluation decision will be published after taking into consideration the comments and information received during the consultation period.

Proposed Re-evaluation Decision for p-menthane-3,8-diol

Under the authority of the *Pest Control Products Act* and based on an evaluation of available scientific information, Health Canada is proposing continued registration of p-menthane-3,8-diol and associated end-use products registered for sale and use in Canada. No additional risk mitigation measures are proposed.

Human health risks from the use of p-menthane-3,8-diol and its associated end-use products were shown to be acceptable, when used according to current label directions. Therefore, Health Canada is proposing that products containing p-menthane-3,8-diol are acceptable for continued registration in Canada.

An environmental assessment is not required for the use of p-menthane-3,8-diol as a personal insect repellent.

p-Menthane-3,8-diol has value as an personal insect repellent by providing an additional choice for mosquito, biting midges, ticks and blackfly repellent users.

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Risk mitigation measures

Registered pesticide product labels include specific directions for use. Directions include risk mitigation measures to protect human health and the environment and must be followed by law. As a result of the re-evaluation of p-menthane-3,8-diol, no additional risk mitigation measures for product labels are proposed.

International context

p-Menthane-3,8-diol is currently acceptable for use in other Organisation for Economic Co-operation and Development (OECD) member countries, including the United States and Australia. No decision by an OECD member country to prohibit all uses of p-menthane-3,8-diol for health or environmental reasons has been identified.

Next steps

Upon publication of this proposed re-evaluation decision, the public, including the registrants and stakeholders are encouraged to submit additional information that could be used to refine risk assessments during the 90-day public consultation period.

All comments received during the 90-day public consultation period will be taken into consideration in preparation of re-evaluation decision document,[2] which could result in revised risk mitigation measures. The re-evaluation decision document will include the final re-evaluation decision, the reasons for it and a summary of comments received on the proposed re-evaluation decision with Health Canada's responses.

Refer to Appendix I for details on specific products impacted by this proposed decision.

Additional scientific information

No additional scientific data are required at this time.

[2] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

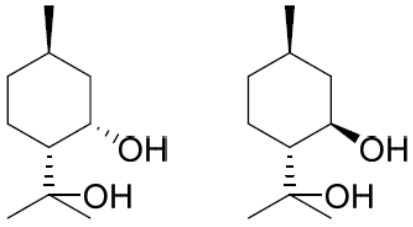
Science evaluation

1.0 Introduction

p-Menthane-3,8-diol is a synthetic analogue of a compound derived from the lemon eucalyptus plant. Products containing p-menthane-3,8-diol can be applied up to twice a day as personal insect repellents and, it repels mosquitoes, biting midges, and ticks for up to two hours, and blackflies for up to five hours following application. There is one technical grade active ingredient and five domestic class end-use products containing p-menthane-3,8-diol currently registered in Canada. The p-menthane-3, 8-diol end-use products are formulated as solutions, or emulsifiable concentrates or emulsions.

2.0 Technical Grade Active Ingredient

2.1 Identity

Common name		p-menthane-3,8-diol
Function		Insect repellent
Chemical Family		Essential oils
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	2-(2-hydroxypropan-2-yl)-5-methylcyclohexanol
2	**Chemical Abstracts Service (CAS)**	2-hydroxy- alpha, alpha, 4-trimethylcyclohexanemethanol
CAS Registry Number		42822-86-6
Molecular Formula		$C_{10}H_{20}O_2$
Structural Formula		
Molecular Weight		172
Purity of the Technical Grade Active Ingredient		99.3%
Registration Number		27193

2.2 Physical and chemical properties

Property	Result
Vapour pressure at 25°C	0.181 Pa
Ultraviolet (UV) / visible spectrum	Not expected to absorb UV at $\lambda > 350$ nm
Solubility in water at 25°C	0.29 g/L
n-Octanol/water partition coefficient at 25°C	Log K_{ow} = 1.37 ± 0.23
Dissociation constant	Molecule does not contain dissociable moiety

