Proposed Re-evaluation Decision PRVD2020-08

Pyrethrins and associated end-use products

Consultation Document

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Proposed re-evaluation decision

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

Pyrethrins are insecticides registered for use on a wide range of commercial and domestic sites including agricultural crops, greenhouses, livestock, companion animals, structural sites (indoor and outdoor), clothing, and stored grains. Pyrethrins products are available in various formulations, including dusts, solutions, emulsifiable concentrates, pastes, solids (coils) and pressurized products. A list of the registered products containing pyrethrins in Canada can be accessed through the PMRA's label transcription service.[1]

Many pyrethrins-containing products were registered prior to the development of modern standardized label language and do not contain comprehensive use directions. Considering the very large amount of pyrethrins products currently registered and the variability with regards to the description of their uses on the labels, pesticide registrants and various stakeholders were consulted on several occasions throughout the re-evaluation process to gather additional information and clarifications on the use pattern of pyrethrins products. Limited information was obtained from theses consultations.

Therefore, a scenario-based approach was used to identify the pyrethrins use pattern, rather than a label-based approach. High-level use pattern summary tables were prepared that outlined the different use scenarios for pyrethrins. These tables were shared with registrants and user groups for consultation on the use pattern that was assessed for the re-evaluation. Clarifications were received which were incorporated into the summary tables.

As a result of this consultation, it was determined that the food uses assessed in the dietary assessment would be limited to the crops and uses specifically identified on commercial class pyrethrins labels, namely greenhouse peppers, blueberry, grape, raspberry, herbs, spices, pears, pinto, snap and wax beans, tomato, stored grains, the direct treatment of livestock, and the use in food handling establishments. In addition, uses where no data was available, such as some indoor or outdoor application methods for residential applicators, were not included in the assessment. Summary tables of the uses at the basis of the risk assessment can be found in Appendix I.

This document presents the proposed regulatory decision for the re-evaluation of pyrethrins including the proposed risk mitigation measures to further protect human health and the environment, as well as the science evaluation on which the proposed decision was based. All products containing pyrethrins registered in Canada are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period, during which the

[1] The PMRA's pesticide label search database is available online in the Pesticides portion of Canada.ca. Pesticide labels can also be accessed on a mobile device using the pesticide label app available in the Pesticides portion of Canada.ca

public including the pesticide manufacturers and stakeholders may submit written comments and additional information to the PMRA. The final re-evaluation decision will be published taking into consideration the comments and information received.

Outcome of science evaluation

Pyrethrins are insecticides registered for use on a wide range of commercial and domestic sites including agricultural crops, greenhouses, livestock, companion animals, structural sites (indoor and outdoor), clothing, and stored grains.

With respect to human health, risks have been shown to be acceptable with mitigation measures required for most uses. However, dietary risks that have not been shown to be acceptable for the use on stored cereal grains. In addition, the risk from the use of domestic-class products used as indoor aerosol space sprays (including total release foggers) were not shown to be acceptable. Also, there were no data available to assess indoor or outdoor application using a mechanically-pressurized handheld sprayer for mists, aerosols, and fogs for residential handlers. Therefore, label directions are proposed to prohibit application using this type of equipment. Exposure from the remaining uses is unlikely to affect human health when used according to the proposed label directions, which include increased personal protective equipment (PPE) and a reduction in the amount handled per day for commercial-class products.

Pyrethrins enter the environment when used to control insects in a variety of agricultural crops, mosquito control uses and outdoor domestic uses. Based on available scientific information, potential risks to the environment have been shown to be acceptable when pyrethrins are used according to the proposed label directions.

Proposed regulatory decision for pyrethrins

Under the authority of the *Pest Control Products Act* and based on the evaluation of currently available scientific information, Health Canada is proposing that products containing pyrethrins are acceptable for continued registration in Canada, provided that the additional proposed risk mitigation measures are in place to further protect human health and the environment.

The use on stored cereal grains, where risks to human health are not shown to be acceptable is being proposed for cancellation. In addition, some indoor or outdoor application methods for residential applicators are proposed for cancellation due to the lack of data to assess their risks to human health. Furthermore, only the uses explicitly identified in the summary tables outlined in Appendix I were included in the risk assessment. All other uses are proposed for cancellation due to lack of data.

Registered pesticide product labels include specific directions for use. Directions include risk mitigation measures to protect human health and the environment that must be followed by law. As a result of the re-evaluation of pyrethrins, Health Canada is proposing further risk-reduction measures in addition to those already included on pyrethrins product labels. Additional revisions to the pyrethrins labels are proposed to update label statements to current policies and language.

Proposed risk mitigation measures

The updated label statements and mitigation measures required, as a result of the re-evaluation of pyrethrins, are summarized below. Refer to Appendix IX for details.

