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Proposed Registration Decision

PRD2019-08

# Hop Beta Acids (Present as Potassium Salts), HopGuard Liquid, HopGuard II

*(publié aussi en français)*

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## Overview

### Proposed Registration Decision for Hop Beta Acids (Present as Potassium Salts)

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the [Pest Control Products Act](#), is proposing registration for the sale and use of Potassium Beta Resin, a manufacturing concentrate HopGuard Liquid and the end-use product HopGuard II, containing the technical grade active ingredient hop beta acids (present as potassium salts), to control varroa mites in honeybee hives.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

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 hop beta acids (present as potassium salts), HopGuard Liquid and HopGuard II.

### 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<sup>1</sup> 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<sup>2</sup> when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the Health Canada regulates pesticides, the assessment process and risk-reduction programs, please visit the [Pesticides](#) section of Canada.ca.

Before making a final registration decision on hop beta acids (present as potassium salts), HopGuard Liquid and HopGuard II, Health Canada's PMRA will consider any comments received from the public in response to this consultation document.<sup>3</sup> Health Canada will then

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<sup>1</sup> "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

<sup>2</sup> "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."

<sup>3</sup> "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

publish a Registration Decision<sup>4</sup> on hop beta acids (present as potassium salts), HopGuard Liquid and HopGuard II, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada'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 Hop Beta Acids (Present as Potassium Salts)?**

Hop beta acids (present as potassium salts) are naturally occurring weak organic acids produced by hop plants (*Humulus lupulus* L.). Hop beta acids (present as potassium salts) are the active ingredient used to formulate HopGuard II, which is used for control of varroa mites in honeybee hives. HopGuard II consists of strips impregnated with hop beta acids (present as potassium salts) which are placed in the brood chamber of bee hives by hanging the strips over hive frames. The mode of action of hop beta acids (present as potassium salts) in killing varroa mite is likely from physical damage to mites leading to death.

## **Health Considerations**

### **Can Approved Uses of Hop Beta Acids (present as potassium salts) Affect Human Health?**

**Hop beta acids (present as potassium salts) is unlikely to affect human health when it is used according to label directions.**

Potential exposure to hop beta acids (present as potassium salts) may occur when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The 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.

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.

In laboratory animal studies, and based on publicly available information, the technical grade active ingredient, Potassium Beta Resin, containing hop beta acids (present as potassium salts), is slightly acutely toxic via the oral route and extremely irritating to the eyes. The manufacturing concentrate, HopGuard Liquid, and the end-use product, HopGuard II, were also considered to be of slight acute oral toxicity and extremely irritating to the eyes.

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<sup>4</sup> "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Requests to waive acute oral, dermal, and inhalation toxicity, skin irritation, and dermal sensitization testing for Potassium Beta Resin, HopGuard Liquid, and HopGuard II, as well as short-term toxicity, prenatal developmental toxicity, and genotoxicity testing of Potassium Beta Resin were accepted in lieu of actual test data. Hop beta acids (present as potassium salts) is not expected to cause adverse health effects when used according to label instructions.

## **Residues in Water and Food**

### **Dietary risks from food and water are acceptable.**

Dietary exposure to hop beta acids (present as potassium salts) to humans is unlikely since application of HopGuard II is limited to brood chambers and not honey supers. Also, users are not to collect honey or wax from the treated brood chambers. It is expected that the proposed use of hop beta acids (present as potassium salts) will not pose a risk to any segment of the population, including infants, children, adults and seniors, from consumption of honey and wax from treated beehives.

Exposure to hop beta acids (present as potassium salts) from drinking water will be negligible. Consequently, the dietary risk from drinking water is acceptable.

## **Risks in Residential and Other Non-Occupational Environments**

### **Estimated risk for residential and other non-occupational exposure is acceptable.**

Residential exposure to individuals coming in contact with hop beta acids (present as potassium salts) during application is not expected. Thus, the risk is considered to be acceptable when HopGuard II is used according to label directions.

Bystander exposure is not expected due to the direct application to beehives. Consequently, the risk to bystanders is acceptable.