3.0 Human health assessment

3.1 Toxicology summary

A detailed review of the toxicology database for p-menthane-3,8-diol was conducted. The database consisted of acute toxicity, skin and eye irritation, and skin sensitization studies with p-menthane-3,8-diol and two end-use products, OFF Botanicals Insect Repellent 1 and OFF Familycare Botanicals Insect Repellent Pump Spray, and repeat-dose dermal toxicity, prenatal developmental toxicity, postnatal neurotoxicity, immunotoxicity screening studies, and an array of genotoxicity studies conducted with p-menthane-3,8-diol. The database is incomplete with respect to studies assessing the potential for reproductive toxicity, and developmental toxicity was assessed in one species only. Published scientific literature was provided on the metabolism, long-term toxicity, and genotoxicity of menthol, on the basis of its structural similarity to p-menthane-3,8-diol and p-menthane-3,8-diol being reported a major urinary metabolite of menthol following oral exposure in rats.

p-Menthane-3,8-diol was determined to be of low acute toxicity by the oral and dermal routes. It was severely irritating to the eyes, mildly irritating to the skin, and was not a dermal sensitizer. The requirement for an acute inhalation study was waived since the technical grade active ingredient is a waxy solid at room temperature, and therefore inhalation is not an expected route of exposure.

In a 90-day short-term dermal toxicity study conducted with p-menthane-3,8-diol in rats, effects at the highest dose tested consisted of decreased body weight and body weight gain in both sexes, increased absolute and relative liver weights in females, and increased relative liver, kidney, and adrenal weights in males. Microscopic lesions in kidneys of high-dose males were observed and included an accumulation of hyaline droplets and chronic progressive nephropathy. These findings were considered to be the result of the male rat-specific protein, α-2-u globulin. A dose-related increase in dermal irritation was observed in both sexes marked by erythema, eschar, and desquamation. Microscopic observations of skin samples revealed acanthosis, chronic inflammation, and parakeratosis at the highest dose.

In a dermal prenatal developmental toxicity study performed with p-menthane-3,8-diol in rats, all females survived to study termination and did not display any treatment-related clinical signs of toxicity. Treatment-related adverse effects on reproductive parameters were not observed. However at the highest dose tested, a reduction in body weight gain was observed during the treatment period, as well as a decrease in food consumption during days 6 to 9 of gestation. Increased skeletal variations (unossified and incompletely ossified sites) in the fetuses (litters) were also observed at the highest dose.

While p-menthane-3,8-diol induced a positive response in an in vitro mammalian cell chromosomal aberration cytogenetics assay in Chinese hamster ovary cells with metabolic activation, a positive response was not induced in a reverse gene mutation assay in *Salmonella typhimurium* (TA98, TA100, TA1535, and TA1537) and *E. coli* (WP2 urvA), an in vitro mammalian cell gene mutation assay in L5178Y mouse lymphoma cells, and an in vivo mouse bone micronucleus assay. Additionally, no concern for genotoxicity of menthol was identified in published scientific literature. Overall, the weight of evidence, which includes an in vivo study, did not suggest p-menthane-3,8-diol to be genotoxic.

Chronic toxicity studies conducted by the National Toxicology Program on menthol in rats and mice were negative for carcinogenicity. Available information for p-menthane-3,8-diol and menthol does not raise concern for carcinogenicity.

In a postnatal developmental neurotoxicity study, p-menthane-3,8-diol was topically administered to rat pups from postnatal day 10 through 21. Reductions in body weight gain occurred at various time points in rat pups of either sex in the mid- and high dose groups. However, no other treatment-related changes in terminal body weights or any other measured parameter occurred. The maternal effect level was not determined in this study as dams were not treated with test substance, and therefore in utero effects were not considered in this study. As this study did not satisfy the guideline requirement for a developmental neurotoxicity study in rats, it was considered to be supplemental.

In a 28-day dermal immunotoxicity study in mice, p-menthane-3,8-diol was dermally applied to the shaved skin of female mice for 28 consecutive days. The antibody plaque forming assay (modified Jerne plaque assay) was used to assess the induction of splenic-antibody forming cells secreting antibodies specific to sheep red blood cells. There was no mortality nor treatment-related clinical signs of toxicity observed in the test animals. While a statistically significant increase in antibody plaque forming cells 10^6, viable spleen cells and per spleen was observed at the mid dose group, an increase was not observed at the high dose. Deficiencies in methodology were identified and accordingly, this study was considered supplemental.