Human health

The following requirements are proposed to reduce potential exposure to workers using pyrethrins for agricultural uses:

- For application to agricultural crops using a mechanically-pressurized handgun, wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides during mixing, loading, application, clean-up and repair.
- For application using handheld airblast/mistblower, wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, socks, chemical-resistant footwear, and a respirator with a NIOSH-approved organic-vapour removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
- When entering treated indoor areas prior to venting after application using a fogger (handheld airblast/mistblower or automatic fogger), wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, chemical-resistant footwear, socks, chemical-resistant gloves, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
- Restriction on the amount handled per day when applying using a handheld airblast/mistblower.

The following requirements are proposed to reduce potential exposure to workers using pyrethrins for non-agricultural/structural uses:

- For application using a mechanically-pressurized handgun, wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides during mixing, loading, application, clean-up and repair.

- For application using mechanically-pressurized handheld sprayer for mists, aerosols, and fogs, wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, socks, chemical-resistant footwear, and a respirator with a NIOSH-approved organic-vapour removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
- For mixing, loading, and application using all dust application equipment, wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and a NIOSH approved N95 (minimum) filtering facepiece respirator (dust mask).
- When entering treated indoor areas prior to venting after applying using a fogger (total release fogger, mechanically-pressurized handheld sprayer for mists, aerosols, and fogs, and automatic fogger), wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, chemical-resistant footwear, socks, chemical-resistant gloves, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
- Restriction on the amount handled per day when applying using mechanically-pressurized handheld sprayer for mists, aerosols, and fogs in indoor scenarios.
- Restrictions on applications to golf course greens, fairways, and tees.
- Restriction on amount applied as a space spray in indoor residential sites.
- A label statement prohibiting use of domestic-class greenhouse end-use products in commercial greenhouses.
- A 2 hour re-entry interval is required after indoor residential space spray applications.
- Structural labels are to be updated as per the 2020 PMRA Guidance Document: *Structural Pest Control Products: Label Updates*.

The following mitigation measures are proposed to reduce exposure to residential handlers and residential postapplication exposure from domestic-class end-use products and from commercial class end-use products used in residential areas:

- For surface spray applications, label directions must be added or revised to:
    - Specify the pests controlled, the application rate and application type (for example, perimeter/spot, crack and crevice) that was shown to have acceptable risk in the human health risk assessment. The maximum assessed rates are presented in Appendix I.
    - The revised label directions must clearly define and establish the conditions of use for residential areas where children may be present versus non-residential areas where children are not expected to be present.
    - For products that are co-formulated with piperonyl butoxide, the acceptable application rates of piperonyl butoxide are presented in PRVD2020-09, Appendix IX, Sections 3.2 and 3.3. Co-formulated products must meet the mitigation requirements for both pyrethrins and piperonyl butoxide.
    - Prohibit application using mechanically-pressurized handheld equipment for mists, aerosols, and fogs.
    - Cancel the use of total release foggers including all domestic-class end-use products that have the “lock-valve” option.
    - Prohibit the use of aerosol indoor space sprays (not including metered release

devices).

- To protect food safety and the health of Canadians, the following measures are proposed:
    - Cancel the use of pyrethrins on stored grains.
    - Revoke the MRL of 3 ppm on raw cereal.
    - Establish a plant-back interval (PBI) of 12 months for all crops other than the ones for which pyrethrins is registered for use.

Environment

To protect the environment, the following risk mitigation measures are proposed:

- Standard environmental hazard statements to inform users of the potential toxic effects on bees, beneficial insects, birds and aquatic organisms.
- Prohibition or restriction of application during crop blooming period to protect pollinators.
- Label directions to minimise spray drift to reduce risk to beneficial insects living in habitats adjacent to the application site.
- Spray buffer zones for non-target aquatic habitats.
- Precautionary statements for sites with characteristics that may be conducive to run-off and when heavy rain is forecasted, in order to reduce the potential for run-off of pyrethrins to adjacent aquatic habitats.

Uses not included in the assessment and proposed for cancellation due to lack of data:

The following crops appear on domestic product labels but were not assessed:

- Apple tree, “fruit” tree (except pear)
- Outdoor and greenhouse applications to asparagus, beets, broccoli, Brussels sprout, cabbage, carrots, cauliflower, celery, cole crops, collards, cranberries, cucumbers, eggplant, kale, lettuce, mustard green, onion, pea, potato, radish, spinach, squash, turnip, “vegetables” (except crops specifically identified on commercial class pyrethrins labels), and vine products
- Outdoor application to peppers
- Greenhouse application to beans, herbs, tomatoes, “Greenhouse plantings” (except peppers)

Value

- Label claims related to killing lice on mattresses, bedding, furniture, and garments are proposed for cancellation.