## **Occupational Risks From Handling HopGuard II**

### **Occupational risks are acceptable when HopGuard II is used according to the label directions, which include protective measures.**

To protect workers from exposure to HopGuard II, the label states that applicators must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, and protective eyewear. The occupational risks are acceptable when the precautionary statements on the label are observed.

## **Environmental Considerations**

An environmental assessment was not required for this evaluation based on the use pattern of HopGuard II.

## **Value Considerations**

### **What Is the Value of HopGuard II?**

**HopGuard II provides control of varroa mites, the most important pest of honeybees, and offers users a new active ingredient for use against this pest.**

Varroa mites are the most important parasitic pest of honeybees, and have a severe economic impact on the Canadian beekeeping industry. Significant varroa mite infestation in a honeybee colony will cause the loss of the infested colony. Based on the mode of action of HopGuard II, varroa mites are not expected to develop resistance, which is a problem with some other varroa mite control products.

### **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 Potassium Beta Resin, HopGuard Liquid and HopGuard II to address the potential risks identified in this assessment are as follows.

### **Key Risk-Reduction Measures**

#### **Human Health**

The signal words “CAUTION POISON” and “DANGER – CORROSIVE TO EYES” are required on the principal display panels of the labels for Potassium Beta Resin, HopGuard Liquid, and HopGuard II.

Standard hazard and precautionary statements are also required on the HopGuard II label to inform workers of the acute oral toxicity and eye irritation of the product. Workers handling packages, as well as the individual strips, of HopGuard II will be required to wear standard personal protective equipment including long-sleeved shirt, long pants, chemical-resistant gloves, shoes with socks, and goggles or face shield.

A restricted-entry interval is not required for HopGuard II.

### **Next Steps**

Before making a final registration decision on hop beta acids (present as potassium salts), HopGuard Liquid and HopGuard II, Health Canada’s PMRA will consider any comments received from the public in response to this consultation document. Health Canada 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). Health Canada will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and Health Canada's response to these comments.

## **Other Information**

When the Health Canada makes its registration decision, it will publish a Registration Decision on hop beta acids (present as potassium salts), HopGuard Liquid and HopGuard II (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

### Hop Beta Acids (Present as Potassium Salts), HopGuard Liquid, HopGuard II

#### 1.0 The Active Ingredient, Its Properties and Uses

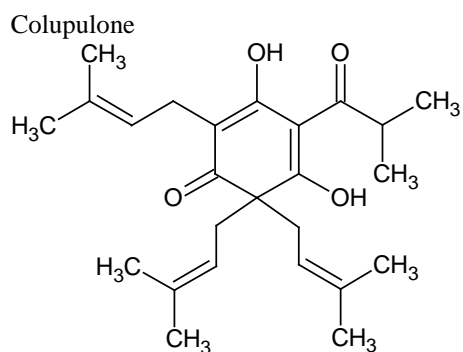
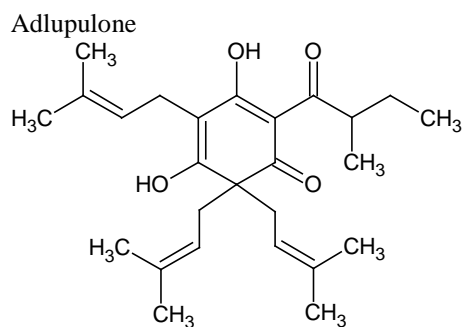
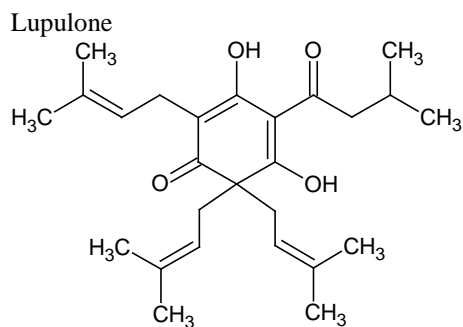
##### 1.1 Identity of the Active Ingredient