An assessment of structural similarities suggests that p-menthane-3,8-diol is more polar than menthol. Consequently, p-menthane-3,8-diol is expected to be more accessible to conjugation and more rapidly excreted than menthol. In Fischer 344 rats, 71% of an oral dose of menthol was recovered in 48 hours with equal amounts in the feces and urine. The majority of the fecal excretion occurred within 48 hours. In bile duct-cannulated rats, approximately 30% was excreted within 6 hours and approximately 70% within 24 hours. The parent compound, menthol, was not detected in the urine, feces, or bile. The metabolite, menthol glucuronide, was predominantly found in the bile, whereas a variety of oxidation products, including p-menthane-

3,8-diol, were predominantly in the urine. A number of products of oxidation of the methyl and isopropyl groups were found as urinary metabolites after the daily administration of menthol to rats for up to 20 days.

Results of the toxicology studies conducted on laboratory animals in support of p-menthane-3,8-diol are summarized in Appendix II, Table 1. Toxicology reference values were not established as the submitted toxicology data for p-menthane-3,8-diol as well as available information for menthol did not identify any toxicological endpoints of concern.

3.2 Dietary exposure and risk assessment

p-Menthane-3,8-diol is not registered for use on any food commodity and is not expected to contaminate drinking water sources when used according to label directions. The dietary risk is not a health concern for all populations. No additional mitigation measures are proposed.

3.3 Occupational and non-occupational exposure and risk assessment

3.3.1 Dermal absorption

The database for p-menthane-3,8-diol includes an in vitro study using pig and rat skin. Previously, in vivo studies were required by the PMRA to determine the dermal absorption value of a pesticide as vitro studies alone were considered insufficient. As such, a refined dermal absorption value for p-menthane-3,8-diol was not established. Recently this policy was revised and moving forward, the PMRA will rely on in vitro studies alone to determine a dermal absorption value for pesticides. While refinement of the dermal risk assessment was not required, the available data may be considered in future assessments of p-menthane-3,8-diol.

3.3.2 Mixer, loader, and applicator exposure and risk assessment

As p-menthane-3,8-diol is an active ingredient used in domestic end-use products that are only registered for use as personal insect repellents, an occupational exposure assessment was not required.

3.3.3 Postapplication exposure and risk assessment

As the end-use products are personal insect repellents, a separate postapplication exposure and risk assessment is not applicable.

3.3.4 Residential and bystander exposure and risk assessment

Exposure to residential users is considered to be high since personal insect repellents are applied directly to the skin, the end-use products can be applied twice daily, and can be used frequently throughout the summer months. Typically, personal insect repellents are used intermittently during the Canadian biting pest season (May to August), and these products are to be used sparingly and only when biting insects are present. Potential exposure would occur in two population groups: adults and children. Toddlers were not considered, as the directions for use indicate that the end-use products are not to be used in children under three years of age. For adults and children, two dermal exposure scenarios were identified for risk assessment of

personal insect repellents: acute (occasional use) and intermediate (prolonged seasonal use) exposure. Potential applicator exposure beyond personal application could take place for adults applying personal insect repellents to young children; however, this exposure is considered to be minimal compared to the exposure from self-application. Exposure is expected to be mainly via the dermal route for consumers. Exposure via the inhalation route is not considered to be significant as the reported vapour pressure of p-menthane-3,8-diol suggests it is relatively non-volatile.

Since no toxicological endpoints of concern were identified, a quantitative risk assessment was not conducted for the proposed use. Based on the results of the toxicology studies conducted with p-menthane-3,8-diol, no adverse effects are expected to occur from the use of the end-use products when applied in accordance with the label instructions. However, without additional information to fully address potential sensitivity to the young including a reproductive toxicity study and a second acceptable developmental study, the label statement restricting the use of the end-use products to not be applied to children under three years of age remains in place. In addition, as noted in PRDD2002-02, the use of the products to a maximum of two applications per day remains as an assurance that exposure to p-menthane-3,8-diol from personal insect repellent use would not exceed exposure to menthol from other sources such as from personal care products, pharmaceuticals, and presence in food. Consequently, risks to residential users are acceptable when the precautionary statements on the labels are followed.

For bystanders (person near a person applying the insect repellent), exposure is expected to be minimal in comparison to exposure to individual users of personal insect repellents. Thus, health risks to bystanders are acceptable.