The proposed label amendments are listed in Section 8.0 and Appendix IX.

International context

Pyrethrins are currently acceptable for use in other Organisation for Economic Co-operation and Development (OECD) member countries, including Australia, European Union, Japan, New Zealand and the United States. No decision by an OECD member country to prohibit all uses of pyrethrins for health or environmental reasons has been identified.

Next steps

The public, including the registrants and other stakeholders are encouraged to submit additional information that could be used to refine risk assessments during the 90-day public consultation period[2] upon publication of this proposed re-evaluation decision.

All comments received during the 90-day public consultation period will be taken into consideration in preparation of re-evaluation decision document,[3] which could result in revised risk mitigation measures. The re-evaluation decision document will include the final re-evaluation decision, the reasons for it and a summary of comments received on the proposed re-evaluation decision with Health Canada's responses.

Additional scientific information

Data are required to confirm that the application rates and use directions on current product labels are consistent with the rates used in the residential, bystander and occupational risk assessments. Many current labels do not have any rate specified, or the rate is presented in a form that cannot be used for risk assessment purposes (for example, spray for 5 seconds). Registrants are required to provide data that bridges the use directions and/or the rate on the label, to a rate that can be expressed in units of the amount of pyrethrins per surface area (for example, mg a.i./cm^2) for surface applications, or amount of pyrethrins per air volume (for example, mg a.i./m^3) for space spray or fogging applications. Data are required for the following products:

- All ready-to-use, commercial-class products for all formulations (for example, pressurized products, dusts) used for structural pest control, unless current label directions have very clear application directions and rates.
- All domestic-class products for all formulations (for example, pressurized products, dusts) for all uses, except pet/livestock and greenhouse uses.

In addition, for several uses where risks were shown to be acceptable at the highest rate assessed, limited label rate use/directions are available. Consequently, additional label information is required to support the risk assessment proposal, and further confirm what use directions/mitigation will be required in the final re-evaluation decision.

Registrants are encouraged to contact the PMRA for guidance on how to meet this data requirement. Only products supported by data demonstrating that the rates used in the risk

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

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

assessments are not exceeded will be considered for continued registration. A Notice, pursuant to paragraph 19(1)(a) of the *Pest Control Products Act*, will be issued to affected registrants in the near future and will include additional guidance on how to satisfy this data requirement.

In addition, although not required, for uses proposed for cancellation, Health Canada is asking stakeholders to provide information on how pyrethrins are typically used, including application rates, frequency of applications, minimum re-application interval, and maximum number of applications per year.

For uses where changes to the use pattern are proposed as mitigation measures, Health Canada is asking stakeholders to comment on the feasibility of the proposed changes, and the potential impact on the associated pest management practice.

Science evaluation

1.0 Introduction

All pyrethrins uses were supported by the registrants at the time of re-evaluation initiation. As of 13 November 2019, there are seven technical grade active ingredient products, 20 manufacturing products, 110 commercial class products (105 of these are co-formulated with piperonyl butoxide), and 326 domestic class products (206 of these are co-formulated with piperonyl butoxide). A list of the registered products containing pyrethrins in Canada can be accessed through the PMRA's label transcription service.[4]

2.0 Technical grade active Ingredient

2.1 Identity

Common name	Pyrethrins
Function	Insecticide
Chemical family	Natural pyrethrin
Chemical name	
1 International Union of Pure and Applied Chemistry (IUPAC)	**Pyrethrin I**: PIN: (1*S*)-2-methyl-4-oxo-3-[(2*Z*)-penta-2,4-dien-1-yl]cyclopent-2-en-1-yl (1*R*,3*R*)-2,2-dimethyl-3-(2-methylprop-1-en-1-yl)cyclopropane-1-carboxylate OR *(Z)-(S)*-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl (l*R*,*3R*)-2,2-dimethyl-3-(2-methylprop-1-enyl)- cyclopropanecarboxylate; OR *(Z)-(S)*-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl (l*R*)-*trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)-cyclopropanecarboxylate; OR *(Z)-(S)*-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl(+) *trans*-chrysanthemate **Cinerin I**: PIN: (1*S*)-3-[(2*Z*)-but-2-en-1-yl]-2-methyl-4-oxocyclopent-2-en-1-yl (1*R*,3*R*)-2,2-dimethyl-3-(2-methylprop-1-en-1-yl)cyclopropane-1-carboxylate OR *(Z)-(S)*-3-(but-2-enyl)-2-methyl-4-oxocyclopent-2-enyl(1*R,3*R)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate; OR *(Z)-(S)*-3-(but-2-enyl)-2-methyl-4-oxocyclopent-2-enyl(1*R*)-*trans*-

[4] The PMRA's pesticide label search database is available online in the Pesticides portion of Canada.ca. Pesticide labels can also be accessed on a mobile device using the pesticide label app available in the Pesticides portion of Canada.ca.

