Proposed Registration Decision PRD2022-08

cis-Jasmone and Trunemco

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Overview

Proposed registration decision for *cis*-Jasmone

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 Jasmone Technical Concentrate and Trunemco, containing the technical grade active ingredient *cis*-jasmone, to be used as a seed treatment in soybean, field corn, popcorn and sweet corn.

Trunemco also contains *Bacillus amyloliquefaciens* strain MBI 600 (previously classified as *Bacillus subtilis* strain MBI 600), which is currently registered for use as a seed treatment. For details, see Proposed Registration Decision PRD2009-17, *Bacillus subtilis* strain MBI 600 and Integral Liquid Biological Fungicide, and Registration Decision RD2010-04, *Bacillus subtilis* strain MBI 600 and Integral Liquid Biological Fungicide.

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 *cis*-jasmone and Trunemco.

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.

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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."*

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 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 *cis*-jasmone and Trunemco, Health Canada's PMRA will consider any comments received from the public in response to this consultation document.[3] Health Canada will then publish a Registration Decision[4] on *cis*-jasmone and Trunemco, 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 *cis*-Jasmone?

cis-Jasmone is a biochemical plant nematicide product able to activate a plant's internal defense system against nematode attacks and can prime treated seed by stimulating expression of genes resistant to nematode infection. In turn, *Bacillus amyloliquefaciens* may induce systemic resistance through the production of bacterial metabolites that protect plants against attacks of pathogenic microbes, viruses and nematodes. The combination of these two active ingredients supresses certain nematodes and provides a consistent yield benefit in soybean and corn.

Health considerations

Can approved uses of *cis*-Jasmone affect human health?

cis-Jasmone is unlikely to affect human health when it is used according to label directions.

Potential exposure to *cis*-jasmone may occur through the diet (food and water) or when handling the product or when handling and planting treated seeds. 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.

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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*.

In laboratory animals, *cis*-jasmone was considered to be of low acute toxicity by the oral, dermal, and inhalation routes, minimally irritating to the eyes and skin, and not a dermal sensitizer.

Short-term dermal toxicity testing, prenatal developmental toxicity testing, and genotoxicity/mutagenicity testing, as well as information from published scientific literature on *cis*-jasmone were also assessed. Adverse effects in animals given repeated high doses of *cis*-jasmone resulted in skin irritation. There was no indication that the young were more sensitive than the adult animal. *cis*-Jasmone is not considered genotoxic or mutagenic.

In laboratory animals, the end-use product, Trunemco, was considered to be of low acute toxicity by the oral, dermal, and inhalation routes, minimally irritating to the eye and slightly irritating to the skin. Since Trunemco contains a microbial pest control agent, *Bacillus amyloliquefaciens* strain MBI 600, the end-use product is considered a potential sensitizer. The Trunemco label also requires a soy allergen warning statement.

Residues in water and food

Dietary risks from food and water are acceptable.

Based on the proposed use pattern as seed treatment, there is no direct application of Trunemco to the edible portions of the plants, and residues are not expected to be present on the harvested crops. In addition, the likelihood of residues of *cis*-jasmone in drinking water will be very low. Consequently, health risks are acceptable for all segments of the population, including infants, children, adults and seniors.

Risks in residential and other non-occupational environments

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

Trunemco will only be applied to seed in commercial seed treatment facilities, therefore, bystander exposure is not expected to occur. There are no residential uses of the product. Residential and non-occupational exposure to Trunemco is expected to be low when label directions are observed. Consequently, the risk to residents and the general public is acceptable.

Occupational risks from handling Trunemco

Occupational risks are acceptable when Trunemco is used according to the label directions, which include protective measures.

Workers handling Trunemco can come into direct contact with *cis*-jasmone on the skin or by inhalation during handling, loading, clean-up and repair, bagging, sewing, stacking, as well as during handling and planting of treated seeds. Minimal eye exposure is also possible.

To protect workers from exposure to Trunemco, the label requires workers to wear a long-sleeved shirt, long pants, waterproof gloves, socks and shoes and a NIOSH-approved particulate filtering facepiece respirator with any N, R or P filter during handling, loading, clean-up and repair, bagging, sewing, stacking, as well as during handling and planting of treated seeds.

Treated seed must be labelled or tagged with instructions for workers handling seed outside of the seed treatment facility.

The occupational risks are acceptable when the precautionary statements on the label are observed.

Environmental considerations

What happens when *cis*-jasmone is introduced into the environment?

cis-Jasmone is a natural product in plants and is ubiquitous in the environment. Jasmone Technical Concentrate, containing two isomeric forms of jasmone, *cis*-jasmone (93%) and *trans*-jasmone (6.9%), enters the environment when the end-use product Trunemco is applied as a seed treatment nematicide for soybean and corn. *trans*-Jasmone is a minor component of Jasmone Technical Concentrate; it is not considered in this assessment. *cis*-Jasmone is found as a natural element in the volatile portion of plant essential oils. Like other terpenoid compounds, *cis*-jasmone is expected to be rapidly broken down by microorganisms; thus, *cis*-jasmone is non-persistent in nature and not likely to travel long distances from where it is applied, or to accumulate in tissues of plants or animals.

When used according to label directions, *cis*-jasmone poses acceptable risks to terrestrial organisms, and potential exposure to aquatic systems from its use on seeds is not expected.

Value considerations

What is the value of Trunemco?

The registration of Trunemco will provide Canadian growers with a new product to manage root-knot nematode in corn, or soybean cyst nematode in soybean, which can cause serious crop and economic losses.

Trunemco is applied as a seed treatment to protect soybean and corn from root damage caused by parasitic soybean cyst nematode or root-knot nematode.

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 Jasmone Technical Concentrate and Trunemco to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Human health

The hazard signal words "WARNING: Contains the allergen soy" are required on the principal display panel of the label for Trunemco. Since Trunemco also contains a microbial pest control agent, which is considered to be a potential sensitizer, the hazard statement "POTENTIAL SENSITIZER" is required on the principal display panel. Standard precautionary statements are also required on the end-use product label to avoid eye and skin contact and inform of the potential for sensitization.

Workers handling, loading, and performing clean-up and repair, and during all other activities involving the handling of treated seeds will be required to wear a long-sleeved shirt, long pants, waterproof gloves, socks and shoes and a NIOSH-approved particulate filtering facepiece respirator with any N, R or P filter.