Active substance

Function acaricide

Chemical name

1. International Union of Pure and Applied Chemistry (IUPAC)	IUPAC chemical names for the major $\beta$ -acids:	
	Lupulone: 3,5-dihydroxy-4-(3-methylbutanoyl)-2,6,6-tris(3-methylbut-2-en-1-yl)cyclohexa-2,4-dien-1-one Adlupulone: 3,5-dihydroxy-2-(2-methylbutanoyl)-4,6,6-tris(3-methylbut-2-en-1-yl)cyclohexa-2,4-dien-1-one Colupulone: 3,5-dihydroxy-2,6,6-tris(3-methylbut-2-en-1-yl)-4-(2-methylpropanoyl)cyclohexa-2,4-dien-1-one	
2. Chemical Abstracts Service (CAS)	CAS chemical names for the major $\beta$ -acids:	
	Lupulone: 2,4-cyclohexadien-1-one, 3,5-dihydroxy-2,6,6-tris(3-methyl-2-buten-1-yl)-4-(3-methyl-1-oxobutyl)- Adlupulone: 2,4-cyclohexadien-1-one, 3,5-dihydroxy-4,6,6-tris(3-methyl-2-buten-1-yl)-2-(2-methyl-1-oxobutyl)- Colupulone: 2,4-cyclohexadien-1-one, 3,5-dihydroxy-2,6,6-tris(3-methyl-2-buten-1-yl)-4-(2-methyl-1-oxopropyl)-	
CAS number	Lupulone	468-28-0
	Adlupulone	28374-71-2
	Colupulone	468-27-9
Molecular formula	Lupulone	C <sub>26</sub> H <sub>38</sub> O <sub>4</sub>
	Adlupulone	C <sub>26</sub> H <sub>38</sub> O <sub>4</sub>
	Colupulone	C <sub>25</sub> H <sub>36</sub> O <sub>4</sub>
Molecular weight	Lupulone	414.6
	Adlupulone	414.6
	Colupulone	400.6

**Structural formula**

**Purity of the active ingredient**

56 %

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

### Technical Product—Potassium Beta Resin

Property	Result
Colour and physical state	dark brown viscous resin
Odour	faint resinous, hop extract aroma
Melting range	92°C for lupulone 93-94°C for colupulone 82-83°C for adlupulone
Boiling point or range	not applicable
Density	1.103 g/mL

Property	Result
Vapour pressure at 20°C	Not required
Ultraviolet (UV)-visible spectrum	<p>pH      <math>\lambda_{\text{max}}</math> (nm)    <math>\epsilon</math> (M<sup>-1</sup>cm<sup>-1</sup>)</p> <p>neutral      355.5      48.15</p> <p>basic      355.5      50.24</p> <p>acidic      333.6      25.49</p>
Solubility in water at 20°C	<p>(for lupulone)</p> <p>pH      solubility (ppm)</p> <p>7.0      48</p> <p>6.2      16</p> <p>5.6      8</p>
Solubility in organic solvents	The beta acids in the free acid form are very soluble in organic solvents; the potassium salt form is not very soluble in organic solvents.
<i>n</i> -Octanol-water partition coefficient ( $K_{ow}$ )	Log $K_{ow}$ = 7.13 (for lupulone)
Dissociation constant ( $pK_a$ )	6.1 (for $\beta$ -acids)
Stability (temperature, metal)	Active degrades slightly under strong acidic and alkaline conditions, and is sensitive to oxidation. Active showed no degradation when exposed to light and high temperature (70 °C).

### Manufacturing Concentrate—HopGuard Liquid

Property	Result
Colour	dark brown
Odour	resinous
Physical state	viscous liquid
Formulation type	SN (solution)
Label concentration	16 %
Container material and description	HDPE Plastic drum
Density	1.069 g/mL
pH of 1% dispersion in water	9.0 – 10.0
Oxidizing or reducing action	no oxidizing or reducing action
Storage stability	stable for three years when stored at room temperature
Corrosion characteristics	not expected to be incompatible with container material
Explosibility	not potentially explosive

## End-Use Product—HopGuard II

Property	Result
Colour	dark brown
Odour	resinous
Physical state	viscous liquid
Formulation type	IF (impregnated fabric)
Label concentration	4 g/strip
Container material and description	Foil and film laminate
Density	1.069 g/mL
pH of 1% dispersion in water	9.0 – 10.0
Oxidizing or reducing action	no oxidizing or reducing action
Storage stability	stable for up to 3 years when stored at room temperature in the original sealed pouches
Corrosion characteristics	not corrosive to packaging material
Explodability	not potentially explosive