2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate;
OR
(*Z*)-(*S*)-3-(but-2-enyl)-2-methyl-4-oxocyclopenten-2-enyl (+)-*trans*-chrysanthemate

Jasmolin I:
PIN: (1*S*)-2-methyl-4-oxo-3-[(2*Z*)-pent-2-en-1-yl]cyclopent-2-en-1-yl (1*R*,3*R*)-2,2-dimethyl-3-(2-methylprop-1-en-1-yl)cyclopropane-1-carboxylate
OR
(Z)-(S)-2-methyl-4-oxo-3-(pent-2-enyl)cyclopent-2-enyl (1*R,*3*R*)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate;
OR
(Z)-(S)-2-methyl-4-oxo-3-(pent-2-enyl)cyclopent-2-enyl (1*R*)-*trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate;
OR
(*Z*)-(*S*)-2-methyl-4-oxo-3-(pent-2-enyl)cyclopent-2-enyl (+)-*trans*-chrysanthemate

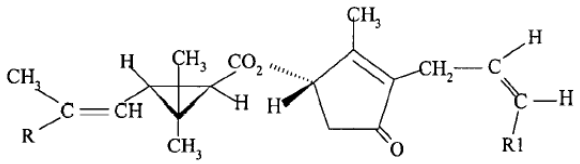
Pyrethrin II:
PIN: (1*S*)-2-methyl-4-oxo-3-[(2*Z*)-penta-2,4-dien-1-yl]cyclopent-2-en-1-yl (1*R*,3*R*)-3-[(1*E*)-3-methoxy-2-methyl-3-oxoprop-1-en-1-yl]-2,2-dimethylcyclopropane-1-carboxylate
OR
(*Z*)-*(S)*-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl *(E)*-(1*R*,3*R*)-3-(2-methoxycarbonylprop-1-enyl)-2,2-dimethdimethylcyclopropanecarboxylate;
OR
(*Z*)-*(S)*-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl *(E)*-(1*R*)-*trans*-3-(2-methoxycarbonylprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate;
OR
(*Z*)-(*S*)-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl pyrethrate

Cinerin II:
PIN: (1*S*)-3-[(2*Z*)-but-2-en-1-yl]-2-methyl-4-oxocyclopent-2-en-1-yl (1*R*,3*R*)-3-[(1*E*)-3-methoxy-2-methyl-3-oxoprop-1-en-1-yl]-2,2-dimethylcyclopropane-1-carboxylate
OR
(Z)-(S)-3-(but-2-enyl)-2-methyl-4-oxocyclopent-2-enyl *(E)*-(l*R*,3*R*)-3-(2-methoxycarbonylprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate;
OR
(Z)-(S)-3-(but-2-enyl)-2-methyl-4-oxocyclopent-2-enyl *(E)*-(l*R*)-*trans*-3-(2-methoxycarbonylprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate;
OR
(Z)-(S)-3-(but-2-enyl)-2-methyl-4-oxocyclopent-2-enyl pyrethrate

Jasmolin II:
PIN: (1*S*)-2-methyl-4-oxo-3-[(2*Z*)-pent-2-en-1-yl]cyclopent-2-en-1-yl (1*R*,3*R*)-3-[(1*E*)-3-methoxy-2-methyl-3-oxoprop-1-en-1-yl]-2,2-