To limit worker and residential bystander exposure, Trunemco and treated seed must be handled in a way that both do not come in contact with workers or residential bystanders. Additionally, only workers wearing personal protective equipment may be in the area where treating, bagging, sewing, stacking or loading for transport is occurring.

Treated seed must be labelled or tagged with instructions for workers handling seed outside of the seed treatment facility.

Next steps

Before making a final registration decision on *cis*-jasmone and Trunemco, 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

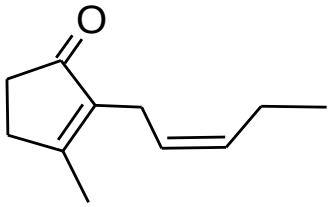
When the Health Canada makes its registration decision, it will publish a Registration Decision on *cis*-jasmone and Trunemco (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room. For more information, please contact the PMRA's Pest Management Information Service.

Science evaluation

cis-Jasmone, Trunemco

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	*cis*-Jasmone
Function	Nematicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	3-methyl-2-[(2Z)-pent-2-en-1-yl]cyclopent-2-en-1-one
2. Chemical Abstracts Service (CAS)	2-Cyclopenten-1-one, 3-methyl-2-[(2Z)-2-penten-1-yl]-
CAS number	488-10-8
Molecular formula	$C_{11}H_{16}O$
Molecular weight	64.246 g/mol
Structural formula	
Purity of the active ingredient	93.0%

The end-use product, Trunemco, also contains *Bacillus amyloliquefaciens* strain MBI 600 (Reg. No. 29452) at a minimum of 2×10^9 colony-forming units (CFU)/mL. The use of *Bacillus amyloliquefaciens* strain MBI 600 as a seed treatment was previously assessed and approved by PMRA (see Proposed Registration Decision PRD2009-17 and Registration Decision RD2010-04, *Bacillus subtilis* strain MBI 600 and Integral Liquid Biological Fungicide). *Bacillus amyloliquefaciens* strain MBI 600 was previously classified as *Bacillus subtilis* strain MBI 600.

1.2 Physical and chemical properties of the active ingredients and end-use product

Technical product—Jasmone Technical Concentrate

Property	Result
Colour and physical state	Pale yellow liquid
Odour	Strong floral
Boiling point	Decomposes at 201.7°C
Density	0.8743–1.0 g/mL at 25°C
Vapour pressure at 20°C	1.33×10^5 mPa
Ultraviolet (UV)-visible spectrum	Maximum absorbance at 235 nm.
Solubility in water at 20°C	1.410 g/L at 20°C
Solubility in organic solvents at 20°C	Soluble in ethanol, ether and carbon tetrachloride.
n-Octanol-water partition coefficient (K_{ow})	Log P: 2.7
Stability (temperature, metal)	Stable in contact with aluminum foil, aluminum acetate, iron and iron acetate. Color of the material changes when stored in iron containers. Stable at 54°C for 2 weeks and at ambient temperature for a year.

End-use product—Trunemco

Property	Result
Colour	Light beige
Odour	Spicy flowery
Physical state	Liquid
Formulation type	Suspension
Label concentration	*Bacillus amyloliquefaciens*, strain MBI 600: not less than 2.0×10^9 CFU/ mL *cis*-Jasmone: 0.88%
Container material and description	Plastic jug, drum or tote (0.1–1000 L)
Density	1.02–1.07 g/cm^3
pH of 1% dispersion in water	6.0–7.5
Oxidizing or reducing action	The end-use product does not exhibit oxidizing properties, and is not expected to exhibit reducing properties.

Property	Result
Storage stability	The active content of the end-use product with respect to *cis*-Jasmone was stable when the end-use product was stored in a 1 L fluorinated HDPE bottle for 2 year at 20°C
Corrosion characteristics	The product was not corrosive to fluorinated HDPE bottles after storage for 24 months at 20°C ± 2°C.
Explodability	Not expected to be explosive.

1.3 Directions for use

Trunemco is applied as a seed treatment to soybean and corn at a rate of 20 mL/100 kg seed. Trunemco may be applied with suitable commercial seed treating equipment.

1.4 Mode of action

The active ingredient *cis*-jasmone is a naturally occurring biochemical plant product, and it activates a plant's internal defense system against nematode attacks. *cis*-Jasmone primes the treated seed via upregulating expression of the genes involved in resistance to nematode infection in plants.

Bacillus amyloliquefaciens may induce systemic resistance through the production of bacterial metabolites that protect plants against nematodes.

2.0 Methods of analysis

2.1 Methods for analysis of the active ingredient

The methods provided for the analysis of *cis*-jasmone and impurities in the technical product have been validated and assessed to be acceptable.

2.2 Method for formulation analysis

The method provided for the analysis of *cis*-jasmone 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 are required to quantify residues of *cis*-jasmone because residue levels on harvested crops are expected to be very low (see Section 3.0 for additional details).

2.4 Methods for identification of the microorganisms

Refer to PRD2009-17, *Bacillus subtilis* strain MBI 600 and Integral Liquid Biological Fungicide, for details.

2.5 Methods for establishment of purity of seed stock

Refer to PRD2009-17, *Bacillus subtilis* strain MBI 600 and Integral Liquid Biological Fungicide, for details.

2.6 Methods to define the content of the microorganism in the manufactured material used for the production of formulated products

For the end-use product, the guarantee of the microbial active ingredient is expressed in units of CFU per mL. Representative data on five batches of the end-use product were submitted. The method for determining CFU counts was adequately described.

2.7 Methods to determine and quantify residues (viable or non-viable) of the active microorganism and relevant metabolites

Refer to PRD2009-17, *Bacillus subtilis* strain MBI 600 and Integral Liquid Biological Fungicide, for details.

2.8 Methods for determination of relevant impurities in the manufactured material

The quality assurance procedures used to limit contaminating microorganisms during the manufacture of Bacillus amyloliquefaciens strain MBI 600 Technical (see PRD2009-17, *Bacillus subtilis* strain MBI 600 and Integral Liquid Biological Fungicide, for details) and the end-use product, Trunemco, are acceptable. These procedures include sterilization of all equipment and media as well as frequent sampling of production batches for purity and contamination.

The absence of human pathogens and below-threshold levels of contaminating microorganisms were shown in the microbial screening of batches of Trunemco using standard methods for detecting and enumerating microbial contaminants of concern. All batches of Trunemco conform to the limits set out in the Organization for Economic Co-operation and Development (OECD) issue paper on microbial contaminants for microbial pest control products [ENV/JM/MONO(2011)43].