### 1.3 Directions for Use

HopGuard II is applied in the brood chamber of honeybee hives by hanging the strips over hive frames. HopGuard II is applied at a rate of 1 strip per 5 frames of bees, rounded up to the nearest multiple of 5 frames (in other words, 1 strip for  $\leq 5$  frames, 2 strips for 6-10 frames of bees, etc.). Two applications, applied at 10 to 15 day intervals, may be required to provide acceptable control of varroa mite. HopGuard II is applied in spring or late summer/fall. Do not apply more than 4 applications per year. HopGuard II should be applied to honeybee hives with little to no brood, as presence of excessive brood will reduce efficacy.

### 1.4 Mode of Action

The mode of action of hop beta acids in killing varroa mite is likely from physical damage to mites leading to death. Hop beta acids are a contact miticide; therefore, bees must come into contact with the strips in order to kill mites on the bees.

## 2.0 Methods of Analysis

### 2.1 Methods for Analysis of the Active Ingredient

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

## **2.2 Method for Formulation Analysis**

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

## **2.3 Methods for Residue Analysis**

No methods (including environmental analytical) are required to quantify residues of hop beta acids (present as potassium salts).

## **3.0 Impact on Human and Animal Health**

### **3.1 Toxicology Summary**

The toxicological database submitted in support of registration of hop beta acids (present as potassium salts), consisted of an animal study on primary eye irritation, and requests to waive acute oral, dermal, and inhalation toxicity, primary skin irritation, dermal sensitization, short-term toxicity, prenatal developmental toxicity, and genotoxicity testing (Appendix I, Tables 1-3). The scientific quality of the data and information submitted was considered adequate to assess the toxic effects that may result from exposure to hop beta acids (present as potassium salts).

The primary eye irritation animal study on hop beta acids solution found it to be extremely irritating and the publicly available information submitted as part of a request to waive acute oral toxicity testing found hop beta acids (present as potassium salts) to be of slight acute oral toxicity (LD<sub>50</sub> of 1500 mg/kg bw in mice, 1800 mg/kg bw in rats, and 1000 to 2000 mg/kg bw in rabbits).

Requests to waive acute oral, dermal, and inhalation toxicity, skin irritation, and dermal sensitization testing for Potassium Beta Resin, HopGuard Liquid, and HopGuard II, as well as short-term toxicity, prenatal developmental toxicity, and genotoxicity testing of Potassium Beta Resin were accepted.

The formulants in HopGuard II are supported for the proposed use.

### **Incident Reports**

As of 1 November 2018, no humans or domestic animal incident reports involving hop beta acids (present as potassium salts) have been reported to the PMRA.

## **3.2 Occupational, Residential and Bystander Exposure and Risk Assessment**

### **3.2.1 Dermal Absorption**

No information on dermal absorption of hop beta acids (present as potassium salts) from HopGuard II was provided, however, dermal exposure is not expected when the precautionary statements on the label are observed.

### **3.2.2 Use Description**

HopGuard II is proposed for use in beehives. The method of application is by applying corrugated cardboard, mylar-backed strips (1 for every 5 frames of comb covered with bees in each brood chamber) impregnated with the manufacturing concentrate, HopGuard Liquid, containing hops beta acids (present as potassium salts) as the active ingredient. HopGuard II may be applied up to a maximum of 2 to 4 strips for a double brood chamber hive, 4 times per season (twice during the spring and twice during late summer or fall). The maximum quantity of active ingredient handled by one individual is 5.6 kg/day and 22.4 kg/year.

### **3.2.3 Mixer, Loader, and Applicator Exposure and Risk**

There are no mixing and loading activities associated with the use of the product. To protect applicators from exposure to HopGuard II, the label states to wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, and protective eyewear. The occupational risks to applicators are acceptable when the precautionary statements on the label are observed.