		dimethylcyclopropane-1-carboxylate OR *(Z)-(S)*-2-methyl-4-oxo-3-(pent-2-enyl)cyclopent-2-enyl *(E)*-(1*R*,3*R*)-3-(2-methoxycarbonylprop-1-enyl)-2,2-dimethyl cyclopropanecarboxylate; OR *(Z)-(S)*-2-methyl-4-oxo-3-(pent-2-enyl)cyclopent-2-enyl *(E)*-(1*R*)-*trans*-3-(2-methoxycarbonylprop-1-enyl)-2,2-dimethyl cyclopropanecarboxylate; OR (*Z*)-(*S*)-2-methyl-4-oxo-3-(pent-2-enyl)cyclopent-2-enyl pyrethrate
2	**Chemical Abstracts Service (CAS)**	**Pyrethrins:** pyrethrins **Pyrethrin I:** (1*S*)-2-methyl-4-oxo-3-(2*Z*)-2,4-pentadien-1-yl-2-cyclopenten-1-yl (1*R*,3*R*)-2,2-dimethyl-3-(2-methyl-1-propen-1-yl)cyclopropanecarboxylate **Cinerin I:** (1*S*)-3-(2*Z*)-2-buten-1-yl-2-methyl-4-oxo-2-cyclopenten-1-yl (1*R*,3*R*)-2,2-dimethyl-3-(2-methyl-1-propen-1-yl)cyclopropanecarboxylate **Jasmolin I:** (1*S*)-2-methyl-4-oxo-3-(2*Z*)-2-penten-1-yl-2-cyclopenten-1-yl (1*R*,3*R*)-2,2-dimethyl-3-(2-methyl-1-propen-1-yl)cyclopropanecarboxylate **Pyrethrin II**: (1*S*)-2-methyl-4-oxo-3-(2*Z*)-2,4-pentadien-1-yl-2-cyclopenten-1-yl (1*R*,3*R*)-3-[(1*E*)-3-methoxy-2-methyl-3-oxo-1-propen-1-yl]-2,2-dimethylcyclopropanecarboxylate **Cinerin II**: (1*S*)-3-(2*Z*)-2-buten-1-yl-2-methyl-4-oxo-2-cyclopenten-1-yl (1*R*,3*R*)-3-[(1*E*)-3-methoxy-2-methyl-3-oxo-1-propen-1-yl]-2,2-dimethylcyclopropanecarboxylate **Jasmolin II**: (1*S*)-2-methyl-4-oxo-3-(2*Z*)-2-penten-1-yl-2-cyclopenten-1-yl (1*R*,3*R*)-3-[(1*E*)-3-methoxy-2-methyl-3-oxo-1-propen-1-yl]-2,2-dimethylcyclopropanecarboxylate
CAS registry number		**Pyrethrins**: 8003-34-7 **Pyrethrin I**: 121-21-1 **Cinerin I**: 25402-06-6 **Jasmolin I**: 4466-14-2 **Pyrethrin II**: 121-29-9 **Cinerin II**: 121-20-0 **Jasmolin II**: 1172-63-0
Molecular formula		Pyrethrin I: $C_{21}H_{28}O_3$ Cinerin I: $C_{20}H_{28}O_3$ Jasmolin I: $C_{21}H_{30}O_3$ Pyrethrin II: $C_{22}H_{28}O_5$ Cinerin II: $C_{21}H_{28}O_5$ Jasmolin II: $C_{22}H_{30}O_5$

Structural formula



R = -CH_3 (chrysanthemates) or -CO_2CH_3 (pyrethrates)
R1 = -CH=CH_2 (pyrethrin) or -CH_3 (cinerin) or -CH_2CH_3 (jasmolin)

Molecular weight

Pyrethrin I: 328.4
Cinerin I: 316.4
Jasmolin I: 330.4
Pyrethrin II: 372.4
Cinerin II: 360.4
Jasmolin II: 374.45

Registration number	**Purity of the Technical Grade Active Ingredient**
25872	20%
29678	51%
28940	54.00%
29956	20%
31787	49.20%
32044	51%
33566	52%

2.2 Physical and chemical properties

Property	**Result**
Vapour pressure at 25°C	pyrethrin I: 2.7 mPa pyrethrin II: 0.053 mPa cinerin I: 0.15 mPa* cinerin II: 0.061 mPa* jasmolin I: 0.064 mPa* jasmolin II: 0.025 mPa* *Estimated value from EPISUITE Estimated using EPISUITE with supporting explanations:

	Pyrethrins	**Pyrethrin I**	**Pyrethrin II**	**Cinerin I**
VP (mm Hg)*	1.41×10^{-6}	2.35×10^{-7}	9.15×10^{-8}	5.20×10^{-7}
VP (Pa)	3.13×10^{-5}	1.88×10^{-4}	1.21×10^{-5}	6.93×10^{-5}
	Cinerin II	**Jasmolin I**	**Jasmolin II**	
VP (mm Hg)*	2.08×10^{-7}	2.19×10^{-7}	8.45×10^{-8}	
VP (Pa)	2.77×10^{-5}	2.92×10^{-5}	1.12×10^{-5}	

Property	Result
Ultraviolet (UV) / visible spectrum	In acidic, neutral and basic isopropanol (since the technical grade active ingredient is not soluble in water or methanol), $\lambda_{max} \simeq 225$ nm. No significant absorption at $\lambda >$ 300 nm. Estimated λ_{max}: Cinerin II 236 nm Pyrethrin II 228 nm Jasmolin II 236 nm Cinerin I 228 nm Pyrethrin I 228 nm Jasmolin I 228 nm
Solubility in water	pyrethrin I: 0.2 ppm pyrethrin II: 9.0 ppm
n-Octanol/water partition coefficient	Technical grade active ingredient at 54 % The range of partition coefficient values for refined pyrethrum extract was found to be 13 000 to 790 000 ($\log_{10}P_{ow}$ = 4.1–5.9), at all three pHs tested (4, 7, 10).
Dissociation constant	Not applicable