2.9 Methods to determine storage stability, shelf-life of the microorganism

Storage stability data were provided for Trunemco. Results support a storage period of two years at 20°C.

3.0 Impact on human and animal health

3.1 Toxicology summary

A detailed review of toxicology information was conducted in support of Jasmone Technical Concentrate (technical grade active ingredient) and Trunemco (end-use product). The data package for Jasmone Technical Concentrate and Trunemco is considered acceptable (Appendix I, Tables 1–2) to assess the toxic effects that may result from exposure to *cis*-jasmone.

The data package consisted of acute toxicity studies (acute oral, dermal and inhalation toxicity, eye and skin irritation, and dermal sensitization) for both Jasmone Technical Concentrate and Trunemco, and short-term dermal toxicity, prenatal developmental toxicity, in vitro bacterial gene mutation and in vitro mammalian gene mutation studies for the technical grade active ingredient, as well as published scientific literature and publicly available information.

Studies conducted with *cis*-jasmone (99.9% *cis*-jasmone) were submitted to evaluate the acute toxicology of Jasmone Technical Concentrate (93% *cis*-jasmone). Jasmone Technical Concentrate is considered to be of low acute toxicity by the oral, dermal, and inhalation routes, minimally irritating to the eyes and skin, and not a dermal sensitizer.

A short-term dermal toxicity study, prenatal developmental toxicity study, genotoxicity and mutagenicity studies in bacterial and mammalian cell lines, as well as information from published scientific literature on *cis*-jasmone, were also assessed.

Treatment-related adverse effects were observed in rats dermally administered repeated doses of *cis*-jasmone for 90 days. Desquamation and erythema were noted at all doses in both males and females. At the end of the study, pathology examination revealed desquamation in treated female rats at all doses while a microscopic examination revealed increased incidence and severity of epidermal hyperplasia and hyperkeratosis in a dose-dependent manner in the treated skin of male and female rats; therefore, the dermal lowest observed adverse effect level (LOAEL) was 85 mg/kg/day, at the lowest dose tested. A dermal no observed adverse effect level (NOAEL) was not established. Additionally, there were increases in red blood cell counts, activated partial thromboplastin time and potassium, and decreases in absolute lymphocytes, white blood cell counts, aspartate amino-transferase, sorbitol dehydrogenase, and bilirubin in female rats. The systemic NOAEL in females was 250 mg/kg/day and in males was >1000 mg/kg/day.

In an oral prenatal developmental toxicity study conducted with *cis*-jasmone, clinical signs of toxicity (slight ataxia) were observed in pregnant animals on Day 5 that resolved between Day 6 and 9. At the highest dose tested, reductions in body weight gains at gestational days (GD) 5-8, 14-17, and for the overall study period (GD 3-20), a decrease in mean daily food consumption between GD 5-8 and 14-17, and an increase in the level of thyroid stimulating hormone (TSH) were noted. The maternal NOAEL was 85 mg/kg bw/day. Developmental effects were observed as reduced fetal body weight and increased incidence of skeletal variations, at a dose level higher than that producing maternal toxicity. The developmental NOAEL was 350 mg/kg bw/day.

While in a non-guideline study *cis*-jasmone enhanced sister chromatid exchange in the presence of a genotoxicant in Chinese hamster ovary K-1 cells, it was not genotoxic alone and it was not mutagenic in a bacterial reverse mutation assay. There is no evidence of carcinogenic potential for *cis*-jasmone in the available published literature.

In addition to *cis*-jasmone, Trunemco also contains the registered technical grade active ingredient *Bacillus amyloliquefaciens* strain MBI 600 Technical (PCP No. 29452) as a co-active ingredient. The use of *B. amyloliquefaciens* strain MBI 600 as a seed treatment was previously assessed and approved by PMRA as *B. subtilis* strain MBI 600. Refer to PRD2009-17, *Bacillus subtilis* strain MBI 600 and Integral Liquid Biological Fungicide, for details on the review.

To address the data requirements for the end-use product, acute toxicity studies with BAS 798 00 F (0.897% *cis*-jasmone, 6.6×10^9 CFU/mL *Bacillus amyloliquefaciens* MBI 600), a seed treatment containing the same two active ingredients found in Trunemco (0.88% *cis*-jasmone, minimum 2×10^9 CFU/mL *Bacillus amyloliquefaciens* MBI 600), were accepted as the two formulations are essentially identical. Given the results of the studies, Trunemco is of low acute toxicity by the oral, dermal, and inhalation routes, minimally irritating to the eye and slightly irritating to the skin. Since Trunemco contains a microbial pest control agent (MPCA), it is considered a potential sensitizer.

3.2. Dermal absorption

No information was submitted on the potential dermal absorption of *cis*-jasmone. The molecular weight, physico-chemical properties including water solubility and octanol-water partition coefficient of *cis*-jasmone suggest that dermal absorption may occur.

3.3 Occupational, residential and bystander exposure and risk assessment

3.3.1 Use description

Trunemco is proposed for registration as a commercial seed treatment on soybean, field corn, popcorn and sweet corn (including seed production). Seeds will be treated at commercial seed treatment facilities before transport to the planting site. Trunemco is loaded into a slurry or holding tank and all mixing activities are carried out automatically. The proposed use pattern permits an application rate of 20 mL/100 kg seed or 0.2 g/100 kg of seed.

3.3.2 Occupational exposure and risk assessment

3.3.2.1 Mixer, loader, and applicator exposure and risk

When Trunemco is used according to label directions, occupational exposure is characterized as short- or intermediate-term in duration with the level of exposure increasing if workers are involved in multiple activities. Occupational exposure will occur primarily by the dermal and inhalation routes during mixing, loading, clean-up and repair. Ocular exposure is expected to be minimal.

To protect workers from exposure to Trunemco during handling, loading, clean-up and repair, workers are required to wear a long-sleeved shirt, long pants, waterproof gloves, socks and shoes and a NIOSH-approved particulate filtering facepiece respirator with any N, R or P filter.

Applicant-submitted dermal exposure estimates for workers performing seed treatment mixing, loading and application activities supported that a single layer of personal protective equipment (PPE) was adequate to protect workers from exposure to Trunemco.