### **3.2.4 Postapplication Exposure and Risk**

Postapplication activities include IPM scouting, harvesting honey, splitting hives, the removal of spent HopGuard II strips, re-queening the hives, removal of queen cells, managing colony growth, and providing bees protein and sugar feed supplements. Given the nature of the postapplication activities, dermal contact with the treated strips is expected, but the wearing of bee keeping equipment (for example, gloves, jacket, pants, and boots) will mitigate this exposure potential. A restricted-entry interval (REI) was not specified on the proposed label and is not required.

### **3.2.5 Residential and Bystander Exposure and Risk**

As HopGuard II is to be applied directly to beehives and does not involve outdoor spraying, bystander exposure due to drift is not expected. Moreover, the volatility of HopGuard II is low, and the overall risk to bystanders is acceptable.

HopGuard II is not proposed for domestic classification as a pest control product, but could be used in beehives near residential areas. The direct application of HopGuard II to beehives, coupled with a low degree of volatility of hop beta acids (present as potassium salts) is such that exposure to humans and companion animals in residential areas is unlikely.

## **3.3 Food Residue Exposure Assessment**

### **3.3.1 Food**

HopGuard II is proposed for use exclusively in the brood chambers, not the honey supers, and workers are not to harvest honey or wax from the brood chambers. Also, hop beta acids have a low degree of volatility and a long history of use in foods without reports of adverse effects.

Thus, dietary exposure to hop beta acids (present as potassium salts) from honey and wax harvested from treated hives is not expected to present a health risk of concern. Consequently, dietary risk is acceptable.

### **3.3.2 Drinking Water**

HopGuard II is proposed for use in brood chambers inside the beehives and is not subject to agricultural run-off during application, postapplication activities, or due to inclement weather. Exposure to hop beta acids (present as potassium salts) from drinking water is expected to be negligible and will not present a health risk of concern.

### **3.3.3 Acute and Chronic Dietary Risks for Sensitive Subpopulations**

Calculations of acute reference doses and acceptable daily intakes are not required for hop beta acids (present as potassium salts).

Based on all the available information and hazard data, the PMRA concludes that hop beta acids (present as potassium salts) is 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.

### **3.3.4 Aggregate Exposure and Risk**

Based on the relevant information in the PMRA's database, there is reasonable certainty that no harm will result from aggregate exposure of residues of hop beta acids (present as potassium salts) to the general population in Canada, including infants and children, when HopGuard II is used according to the label. This includes all anticipated dietary (food and drinking water) exposures and all other non-occupational exposures (dermal and inhalation) for which there is reliable information.

### **3.3.5 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. For the current evaluation, the PMRA did not identify the potential for dietary or residential exposure for hop beta acids (present as potassium salts). Therefore, there is no requirement for a cumulative health risk assessment at this time.

### **3.3.6 Maximum Residue Limits**

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



The dietary risks from food and drinking water are considered to be negligible given that HopGuard II is proposed for use in the brood chambers and not the honey supers, that honey or wax are not to be harvested from the brood chambers, that hop beta acids have a low degree of volatility, and a long history of use in foods without reports of adverse effects. Consequently, the specification of a maximum residue limit (MRL) under the *Pest Control Products Act* is not required.

## **4.0 Impact on the Environment**

An environmental assessment was not required for this evaluation based on the use pattern of HopGuard II.

## **5.0 Value**

Efficacy trials demonstrated the level of control provided by HopGuard II is affected by presence of brood in the hive and by the number of applications. The data supported the application of one strip per five frames of bees for a period of 10–15 days, applied when little to no brood are present in the hive. While only one application may provide control, the results were not as consistent as when two sequential applications were applied. Therefore, two applications applied at 10-15 day intervals may be required to provide control of varroa mite. HopGuard II should be applied in spring or late summer/fall when there are little to no brood in the treated hives.

Tolerance of honeybees to HopGuard II was supported based on observations on adverse effects in the efficacy trials and 6 additional adverse effects studies. In one adverse effect study, when the product was applied to hives with brood present injury to brood directly adjacent to the strips was observed; brood injury was not observed in areas not directly adjacent to strips. Based on this evidence, the supported application rate and application timing (little to no brood present) is not expected to result in any significant injury to treated honeybee hives. A warning on the HopGuard II label regarding potential brood injury is required.