3.4 Aggregate exposure and risk assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation).

The use pattern of the end-use products formulated with p-menthane-3,8-diol is limited to use as personal insect repellents and thus, exposure from the diet (food and water) is considered to be negligible. Given that the personal insect repellent use of p-menthane-3,8-diol is acceptable and that there are no other sources of exposure, an aggregate assessment is not required.

3.5 Cumulative assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pesticides was undertaken. p-Menthane-3,8-diol is derived from the lemon eucalyptus plant.

Although there is another registered pesticide derived from the same plant, p-menthane-3,8-diol and related oil of lemon eucalyptus compounds, given that both active ingredients are registered uniquely as personal insect repellents, co-exposure is unlikely. Therefore, a cumulative assessment for p-menthane-3,8-diol is not required at this time.

3.6 Health incident reports

As of 29 March 2021, 9 human and 1 domestic animal incident involving the active ingredient p-menthane-3,8-diol, a synthetic version of a component found in lemon eucalyptus oil, were submitted to the PMRA.

All incidents were considered to be related to the reported insect repellent product. The reported incidents were either minor or moderate in severity. Six adults and three children (less than 6 years of age) experienced either skin or eye irritation effects following the use of a insect repellent product containing p-menthane-3,8-diol. The reported signs include swelling near eyes, rash or hives. In the domestic animal incident, a dog bit into a insect repellent product containing p-menthane-3,8-diol and later developed swelling around the eyes.

Overall, given the minor nature of symptoms reported in the incidents as well as the low volume of incidents reported over a 12-year period, no serious health concerns were identified in the incidents involving p-menthane-3,8-diol. The labels of p-menthane-3,8-diol products reported in the incidents do contain appropriate precaution and use direction statements to minimize potential for skin and eye effects in people when using insect repellent products. Hence, no additional mitigation measures are being proposed based on the incident report review.

4.0 Environmental assessment

An environmental assessment is not required for the use of p-menthane-3,8-diol as a personal insect repellent.

4.1 Toxic substances management policy considerations

In accordance with the PMRA Regulatory Directive DIR99-03,[3] the assessment of p-menthane-3,8-diol against Track 1 criteria of Toxic Substances Management Policy (TSMP) under Canadian Environmental Protection Act was conducted. Health Canada has reached the conclusions that: p-menthane-3,8-diol does not meet all Track 1 criteria, and is not considered a Track 1 substance.

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

4.2 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.[4] The list is used as described in the Health Canada's Science Policy Note SPN2020-01[5] and is based on existing policies and regulations, including the Toxic Substances Management Policy**Error! Bookmark not defined.** and Formulants Policy,[6] and taking into consideration the Ozone-depleting Substances and Halocarbon Alternatives Regulations under the *Canadian Environmental Protection Act*, 1999 (substances designated under the Montreal Protocol). Health Canada has reached the following conclusions:

p-Menthane-3,8-diol and its end-use products do not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants and Contaminants 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 Regulatory Directive DIR2006-02.

5.0 Value assessment

p-Menthane-3,8-diol products have value as personal insect repellents by providing an additional choice for mosquito, biting midges, ticks and blackfly repellent users.

4 SI/2005-114, last amended on June 24, 2020. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

5 PMRA's Science Policy Note SPN2020-01, *Policy on the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under paragraph 43(5)(b) of the Pest Control Products Act*

6 DIR2006-02, *Formulants Policy and Implementation Guidance Document*

List of abbreviations

↑	increased
↓	decreased
♂	male
♀	female
bw	body weight
bwg	body weight gain
CAS	Chemical Abstracts Service
d	day
g	gram(s)
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
L	litre
LD_{50}	dose estimated to be lethal to 50% of the test population
mg	milligram(s)
MAS	maximum average score for 24, 48 and 72 hours
MIS	maximum irritation score
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
TSMP	Toxic Substances Management Policy
UV	ultraviolet
wt	weight

Appendix I Registered products containing p-menthane-3,8-diol in Canada

Table 1 Registered products containing p-menthane-3,8-diol in Canada[1]