Precautionary statements on the end-use product label, such as the wearing of PPE, aimed at mitigating exposure are adequate to protect individuals from any risk due to occupational exposure. Overall, occupational risks to workers are acceptable when the precautionary statements on the labels are followed which include PPE.

Methyleugenol is a genotoxic carcinogen and is a naturally occurring substance found in some spices, herbs, fruit, and essential oils. Based on submitted batch analysis data for the technical grade active ingredient, methyleugenol was not detected at levels above the limit of detection (0.0003% w/w) in the technical grade active ingredient, and the estimated level in the end-use product (at approximately 1/90th the level in the technical grade active ingredient) is less than the maximum concentration of methyleugenol permitted in personal care products (in other words, fine fragrances, eau de toilette, fragrance creams, leave-on products, oral hygiene products and rinse-off products). Therefore, the risk from worker exposure to the level of methyleugenol in Trunemco is considered acceptable.

3.3.2.2 Postapplication exposure and risk

Postapplication activities inside the seed treatment facility include bagging, sewing, stacking, and loading for transport of treated seed. Postapplication activities outside of the seed treating facility include delivery and planting of treated seed, equipment maintenance or entry into seeded fields to check seeding depth. Postapplication exposure can be characterized as short-term in duration, with the primary routes of exposure by the dermal and inhalation routes. All handlers of treated seed must wear a long-sleeved shirt, long pants, waterproof gloves, socks and shoes and a NIOSH-approved particulate filtering facepiece respirator with any N, R or P filter. Additionally, Trunemco and treated seed must be handled in a way that both do not come in contact with workers or residential bystanders, and only workers wearing PPE may be in the area where treating, bagging, sewing, stacking or loading for transport is occurring. Ocular exposure is expected to be minimal.

Treated seed leaving the seed treatment facility must be labelled to inform the workers the seed has been treated with Trunemco and that handling of treated seed requires precautions (including PPE).

Precautionary (for example, wearing of PPE) statements on the end-use product label aimed at mitigating exposure are adequate to protect workers from risk due to postapplication exposure.

3.3.3 Residential and bystander exposure and risk

Trunemco will only be applied to seed in commercial seed treatment facilities, therefore bystander exposure is not expected to occur. There are no residential uses of the product. Residential bystander exposure to Trunemco is expected to be low when label directions are

observed. Health Canada requires statements on the label that specify that Trunemco must be applied in such a way that there will be no contact to workers or other persons, either directly or through drift; and as per Canada's *Seeds Act*, treated seed must be unnaturally coloured as an indicator that the seed has been treated with a substance. Consequently, the health risks to bystanders and individuals in residential areas to Trunemco are considered acceptable.

3.4 Dietary exposure and risk assessment

3.4.1 Food

The proposed use pattern as seed treatment is not expected to result in dietary exposure since the residue levels on harvested crops are expected to be very low. To characterize the *cis*-jasmone residues remaining on harvested plants, the applicant submitted residue data obtained from bean seeds treated with ^{14}C-labelled *cis*-jasmone, as well as *cis*-jasmone-treated soybean, corn or cotton seeds. Both studies treated the starting seed at the proposed application rate of Trunemco, and the resulting study data were adequate to provide information on the amount of *cis*-jasmone residue remaining on plants after harvest.

Bean pods were harvested 97 days after sowing and separated into bean seeds, bean hulls and leaves and stems (rest of plant). The Total Radioactive Residues (TRR) in the matrices of bean seeds, bean hulls and bean rest of plant was determined by combustion analysis of homogenized samples, 179 days after planting. The TRR measured in the bean seed matrix was higher than the values in bean hulls and the rest of the plant matrices but residue levels were all less than 0.01 mg/kg. When the bean seed matrix was extracted three times with methanol and then three times with water, the sum of Extractable Radioactive Residues (ERR) and Residual Radioactive Residues (RRR) remaining after solvent extraction was less than 0.01 mg/kg. All labelled *cis*-jasmone residues (measured and calculated) for bean seed, hulls and rest of plant were less than 0.01 mg/kg.

Five field studies with soybean seeds, corn grain and cotton seed treated with *cis*-jasmone were conducted in the United States. Corn, soybean and cotton crops were harvested 167 days, 124-140 days and 150 days, respectively, after planting of treated seed. Harvested samples were frozen until analysis using a liquid chromatography-differential mobility spectrometry tandem mass spectrometry (LC-DMS/MS/MS) analytical method able to determine residues of *cis*-jasmone. The limit of quantitation (LOQ) was 0.01 ppm for *cis*-jasmone. No residues of *cis*-jasmone were detected above the LOD of 0.002 ppm in any of the 32 harvested corn, soybean seed or cotton seed samples grown from the treated seeds.

Considering the use pattern and the submitted residue data, residues of *cis*-jasmone are not expected to be present on the edible portions of the plant after harvest when applied as a seed treatment at a rate of 0.2 g *cis*-jasmone/100 kg seeds.

Therefore, when the end-use product is applied as directed by the label, the health risk is acceptable for the general population, including infants and children, and domestic animals.

Methyleugenol is a naturally occurring substance found in spices, herbs, fruit, and essential oils. Based on submitted batch analysis data for the technical grade active ingredient, the level of methyleugenol in the end-use product would be several orders of magnitudes below published estimates of background dietary intakes from flavourings, spices and other sources. In addition, the residues of methyleugenol remaining on edible portions of the crops are expected to be further reduced before harvest as Trunemco is a seed treatment and methyleugenol has an estimated dissipation half-life of 16 hours in the soil. Consequently, it is not expected that the use of Trunemco will result in dietary intakes of methyleugenol greater than existing background dietary intakes.

3.4.2 Exposure from residues in drinking water

Dietary exposure from drinking water is expected to be low as the use pattern is limited to seed treatment. The treatment is performed indoors in a commercial facility, and leaching from the treated seed in the field is expected to be minimal due to the low soil mobility and low environmental persistence of *cis*-jasmone. Moreover, the end-use product has a low toxicity profile, and the label has the necessary mitigative measures to limit contamination of drinking water. Consequently, health risks are acceptable for all segments of the population, including infants, children, adults and seniors.

3.4.3 Acute and chronic dietary risks for sensitive subpopulations

As noted above, when the end-use product is applied as directed by the label, the health risk is acceptable for the general population, including infants and children, and domestic animals.

3.5 Aggregate exposure and risk

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).