Alternative active ingredients registered to treat honeybee hives infested with varroa mites include oxalic acid, formic acid, amitraz, thymol, fluvalinate-tau, coumaphos, and flumethrin. Varroa mites have historically developed resistance to conventional miticides such as fluvalinate-tau and coumaphos, resulting in difficulty in controlling this pest. Based on the mode of action of hop beta acids (present as potassium salts) as a contact miticide which causes physical damage to mites, resulting in mite mortality, varroa mites are unlikely to develop resistance to HopGuard II.

HopGuard II has value as it controls varroa mites in honeybee hives with a mode of action which is unlikely to lead to resistance. HopGuard II is compatible with current management practices and will be a useful addition to the integrated pest management of varroa mites and aid in the control of resistant mites.

## 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, in other words, those that meet all four criteria outlined in the policy: persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*. The *Pest Control Products Act* requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, hop beta acids (present as potassium salts) and their transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03<sup>5</sup> and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

Hop beta acids (present as potassium salts) do not meet Track 1 criteria, and are not considered Track 1 substances.

### 6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical as well as formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.<sup>6</sup> The list is used as described in the PMRA Notice of Intent NOI2005-01<sup>7</sup> and is based on existing policies and regulations including DIR99-03 and DIR2006-02,<sup>8</sup> and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act*, 1999 (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

Technical grade Potassium Beta Resin does not contain any contaminants identified in the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.

The manufacturing concentrate, HopGuard Liquid, and the end-use product, HopGuard II, both contain ethylene oxide and 1,4-dioxane, contaminants of health or environmental concern identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*. However, the contaminants are present at acceptable levels.

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

<sup>6</sup> SI/2005-114

<sup>7</sup> NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*

<sup>8</sup> DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

## **7.0 Summary**

### **7.1 Human Health and Safety**

The toxicology database for hop beta acids (present as potassium salts) is adequate to define the toxic effects that may result from exposure to hop beta acids (present as potassium salts). Based on publicly available information provided in a request to waive acute oral toxicity testing, the active ingredient, hop beta acids (present as potassium salts), is of slight acute toxicity by the oral route. There was evidence of extreme irritation to the eyes of rabbits after acute dosing. Requests to waive acute oral, dermal, and inhalation toxicity, dermal irritation, and dermal sensitization testing for Potassium Beta Resin, HopGuard Liquid, and HopGuard II, as well as requests to waive short-term toxicity, prenatal developmental toxicity, and genotoxicity testing for Potassium Beta Resin were accepted based on a long history of use without reports of adverse effects.

Applicators will not be exposed to unacceptable levels of hop beta acids (present as potassium salts) when HopGuard II is used according to label directions.

Bystander and residential exposure during application of HopGuard II is not expected. Consequently, the risk to bystanders and residents is considered acceptable.

Exposure to hop beta acids (present as potassium salts) from food and drinking water will be negligible. Consequently, the dietary risk from food and drinking water is acceptable.

The specification of an MRL under the *Pest Control Products Act* is not required.

### **7.2 Value**

Varroa mites are the most important parasitic pest of honeybees, and have a severe economic impact on the Canadian beekeeping industry. Significant varroa mite infestation in a honeybee colony will cause the loss of the infested colony. Based on the mode of action of HopGuard II, varroa mites are not expected to develop resistance, which is a problem with some other varroa mite control products. HopGuard II provides control of varroa mites when applied at a rate of one strip for every five frames of bees in spring or late summer/fall, for an application period of 10–15 days. Two applications, applied at 10 to 15 day intervals, may be required to provide control of varroa mite.