Registration number	Class	Registrant	Product name	Formulation type	Guarantee
27193	Technical	S. C. Johnson and Son, Limited	p-Menthane-3,8-Diol Technical	Dust or powder	p-Menthane-3,8-diol 99 %
27194	Domestic	S. C. Johnson and Son, Limited	OFF! Botanicals Insect Repellent 1	Emulsifiable concentrate or emulsion	p-Menthane-3,8-diol 10 %
29313	Domestic	S. C. Johnson and Son, Limited	OFF!® Familycare Botanicals Insect Repellent Lotion	Emulsifiable concentrate or emulsion	p-Menthane-3,8-diol 10 %
33948	Domestic	S. C. Johnson and Son, Limited	OFF!® Familycare® Botanicals® Insect Repellent Pump Spray	Solution	p-Menthane-3,8-diol 10 %
34004	Domestic	S. C. Johnson and Son, Limited	OFF!® Botanicals Insect Repellent Spritz	Solution	p-Menthane-3,8-diol 10 %
34008	Domestic	S. C. Johnson and Son, Limited	OFF!® Botanicals Insect Repellent Lotion	Emulsifiable concentrate or emulsion	p-Menthane-3,8-diol 10 %

[1] as of 30 June 2021, excluding discontinued products or products with a submission for discontinuation

Appendix II

Table 1 Toxicity profile of p-Menthane-3,8-diol Technical

Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to body weights unless otherwise noted. Unless otherwise noted, studies were conducted with p-menthane-3,8-diol.

Study type/Animal/PMRA#	Study results
Acute toxicity studies	
Acute oral toxicity Crl:CD BR VAF/Plus rats PMRA# 1132384	LD_{50} > 5000 mg/kg bw Clinical signs of toxicity included reduced fecal volume, hypoactivity, irregular respiration, ocular discharge, dark material around the nose, and hair loss. **Low acute toxicity**
Acute dermal toxicity New Zealand white rabbits PMRA# 1132385	LD_{50} > 5000 mg/kg bw Dermal irritation (edema, erythema, eschar, blanching, desquamation, eschar exfoliation, and/or necrosis and superficial lightening) was observed in all of the test animals at the application site. Dermal irritation was also observed beyond the application site. Clinical observations were limited to dark material around the mouth. **Low acute toxicity**
Eye irritation New Zealand White rabbits PMRA# 1132387	MAS = 48.8, MIS = 51.3 (at 48 h) **Severely irritating**
Skin irritation New Zealand White rabbits PMRA# 1132388	MAS = 1.06, MIS = 1.67 (at 24 h) **Mildly irritating**
Dermal sensitization (Buehler) Hartley Albino guinea pigs PMRA# 2720616	Negative **Not a dermal sensitizer**
Short-term toxicity studies	
90-day dermal toxicity Sprague Dawley rats PMRA# 2720619	**Systemic toxicity:** NOAEL = 1000 mg/kg bw/day **3000 mg/kg bw/day:** ↓ bw/bwg, ↑ liver wt (♂/♀), ↑ kidney wt, kidney lesions (hyaline droplet formation, chronic nephropathy), ↑ adrenal wt (♂)

	Dermal irritation: **>1000 mg/kg bw/day:** dose-related ↑ skin irritation (erythema, eschar, desquamation) **3000 mg/kg bw/day:** skin damage (acanthosis, parakeratosis, chronic inflammation)
Developmental studies	
Prenatal developmental toxicity Sprague Dawley rats PMRA# 1132391	**Maternal toxicity:** **NOAEL = 1000 mg/kg bw/day** **3000 mg/kg bw/day:** ↓ bwg (days 6-19), ↓ food consumption (days 6-9) **Developmental toxicity:** **NOAEL = 1000 mg/kg bw/day** **3000 mg/kg bw/day:** ↑ skeletal variations (incomplete and unossified sites)
Genotoxicity studies	
Bacterial reverse mutation assay *S. typhimurium* TA98, TA100, TA1535, TA1537, *E. coli* WP2 urvA PMRA# 1132391	**Negative ± metabolic activation**
In vitro mammalian cytogenetics (chromosomal aberration) assay Chinese hamster ovary CHO-K1 cells PMRA# 1132393	**Negative without metabolic activation** **Positive with metabolic activation**
In vitro mammalian cell assay (TK locus) L5178Y mouse lymphoma cells PMRA# 1145195	**Negative ± metabolic activation**
In vivo micronucleus assay (intraperitoneal) ICR mice PMRA# 1132392	**Negative** **> 208 mg/kg bw/day:** lethargy **416 mg/kg bw/day:** convulsions, prostration