In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential exposure pathways is assessed. A major consideration is the likelihood of co-occurrence of exposures. Additionally, only exposures from routes that share common toxicological endpoints can be aggregated.

cis-Jasmone is considered to be of low acute oral, dermal, and inhalation toxicity, minimally irritating to the eyes and skin, and not a dermal sensitizer. The proposed use pattern (seed treatment) is not expected to result in dietary exposure since the end-use product will not be applied to the edible portions of crops. Based on available information, there is reasonable certainty that no harm will result from aggregate exposure of residues of *cis*-jasmone to the general population in Canada, including infants and children, when Jasmone Technical Concentrate and Trunemco are used as labelled. 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.

3.6 Cumulative assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. Accordingly, assessment of potential common mechanisms of toxicity with other pesticides was undertaken.

While *cis*-jasmone is structurally similar to components found in essential oil-based pest control products, it is difficult to determine whether constituents share a common mechanism of action as it is often not possible to fully identify and characterize the constituent(s) responsible for toxicity. However, based on the low toxicity profile, and given that dietary or residential exposure to *cis*-jasmone is not expected under the proposed conditions of use (seed treatment), there is no requirement for a cumulative risk assessment at this time.

In its assessment of common mechanism of toxicity, the PMRA considers both the taxonomy of MPCAs and their production of any potentially toxic metabolites. For the current evaluation, the PMRA has determined that *B. amyloliquefaciens* strain MBI 600 shares a common mechanism of toxicity with other strains of *B. amyloliquefaciens*, *B. licheniformis*, and *B. subtilis* that are used as MPCAs; *B. amyloliquefaciens* strain F727, *B. amyloliquefaciens* strain FZB42, *B. amyloliquefaciens* strain D747, *B. velezensis* strain RTI301, *B. subtilis* strain RTI477, B. *amyloliquefaciens* strain PTA-4838, *B. subtilis* strain QST 713, *B. subtilis* strain GB03, *B. subtilis* strain FMCH 001, *B. licheniformis* FMCH 002 and *B. subtilis* var. *amyloliquefaciens* strain FZB24. The potential health risks from cumulative exposure of *Bacillus amyloliquefaciens* strain MBI 600 and these other MPCAs are acceptable when used as labelled given their low toxicity and pathogenicity.

3.7 Maximum residue limits

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether dietary risks are acceptable from the consumption of foods treated with the pesticide when used according to the supported label directions. If acceptable, this means food containing that amount of residue is safe to eat, and maximum residue limits (MRLs) may be proposed. MRLs are the maximum amount of pesticide residue legally permitted to remain in/on food sold in Canada and are specified under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act.*

Dietary risk from the proposed use of *cis*-jasmone is acceptable, given the low toxicity profile of *cis*-jasmone and the proposed use as a seed treatment, which would result in negligible residues on the edible portions of the plant after harvest. Consequently, the specification of MRLs, under the *Pest Control Products Act*, will not be required for *cis*-jasmone because residues of *cis*-jasmone are not expected on foods.

3.8 Health incident reports

cis-Jasmone is a new active ingredient pending registration for use in Canada, and as of 7 December 2021, no human or domestic animal incident reports had been submitted to the PMRA.

The proposed end-use product also contains a registered active ingredient *Bacillus amyloliquefaciens*, strain MBI 600, in addition to *cis*-jasmone. Therefore, a query was also conducted for incidents involving the active *Bacillus amyloliquefaciens* and the related strains, *Bacillus licheniformis* and *Bacillus subtilis.* As of 7 December 2021, there was one human incident involving *Bacillus subtilis* QST 713. In this incident, a person reported minor symptoms of rash and cough when applying a product containing *Bacillus subtilis* strain QST 713. The label of the proposed product, Trunemco, contains appropriate hazard signal words, precaution statements and personal protective equipment aimed at reducing pesticide exposure when mixing, loading or applying the product or when handling treated seeds. Hence, no additional mitigation measures are proposed based on the incident report review.

4.0 Impact on the environment

4.1 Fate and behaviour in the environment

cis-Jasmone is soluble in water with a solubility of 1.41 g/L. *cis*-Jasmone belongs to the group of sesquiterpenes known as jasmonates, all of which are naturally occurring substances expected to dissipate through microbial degradation. In an aerobic biodegradation study of some terpene compounds similar to jasmone, their levels decreased below the detection limit within 40 hours of incubation. An estimated K_{oc} of 295 L/g indicates *cis*-jasmone is expected to have moderate soil mobility. An estimated Henry's law constant of 1.53×10^{-4} atm. m^3/mol suggests that it will volatilize from wet or dry soil or water surfaces. Run-off and leaching of *cis*-jasmone from treated soils is not expected due to its non-persistent nature in the environment. Thus, surface and ground water sources are not expected to be contaminated as a result of soil application of *cis*-jasmone as seed treatment. In the atmosphere, *cis*-jasmone will not be subject to long-range transport as it is expected to undergo rapid degradation by reactions with ozone, nitrate and hydroxyl radicals (Appendix I, Table 3).

4.2 Environmental risk characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models, which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates,

vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to terrestrial organisms

A summary of toxicity data are presented in Appendix I, Table 4.

cis-Jasmone is relatively non-toxic to honey bees on an acute oral and contact basis with LD_{50} values greater than 100 µg a.i./bee. *cis*-Jasmone was slightly toxic to the northern bobwhite quail on acute and dietary basis with LD_{50} values of 1432 mg a.i./kg bw and greater than 902 mg a.i./kg bw/day, respectively. *cis*-Jasmone is relatively non-toxic to the rat on an acute oral basis with an LD_{50} of 4300 mg/kg bw.

A risk assessment for bees was not required because *cis*-jasmone was found to be relatively non-toxic to bees at doses much higher than those to which bees would be exposed. In addition, this naturally occurring substance derived from jasmine flowers is expected to undergo rapid microbial degradation in soil. It is unlikely that *cis*-jasmone would translocate into pollen and nectar at levels that would exceed its natural background following the contact of treated seeds with soil. The risk quotients (RQs) for birds and mammals resulting from acute oral exposure to *cis*-jasmone through consumption of treated seeds did not exceed the level of concern at the screening level (RQ $\leq$0.0029). Screening level estimated dietary exposure (EDE) and RQ calculations for birds and mammals are presented in Appendix I, Table 5.