## **8.0 Proposed Regulatory Decision**

Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing registration for the sale and use of Potassium Beta Resin, HopGuard Liquid and HopGuard II, containing the technical grade active ingredient hop beta acids (present as potassium salts), to control varroa mites in honeybee hives.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

## List of Abbreviations

♂	male
ADI	acceptable daily intake
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetres
g	gram
ha	hectare(s)
HDPE	High Density Polyethylene
HPLC	high performance liquid chromatography
hrs	hours
IPM	integrated pest management
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
$K_{ow}$	<i>n</i> -octanol-water partition coefficient
L	litre
LD <sub>50</sub>	median lethal dose
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation
mg	milligram
mL	millilitre
MAS	maximum average score
MIS	maximum irritation score
MOE	margin of exposure
MRL	maximum residue limit
N/A	not applicable
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
OC	organic carbon content
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

## Appendix I Tables and Figures

**Table 1 Toxicity Profile of HopGuard II Containing Hop Beta Acids (present as potassium salts)**  
(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons)

Study Type/Animal/PMRA#	Study Results
Acute oral toxicity  Rat  PMRA# 2783883	LD <sub>50</sub> 1800 mg/kg bw   Slight toxicity
Acute dermal toxicity Acute inhalation toxicity Primary skin irritation Dermal sensitization  PMRA# 2783883	Based on a long history of safe use, waivers were requested and granted.
Eye irritation  Rabbit, New Zealand White (♂)  PMRA# 2783804	MAS <sup>a</sup> = 48.6/110 MIS <sup>b</sup> = 84.4/110 (10 days)  The irritation was not resolved by Day 21 of the study.  Extremely irritating

<sup>a</sup> MAS = Maximum Average Score for 24, 48, and 72 hrs

<sup>b</sup> MIS = Maximum Irritation Score (average)

**Table 2 Toxicity Profile of HopGuard Liquid Containing Hop Beta Acids (present as potassium salts)**  
(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons)

Study Type/Animal/PMRA#	Study Results
Acute oral toxicity  Rat  PMRA# 2783883	LD <sub>50</sub> 1800 mg/kg bw   Slight toxicity
Acute dermal toxicity Acute inhalation toxicity Primary skin irritation Dermal sensitization  PMRA# 2783883	Based on a long history of safe use, waivers were requested and granted.

Study Type/Animal/PMRA#	Study Results
Eye irritation Rabbit, New Zealand White (♂) PMRA# 2783804	MAS <sup>a</sup> = 48.6/110 MIS <sup>b</sup> = 84.4/110 (10 days)  The irritation was not resolved by Day 21 of the study.  Extremely irritating

<sup>a</sup> MAS = Maximum Average Score for 24, 48, and 72 hrs

<sup>b</sup> MIS = Maximum Irritation Score (average)

**Table 3 Toxicity Profile of Potassium Beta Resin**  
(Effects are known or assumed to occur in both sexes unless otherwise noted)

Study Type/Animal/PMRA#	Study Results
Acute oral toxicity Rat PMRA# 2783883	LD <sub>50</sub> 1800 mg/kg bw  Slight toxicity
Acute dermal toxicity Acute inhalation toxicity Primary skin irritation Dermal sensitization PMRA# 2783883	Based on a long history of safe use, waivers were requested and granted.
Eye irritation Rabbit, New Zealand White (♂) PMRA# 2783804	MAS <sup>a</sup> = 48.6/110 MIS <sup>b</sup> = 84.4/110 (10 days)  The irritation was not resolved by Day 21 of the study.  Extremely irritating
Short-term oral toxicity Short-term dermal toxicity Short-term inhalation toxicity Prenatal developmental toxicity Gene mutations in bacteria Gene mutations in mammalian cells (in vitro) Chromosome aberrations (in vitro) PMRA# 2783883	Based on a long history of safe use, waivers were requested and granted.

## References

### A. List of Studies/Information Submitted by Registrant

PMRA  
Document  
Number

References

#### 1.0 Chemistry

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#### 2.0 Human and Animal Health

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**3.0 Value**

- 2783869 2017, Value summary spreadsheet, DACO: 10.1, 10.3.1
- 2783870 2017, DACO 10 Value Assessment, DACO: 10.1, 10.2.1, 10.2.2, 10.2.3.1, 10.2.3.3, 10.3.1, 10.3.2, 2.10
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- 2783878 2017, Value Dossier, DACO: 10.1, 3.0, 3.1, 4.1, 5.2, 6.1, 7.1, 8.1, 9.1 CBI