Neurotoxicity studies	
Postnatal developmental neurotoxicity (dermal) Crl :CD(SD)IGS BR VAF/Plus rats PMRA# 2910522	Supplemental **Offspring toxicity:** **NOAEL = 400 mg/kg bw/day** **>800 mg/kg bw/day:** ↓ bwg Limitations: The maternal effect level was not determined as dams were not treated with test substance. This study did not satisfy the guideline requirement for a developmental neurotoxicity study in rats.
Immunotoxicity studies	
28-day immunotoxicity (dermal) $B_6C_3F_1$ mice PMRA# 1145183	Supplemental LOAEL and NOAEL could not be determined due to absence of a dose-related response. Limitations: Only one immunologic parameter was measured and deficiencies in methodology were identified.

References

A. Information considered in the updated chemistry assessment

Studies/Information submitted by the registrant(s)

PMRA document number	Title
1853898	1997, Physical and Chemical Characteristics of Granola 97, DACO: 2.14
1853900	Solvent Solubility, Dissociation Constant, UV/Visible Absorption Spectra, DACO: 2.14.10,2.14.12,2.14.8
1853903	1998, PMK-TKI-4 Vapor Pressure Determination of Granola 97, DACO: 2.14.9
2910519	2018, Description of Starting Materials and Production Process for p-Menthane-3,8-diol, DACO: 2.11
2946498	2018, Validation of Method MV208, DACO: 2.13.4
2946500	2018, Determination of the Content in 5 Batches of PMD PURE, DACO: 2.13.4
3169606	2020, Batch Data, DACO: 2.13.3

B. Information considered in the toxicological assessment

Studies/Information submitted by the registrant(s)

PMRA document number	Title
1145175	1997, An Acute Oral Toxicity Study of Granola 97 in Rats, DACO: 4.2.1
1145176	1997, An Acute Dermal Toxicity Study of Granola 97 in Rabbits, DACO: 4.2.2
1145177	1997, Data Waiver Request for Acute Inhalation Toxicity Study (OPP Guideline 152-12), DACO: 4.2.3
1145178	1997, A Primary Eye Irritation Study of Granola 97 in Rabbits, DACO: 4.2.4
1145179	1997, A Primary Skin Irritation Study of Granola 97 in Rabbits, DACO: 4.2.5
1145180	1997, A Dermal Sensitization Study of Granola 97 in Guinea Pigs - Modified Buehler Design, DACO: 4.2.6
1145182	1997, A 90-Day Dermal Toxicity Study of Granola 97 in Rats, DACO: 4.3.4
1145183	1997, Immunotoxicity Screening Study in Mice Exposed Dermally to Granola 97, DACO: 4.3.5
1145192	1997, Rat Prenatal Developmental Toxicity Study with Granola 97, DACO: 4.5.2
1145194	1997, Bacterial Reverse Mutation Assay with Granola 97 , DACO: 4.5.4
1145195	1997, In Vitro Mammalian Cell Gene Mutation Test with Granola 97 , DACO: 4.5.5
1145196	1997, In Vitro Mammalian Cytogenetic Test Using Chinese Hamster Ovary (CHO) Cells with Granola 97 , DACO: 4.5.6
1145197	1997, Mammalian Erythrocyte Micronucleus Test with Granola 97, DACO: 4.5.7
2910521	2004, Percutaneous Postnatal Developmental Neurotoxicity study of p-menthan-3,8-diol in Crl:CD® (SD)IGS BR VAF/PLUS® Rats, DACO: 4.5.14

C. Information considered in the occupational and non-occupational assessment

Studies/Information submitted by the registrant(s)

PMRA document number	Title
2910531	2009, Percutaneous Absorption of an Insect Repellent p-Menthane-3,8-diol: A Model for Human Dermal Absorption, DACO: 5.8

D. Information considered in the environmental assessment

Additional information considered

Published information

PMRA document number	Title
654881	Health Canada, 2002. Proposed Regulatory Decision Document. *P-Menthane-3,8-diol*. PRDD2002-02. September 18, 2002.
660877	Health Canada, 2002. Registration Decision. *P-Menthane-3,8-diol*. RDD2002-04. November 29, 2002.