No toxicity data were available for freshwater algae and vascular plants. The PMRA agrees with the applicant's rationale that jasmonates such as *cis*-jasmone are naturally present in both terrestrial and aquatic vascular plants and algae and the environmental exposure through use of Trunemco as seed treatment is not expected to exceed the natural background levels of *cis*-jasmone in both terrestrial and aquatic habitats.

4.2.2 Risks to aquatic organisms

A summary of toxicity data are presented in Appendix I, Table 4.

cis-Jasmone was slightly toxic to rainbow trout (*Oncorhynchus mykiss*) and water flea (*Daphnia magna*) on an acute basis with 96-h LC_{50} values of 35.8 mg a.i./L and 48-h EC_{50} of 70.8 mg a.i./L, respectively.

The risk quotients for freshwater invertebrates (*D. magna*) and fish (*O. mykiss*) from acute exposure to *cis*-jasmone did not exceed the level of concern at the screening level (RQ = 7.4×10^{-7} and 7.3×10^{-6}, respectively). Thus, the use of *cis*-jasmone is not expected to pose a risk to freshwater invertebrates and fish.

Using a surrogate endpoint from the acute study with the rainbow trout, along with EECs for *cis*-jasmone in a 15-cm deep body of water, the risk quotient for amphibians resulting from acute exposure to *cis*-jasmone did not exceed the level of concern at the screening level (RQ =3.9×10^{-5}). The use of *cis*-jasmone is, therefore not expected to pose a risk to amphibians. Risk quotients are summarized in Appendix I, Table 6.

Overall conclusion about potential risks to non-target organisms

Based on the proposed use as seed treatment, it is unlikely that aquatic and terrestrial organisms would be exposed to significant amounts of *cis*-jasmone that would exceed its natural background in the environment. Therefore, environmental risk is acceptable for the use of Trunemco, containing Jasmone Technical Concentrate, when used in accordance with label directions. No mitigation measures are required.

4.3 Environmental incident reports

cis-Jasmone is a new active ingredient pending registration for use in Canada, and as of 7 December 2021, no environment incident reports had been submitted to the PMRA.

A query was also conducted for environment incidents involving the active *Bacillus amyloliquefaciens* and the related strains, *Bacillus licheniformis* and *Bacillus subtilis.* As of 7 December 2021, no environment incidents involving *B. amyloliquefaciens* and related strains were submitted to the PMRA.

5.0 Value

Both *Bacillus amyloliquefaciens* strain MBI 600 and *cis*-Jasmone are new active ingredients for nematode management in Canada. There are a limited number of conventional and non-conventional products registered in Canada for suppression of soybean cyst nematode in soybean and/or root-knot nematode in corn. The availability of Trunemco will provide Canadian growers with a new nematicide for use on soybean and corn to manage soybean cyst nematode in soybean or root-knot nematode in corn.

Value information was submitted as 15 field studies in which the efficacy of Trunemco against soybean cyst nematode or root-knot nematode was evaluated. Data assessing the number of soybean cyst nematodes, number of cysts caused by soybean cyst nematode on soybean roots, corn root gall rating and number of corn plants infected by root-knot nematodes, collectively demonstrated that Trunemco can be expected to consistently suppress soybean cyst nematode in soybean and root-knot nematode in corn. The Trunemco treatment also demonstrated a consistent yield benefit in both soybean and corn. As no phytotoxicity or crop injury was reported in any of the submitted studies conducted at application rates equal to or greater than rates proposed for registration, application of Trunemco is not expected to result in adverse effects to the crops.

The supported uses are summarized in Appendix I, Table 7.

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, Jasmone Technical Concentrate and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that Jasmone Technical Concentrate and its transformation products do not meet all of the TSMP Track 1 criteria.

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

For pest control product policy considerations relating to the microbial active ingredient, refer to PRD2009-17, *Bacillus subtilis strain MBI 600 and Integral Liquid Biological Fungicide*.

6.2 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.*[6] The list is used as described in the PMRA Science Policy Note SPN2020-01[7] and is based on existing policies and regulations, including the *Toxic Substance Management Policy*[2] and *Formulants Policy,*[8] 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*). The PMRA has reached the following conclusions:

- Jasmone Technical Concentrate does not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.
- The end-use product, Trunemco, contains the allergen, soy, which is on the *List of Pest Control Product Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions*.

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 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 Jasmone Technical Concentrate and Trunemco, containing the technical grade active ingredient *cis*-jasmone, to be used as a seed treatment in soybean, field corn, popcorn and sweet corn.

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.

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[6] 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*.

[7] 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 New Pest Control Products Act.*

[8] DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

List of abbreviations

°C	degrees Celsius
^{14}C	Carbon-14
♀	female
♂	male
a.i.	active ingredient
atm	Atmosphere
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BCFBAF	Windows based program model that estimates the fish bioconcentration factors
bw	body weight
bwg	body weight gain
CFU	colony-forming units
C.I.	confidence interval
cm	Centimeter(s)
d	Day(s)
DACO	Data code
DIR	(Regulatory) Directive
DMS	Differential mobility spectrometry
EC_{50}	Effective concentration 50%
EDE	Estimated dietary exposure
EEC	Estimated environmental concentration
EIIS	Ecological Incident Information System
ERR	extractable radioactive residues
fc	food consumption
FIR	Food ingestion rate
g	gram
GD	gestation day
HDPE	High density polyethylene
hr	hour
hrs	hours
kg	kilogram
K_{oc}	Adsorption quotient normalized to organic carbon
KOCWIN	Windows based program model that estimates the K_{oc} for soil and sediment
L	litre
LC	Liquid Chromatography
LC_{50}	Lethal concentration 50%
LD_{50}	Lethal dose 50%
LOAEL	lowest observed adverse effect level
LOC	Level of concern
LOD	level of detection
LOQ	level of quantification
m^3	Cubic metre(s)
mg	Milligram(s)
MMAD	mass median aerodynamic diameter

MAS	maximum average score
mg	milligram
MIS	maximum irritation score
mL	millilitre
MOE	margin of exposure
MPCA	Microbial Pest Control Agent
MRL	maximum residue limit
MS	mass spectrometry
MS/MS	tandem mass spectrometry
OECD	Organization for Economic Co-operation and Development
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no observed adverse effect level
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
RRR	residual radioactive residues
RQ	Risk quotient
SPN	Science Policy Note
TRR	total radioactive residues
TSH	thyroid stimulating hormone
TSMP	Toxic Substances Management Policy
UF	Uncertainty factor
µg	micrograms
USEPA	United Stated Environmental Protection Agency

Appendix I Tables and figures

Table 1 Toxicity profile of *cis*-Jasmone (99.9%)

(Effects are known or assumed to occur in both sexes unless otherwise noted.)