2.3 Description of registered pyrethrins uses

Pyrethrins are registered for use on a wide range of commercial and domestic sites including agricultural crops, greenhouses, livestock, companion animals, structural sites (indoor and outdoor), clothing, and stored grains. Pyrethrins products are available in various formulations, including dusts, solutions, emulsifiable concentrates, pastes, solids (coils) and pressurized products. As of 13 November 2019, there are seven technical grade active ingredient products, 20 manufacturing products, 110 commercial class products (105 of these are co-formulated with piperonyl butoxide), and 326 domestic class products (206 of these are co-formulated with piperonyl butoxide). A list of the registered products containing pyrethrins in Canada can be accessed through PMRA's label transcription service.[5]

A summary of the registered uses of pyrethrins at the basis of the risk assessment is outlined in Appendix I. Only the uses explicitly identified in the summary tables were considered for continued registration. All other uses are proposed for cancellation.

3.0 Impact on human and animal health

3.1 Toxicology summary

Pyrethrum extract is a botanical insecticide derived from the dried flowers of the pyrethrum plant, *Chrysanthemum cinerariaefolium*. It is an enriched mixture containing six compounds: pyrethrin I, pyrethrin II, cinerin I, cinerin II, jasmolin I and jasmolin II, which are collectively known as the pyrethrins. Pyrethrum extract and the pyrethrins belong to a group of chemicals,

[5] The PMRA's pesticide label search database is available online in the Pesticides portion of Canada.ca. Pesticide labels can also be accessed on a mobile device using the pesticide label app available in the Pesticides portion of Canada.ca.

namely the pyrethroid/pyrethrins group. These chemicals induce neurotoxic effects in insects and mammals by binding to voltage-dependent sodium channels in neurons, thereby delaying the closing of sodium channels and causing the depolarization of neurons.

This affects action potentials and results in repetitive activity, similar to Type I synthetic pyrethroids. Pyrethrum extract and Type I pyrethroids typically induce the "T syndrome" which is characterized by aggressive sparring, sensitivity to external stimuli, and fine tremors progressing to whole body tremors and prostration.

A detailed review of the toxicology database for the pyrethrins was conducted. The human health risk assessment for pyrethrum extract and the pyrethrins is based primarily on studies conducted with pyrethrum extract. The pyrethrum extract used in toxicology studies was produced by the Pyrethrin Joint Venture industry task force, and is a blend of refined pyrethrum extract from the four main growing areas of the world. In addition to the core toxicity studies currently required for hazard assessment, a number of mechanistic studies were also submitted to support proposed modes of action. The majority of the studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practice. The human health risk assessment also considered information found in the published literature. Overall, the scientific quality of the toxicology database is acceptable, and the database is considered adequate to characterize the majority of the toxic effects that may result from exposure.

Pyrethrum extract and the pyrethrins are lipophilic compounds, thus bioavailability and toxicity are expected to be significantly enhanced with digestible oils, compared to aqueous vehicles. Available toxicokinetic data are derived from radiolabel studies in which rats were treated by gavage with a single- or repeated-dose of pyrethrin I (in corn oil). Slightly higher absorption was observed in females, compared to males, 24 hours or 7 days following a single low dose. With increasing oral dose, absorption was slower and less extensive, with a greater proportion of the administered dose eliminated in feces (more pronounced in males, compared to females). Peak levels in blood were noted slightly later in females (6–8 hours), compared to males (5–6 hours), while the elimination half-life in blood ranged from 5–7 hours in both sexes.

Pyrethrin 1 was rapidly and extensively distributed, metabolized and eliminated, with elevated concentrations of radioactivity detected in the fat of both sexes, and the ovary, irrespective of the dosing regimen. Concentrations of radioactivity in female adipose tissue were approximately 2-fold higher than levels in males, following single- or repeated-exposure to a low oral dose. Dose-related levels of radioactivity were detected in the brain of male and female rats, irrespective of the dosing regime in this investigation.

Pyrethrin 1 was extensively metabolized (and detoxified) in rats via hydrolysis of the ester bond and oxidative processes. In both sexes, chrysanthemum dicarboxylic acid (CDCA) was the major metabolite identified in urine and feces, with smaller amounts of other metabolites isolated from urine and feces. Oral administration of a single- or repeated-dose of pyrethrin I in rats resulted in rapid elimination in both sexes; fecal elimination increased with increasing oral dose and was more pronounced in males, compared to females. Negligible amounts of the administered dose were recovered in expired air. While toxicology studies on the metabolic products of pyrethrum extract were not available, the resulting degradates are not anticipated to have neurotoxic activity, and thus were not considered in the human health risk assessment.