Study Type/Animal/PMRA#	**Study results**
Acute toxicity studies	
Acute oral toxicity (Up and Down study) Rat, Sprague-Dawley (♀) PMRA# 2989290	LD_{50} of 3129 mg/kg (95% C.I. of 1750–5000 mg/kg) On day of dosing animals dosed at 1750 mg/kg, exhibited signs of decreased activity, piloerection or head bobbing while animals dosed at 5000 mg/kg exhibited extreme decreases in activity, piloerection and leg spasms. Animals dosed at 5000 mg/kg were deceased by Day 1. Low toxicity
Acute dermal toxicity Rat, Sprague-Dawley PMRA# 2989291	LD_{50} > 5050 mg/kg bw (combined) Low toxicity
Acute inhalation toxicity (Nose-only exposure) Rat, Sprague-Dawley PMRA# 2989292	LC_{50} (combined) > 2.24 mg/L MMAD = 3.3 at 1 h and 2.7 at 2 h Signs of piloerection and decreased activity resolved by Day 2 Low toxicity
Eye irritation Rabbit, New Zealand PMRA# 2989293	MAS = 2.22/110 (at 24, 48 and 72 hrs) MIS = 12.67/110 (1 hr) Signs of irritation at 72 hours. Minimally irritating
Skin Irritation Rabbit, New Zealand (♂) PMRA# 2561759	MAS = 0/8 (at 24, 48 and 72 hrs) MIS = 1/8 (1 hr) All signs of irritation resolved by 24 hours. Minimally irritating
Dermal sensitization (modified Buehler)	Negative

Guinea pigs, Hartley PMRA# 2989295	Not a dermal sensitizer
Short-term toxicity studies	
90-Day dermal Rat, Sprague-Dawley PMRA# 3261267	LOAEL (systemic) = 1000 mg/kg/day (♀) 1000 mg/kg/day: ↑ red blood cell, activated partial thromboplastin time and potassium; ↓ absolute lymphocyte, white blood cell, aspartate amino-transferase, sorbitol dehydrogenase and bilirubin (♀) NOAEL (systemic) = 250 mg/kg/day (♀) NOAEL (systemic) > 1000 mg/kg/day (♂) LOAEL (dermal) = 85 mg/kg/day (♂/♀) ≥ 85 mg/kg/day: increase in incidence and severity epidermal hyperplasia and hyperkeratosis and desquamation (clinical signs) (♂/♀) NOAEL (dermal) not established (♂/♀)
Developmental/Reproductive toxicity studies	
Prenatal Developmental Toxicity Rat, Sprague-Dawley PMRA# 3257834	Maternal NOAEL = 85 mg/kg bw/day ≥ 350 mg/kg bw/day: slight ataxia 850 mg/kg bw/day: ↓ bwg at GD 5-8, 14-17 and overall (GD 3-20), ↓ fc at GD 5-8, 14-17, ↑ in TSH Developmental NOAEL = 350 mg/kg bw/day 850 mg/kg bw/day:↓ fetal bw (♂/♀), increased in skeletal variations No evidence of sensitivity of the young
Genotoxicity studies	
Bacterial Reverse Mutation Assay S. typhimurium (TA98, TA100, TA102, TA1535, TA1537) PMRA# 3257836	Negative ± metabolic activation
Sister Chromatid Exchange (SCE) Assay	Enhanced SCE in the presence of a genotoxicant, not genotoxic alone (Non-guideline study)

Chinese hamster ovary K-1 (CHO K-1) cells treated with X-rays or UV PMRA# 3033708	

Table 2 Toxicity Profile of BAS 798 00 F (0.897 % *cis*-jasmone, 6.6×10^9 CFU/mL *Bacillus amyloliquefaciens* MBI 600)

(Effects are known or assumed to occur in both sexes unless otherwise noted.)

Study Type/Animal/PMRA #	Study results
Acute Oral Toxicity (Limit Test) Rat, Sprague-Dawley PMRA # 2989362	LD_{50} > 5000 mg/kg bw Low toxicity
Acute Dermal Toxicity Rat, Sprague-Dawley PMRA # 2989363	LD_{50} > 5000 mg/kg bw (combined) Signs of very slight erythema Days 1–2 (♂ and ♀) and desquamation Days 3–5 (♂). Irritation resolved by Day 2 (♀) and Day 6 (♂). Low toxicity
Acute Inhalation Toxicity (Nose-only exposure) Rat, Wistar PMRA # 2989364	LC_{50} (combined) > 5.51 mg/L MMAD = 2.40 No mortality. Irregular respiration within 2 hours after removal of the exposure tube. Respiration normal for all animals by Day 2. Animals lost weight initially but recovered by Day 3. Low toxicity
Eye Irritation Rabbit, New Zealand PMRA # 2989365	MAS = 0.44/110 (at 24, 48 and 72 hrs) MIS = 7.32/110 (1 hr) All signs of irritation resolved by 48 hours. Minimally irritating

Study Type/Animal/PMRA #	Study results
Skin Irritation Rabbit, New Zealand PMRA # 2989366	MAS = 1.45/8 (at 24, 48 and 72 hrs) MIS = 2.33/8 (immediately after application) Signs of irritation until 72 hours but resolved by Day 7. Slightly irritating
Dermal Sensitization (Buehler Method) Guinea pigs, Hartley PMRA# 2989367	No signs of irritation 24 or 48 hours after challenge. Trunemco contains a MPCA and is considered a potential sensitizer.

Table 3 Fate and behaviour in the environment

Property	Value[1]	Comment
BCF	102–180 (BCFBAF, EpiSuite 4.1)	Low potential for bioconcentration.
logK_{oc}	2.47 (KOCWIN v2.00)	Low potential for adsorption to particles present in soil and sediment
Volatilization half-life	2.3 hr (model river); 21 days (model lake)	Not expected to be subject to undergo long range transport in the atmosphere.
Atmospheric hydroxyl photodegradation half-life	2.4 hours	
Atmospheric reaction with ozone half-life	0.5 hours	
Atmospheric reaction with nitrate half-life	0.8 hours	

[1]EpiSuite estimates from the United States National Library of Science - TOXNET HSDB.