Acute oral toxicity studies conducted in rats with pyrethrum extract (undiluted or in aqueous suspension) indicated slight to moderate oral toxicity. Clinical signs of toxicity following acute oral exposure were consistent with Type I pyrethroids and included tremors, hunched posture, ruffled fur and hyperactivity. Since acute oral toxicity studies conducted with oil vehicle were not available, there is some concern that the acute toxicity of pyrethrum extract may be underestimated in the toxicology database, based on evidence with some pyrethroids that the choice of vehicle can significantly enhance bioavailability and toxicity. In an acute dermal toxicity study conducted in rabbits, undiluted pyrethrum extract was of low toxicity and did not induce clinical signs at the limit dose. Undiluted pyrethrum extract produced minimal dermal or ocular irritation in rabbits, and was not a dermal sensitizer in the modified Buehler assay in guinea-pigs. While aerosolized pyrethrum extract (in acetone) produced low acute inhalation toxicity in rats following whole-body exposure, tremors were noted in females and lung edema and reddening of the lung and nasal turbinates were observed in both sexes following a single exposure. Based on clinical signs including lethality, female rats appear to be more sensitive to the acute oral and inhalation toxicity of pyrethrum extract, compared to male rats.

Repeat-dose oral toxicity studies were conducted in various species (mice, rats, dogs) with pyrethrum extract administered via the diet. Dose-related thyroid (rats) and liver (mice, rats, dogs) effects were noted throughout the database, with the most sensitive endpoints including thyroid follicular cell hyperplasia in males and bile duct hyperplasia in females in a 2-year rat dietary study. A subchronic oral toxicity study conducted with pyrethrum extract in rats was not available to investigate the progression of thyroid and liver lesions over time. Mortality (all species), decreased body weight (rats, dogs), clinical signs of neurotoxicity (all species), decreased testes weight (dogs) and haematological changes (rats, dogs) were also observed following oral exposure to higher doses of pyrethrum extract. No significant sex-related differences in non-neoplastic effects were noted, despite evidence of higher concentrations of pyrethrin I in female rat adipose and reproductive tissues in toxicokinetic studies, compared to males; however, the assessment of ovarian endpoints was generally limited in the toxicology database for pyrethrum extract.

Subchronic inhalation exposure of rats to aerosolized undiluted pyrethrum extract resulted in histopathology of the laryngeal mucosa in both sexes at all administered concentrations. At higher exposure levels, histopathological lesions of the nasal mucosa and lung were also observed in both sexes, in addition to mortality, decreased body weight, clinical signs of neurotoxicity (tremors, lacrimation, laboured breathing, matted coat) and increased kidney weight. Short-term dermal exposure in rabbits to pyrethrum extract (in corn oil) did not induce systemic toxicity, though signs of dermal irritation, including erythema and desquamation, were noted at the limit dose.

In acute oral neurotoxicity studies conducted via gavage, pyrethrum extract (in corn oil) induced neurological effects in rats consistent with Type I pyrethroids. Decreased motor activity in male and female rats was the most sensitive endpoint in the only adequate acute oral neurotoxicity study identified. At higher dose levels in this study, neuropathology was evident in male and female rats including degenerative changes in the sciatic, peroneal and tibial nerves. A subchronic oral neurotoxicity study conducted with pyrethrum extract was not available, nor was a developmental neurotoxicity (DNT) study conducted with pyrethrum extract. Studies from the published literature indicate that toxicodynamic and toxicokinetic factors, notably age-dependent

maturation of key metabolic processes, may lead to increased sensitivity of the young to pyrethroid toxicity. Young animals have incomplete maturation of the enzyme systems that detoxify pyrethroids, particularly the carboxylesterase and cytochrome P450 enzyme families. Consequently, pyrethroid concentrations in target tissues may be higher in young animals than in adults given the same dose level. In general, pyrethroid neurotoxicity is correlated with peak plasma concentrations of the compound, and gavage dosing results in greater internal doses compared to dietary administration. The pyrethroids are regarded as having a narrow window of time-to-peak effect. The design of a developmental neurotoxicity study does not consider time-to-peak effect and may, therefore, miss the window of peak toxicity for the pyrethroids, resulting in residual uncertainty regarding sensitivity of the young. Since the pyrethrins cause neurotoxicity via the same mode of action (MOA) involving voltage-gated sodium channels as the pyrethroids, the same uncertainty regarding sensitivity of the young was identified for the pyrethrins.

Recently, the results of work undertaken by the Council for Advancement of Pyrethroid Human Risk Assessment (CAPHRA) to address potential sensitivity of the young were submitted to the PMRA. The CAPHRA data may have implications on the entire class of pyrethroids/pyrethrins, and consequently these data are being addressed separately from assessments for individual pyrethroids. Until these data are evaluated, residual uncertainty regarding sensitivity of the young is reflected in the form of a database uncertainty factor.