Table 4 Toxicity to non-target species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Bees					
Honey bees (*Apis mellifera* L.)	48 h – Acute Contact	BAS 576 00 S[b]	LD_{50}>100 µg a.i./bee	Relatively non-toxic	2989304
Honey bees (*Apis mellifera* L.)	48 h – Acute Oral	BAS 576 00 S	LD_{50}>100 µg a.i./bee		2989305

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Birds					
Bobwhite quail (*Colinus virginianus*)	14 d – Acute oral	BAS 576 00 S	LD_{50}: 1432 mg a.i./kg bw	Slightly toxic	2989308
Bobwhite quail (*Colinus virginianus*)	5 d – Acute dietary	BAS 576 00 S	LD_{50} > 902 mg a.i./kg bw/day	Slightly toxic	2989309
Mammals					
Wistar rat	14 d – Acute oral	*cis*-Jasmone	LD_{50}: 4300 mg/kg bw	Relatively non-toxic	Scognamiglio et al. 2012
Freshwater species					
Daphnia magna	48 h – Acute	BAS 576 00 S	EC_{50}: 70.8 mg a.i./L	Slighty toxic	2989306
Rainbow trout (*Oncorhynchus mykiss)*	96 h – Acute	BAS 576 00 S	LC_{50}: 35.8 mg a.i./L		2989307

[a] USEPA classification, where applicable

[b] BAS 576 00 S contains 94.67% *cis*-jasmone and 6.26% *trans*-jasmone

Table 5 Screening level risk assessment of *cis*-jasmone for birds and mammals

	Study endpoint (mg a.i./kg bw/day / UF)	EDE[1] (mg a.i./kg bw/day)	RQ
Small bird (0.02 kg)			
Acute	143.20	0.419	0.0029
Medium bird (0.10 kg)			
Acute	143.20	0.329	0.0023
Large bird (1.00 kg)			
Acute	143.20	0.096	0.0006
Small mammals (0.015 kg)			
Acute	430.00	0.239	0.0005
Medium mammals (0.035 kg)			
Acute	430.00	0.206	0.0004
Large mammals (1.00 kg)			
Acute	430.00	0.113	0.0002

[1]EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/bw) × EEC, where: FIR: Food Ingestion Rate. For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used:

Passerine Equation (body weight <or = 200 g): FIR (g dry weight/day) = 0.398(bw in g)$^{0.850}$. All birds Equation (body weight >200 g): FIR (g dry weight/day) = 0.648 (bw in g) 0.651.
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235(bw in g)$^{0.822}$
bw: Generic Body Weight
EEC: Concentration of pesticide on food item. At the screening level, relevant food items representing the most conservative EEC for each feeding guild are used.

Table 6 Screening level risk assessment of *cis*-jasmone for aquatic organisms

Organism	Exposure	Endpoint value	EEC*	RQ	LOC exceeded
Daphnia magna	Acute	$EC_{50}/2$ = 35.4 mg a.i./L	0.000026 mg a.i./L	7.4×10^{-7}	No
Rainbow trout (*Oncorhynchus mykiss)*	Acute	$LC_{50}/10$ = 3.58 mg a.i./L	0.000026 mg a.i./L	7.3×10^{-6}	No
Amphibians	Acute	$LC_{50}/10$ = 3.58 mg a.i./L	0.000139 mg a.i./L	3.9×10^{-5}	No

*estimated environmental concentrations are calculated assuming a maximum seeding application rates of 209 mg a.i./ha to water bodies of 80 cm depth (fish) and 15 cm depth (amphibian).

Table 7 List of supported uses

Supported use claims for Trunemco
Crop: Soybean **Pest:** soybean cyst nematode (*Heterodera glycines*) **Claim:** Suppression **Rate:** 20 mL/100 kg seed **Application instructions:** Apply Trunemco through suitable commercial seed treating equipment. Read and follow all label guidelines (including precautions, limitations, rates and directions for use) for all mix partners.
Crop: Corn (field, pop, sweet, seed) **Pest:** Root-knot nematode (*Meloidogyne incognita*) **Claim:** Suppression **Rate:** 20 mL/100 kg seed **Application instructions:** Apply Trunemco through suitable commercial seed treating equipment. Read and follow all label guidelines (including precautions, limitations, rates and directions for use) for all mix partners.

References

A. List of studies/Information submitted by registrant

1.0 Chemistry

PMRA No.	Reference
2989287	2019, Selected technical grade active ingredient chemistry information - Jasmone Technical Concentrate, DACO: 2.1,2.14.4,2.14.8,2.2,2.3,2.3.1,2.4,2.5,2.6, 2.7,2.8,2.9 CBI.
2989288	2017, Analytical characterization of 5 representative batches of cis- Jasmone Technical Material with determination of [CBI Removed], DACO: 2.13.4 CBI.
2989289	2017, Determination of physical and chemical characteristics of [CBI Removed], DACO: 2.14,2.14.1,2.14.11,2.14.12,2.14.2,2.14.3,2.14.5,2.14.6, 2.14.7,2.14.9, 2.16.
2990495	2019, Jasmone Technical Concentrate manufacturing summary 2.11.1, DACO: 2.11.1 CBI.
2990497	2019, Jasmone Technical Concentrate detailed process description 2.11.3, DACO: 2.11.3 CBI.
2990498	2019, Jasmone Technical Concentrate discussion of formation of impurities, DACO: 2.11.4 CBI.
2990501	2019, Jasmone Technical Concentrate 5 batch and methodology report, DACO: 2.13.3 CBI
2990504	2019, Jasmone Technical Concentrate metal stability, DACO: 2.14.13 CBI.
2990505	2019, Jasmone Technical Concentrate stability study, DACO: 2.14.14 CBI.
3006266	2019, Jasmone Technical Concentrate_PMRA_2.13.2, DACO: 2.13.2 CBI.
3098823	2020, Manufacturing summary, DACO: 2.11.1 CBI
3098825	2020, Detailed production process description, DACO: 2.11.3 CBI.
3098826	2020, Batch Data, DACO: 2.13.3 CBI
2989353	2017, [CBI Removed] - Product identity, composition and analysis, DACO: 3.1,3.2.1,3.2.2,3.2.3,3.3.1,3.4.1.
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2.0 Human and animal health

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3.0 Environment

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4.0 Value

PMRA No.	Reference
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B. Additional information considered

i) Published information

1.0 Human and animal health

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2.0 Environment

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