In in vitro genotoxicity studies, pyrethrum extract (in acetone or DMSO) was negative for reverse mutation in the Ames test, forward mutation in mouse lymphoma cells, unscheduled DNA synthesis in rat hepatocytes, and sister chromatid exchange in Chinese hamster ovary cells. No in vivo genotoxicity studies conducted with pyrethrum extract were identified.

In a 2-year carcinogenicity bioassay, dietary administration of pyrethrum extract resulted in an increased incidence of hepatocellular adenomas in female rats and thyroid follicular cell adenomas in male and female rats. With respect to liver tumour induction in female rats, it was proposed that pyrethrum extract activated the constitutive androstane receptor (CAR), thereby inducing CYP2B enzymes and producing liver hypertrophy, increased cell proliferation and hepatocellular tumors. Short-term in vivo and in vitro evidence supported the key events of the proposed MOA: increased CYP450 mRNA and biomarker activity, increased liver DNA synthesis, and liver hypertrophy. Limitations of the proposed MOA were the lack of evidence of hepatocellular hypertrophy, proliferation or altered foci in the rat carcinogenicity assay, and the absence of in vivo genotoxicity data and apoptosis inhibition data. However, these limitations were not of sufficient concern to discredit the proposed threshold MOA for liver tumours in female rats. The CAR MOA was considered plausible, and notwithstanding some species- and sex-related differences, was consistent with that of phenobarbital. Given the lack of human cancer concerns with phenobarbital and the similarity of the pyrethrins to phenobarbital in terms of hepatic response, a threshold approach to cancer risk assessment is supported.

It was proposed that the thyroid tumors in male and female rats treated with pyrethrum extract in the 2-year dietary study were secondary to the dysregulation of the pituitary-thyroid axis via increased hepatic microsomal enzyme activity. The induction of hepatic enzyme activity increases hepatic clearance of thyroxine (T4) resulting in decreased T4 levels, increased thyroid stimulating hormone (TSH) levels, thyroid hypertrophy, increased thyroid cell proliferation,

thyroid follicular cell hyperplasia and ultimately the formation of thyroid tumours. The short-term in vivo evidence largely supported the key events of the proposed MOA, namely, hepatic microsomal enzyme induction, increased hepatic clearance of T4, a compensatory increase in serum TSH levels and thyroid cell proliferation. Limitations in the supporting evidence included the lack of mechanistic data in male rats at doses relevant to tumour induction and lack of in vivo genotoxicity data. The absence of an effect on serum T3 or T4 levels in female rats was also considered a limitation, though this was not critical as increased serum TSH levels were demonstrated in female rats in short-term dietary studies conducted with pyrethrum extract. It was concluded that the data limitations were insufficient to discredit the proposed threshold MOA for thyroid tumour development in rats treated with pyrethrum extract. Based upon the qualitative and quantitative differences in thyroid homeostasis between rats and humans, a threshold approach to cancer risk assessment is supported.

Statistically significant increased incidences of lung adenomas and combined lung adenomas/carcinomas were observed in high-dose female mice treated in the diet with pyrethrum extract for 78-weeks. There was no increase in the incidence of lung carcinomas in high-dose female mice in this study. It is noteworthy that treatment-related lung tumours were also reported in female mice treated orally with some synthetic pyrethroids. However, the evidence for a treatment-related increase in lung tumours in female mice treated with pyrethrum extract was considered to be equivocal, owing to the lack of increased lung tumour incidences in male mice or male or female rats, lack of statistical significance of tumour incidences in re-sectioned lungs of high-dose female mice, lack of pre-neoplastic histopathology in the lung of mice treated with pyrethrum extract in the 13-week dietary study and no evidence of genotoxicity in in vitro studies. It is noted that the evidence did not suggest progression of the lung tumours to malignancy. For these reasons, there was a low level of concern for these findings.

There was no evidence of adverse effects on mating performance or fertility in a dietary multi-generation reproductive toxicity study in rats conducted with pyrethrum extract, although this investigation lacked estrus cycle and sperm measurements. Effects in parental animals were similar to those in repeat-dose dietary toxicity studies (for example, decreased body weight) and were evident at dose levels which were similar to those producing toxicity in non-pregnant females. There was some evidence of sensitivity of the young in this study, namely a slight decrease in pup body weight during the lactation period, which occurred in the absence of maternal toxicity. The evidence supporting the sensitivity of the young in this study was considered marginal given that the slight pup body weight changes at the offspring Lowest-Observed-Adverse-Effect-Level (LOAEL) reflected the lower initial birth weight of these animals, occurred in only one sex (females) and in one of four matings, and non-adverse body weight effects in parental animals (decreased body weight gain) were also observed at the offspring LOAEL.

At the LOAELs in range-finding developmental toxicity studies conducted by gavage in rats and rabbits treated with pyrethrum extract, signs of toxicity in dams included decreased body weight gain, tremors, salivation and head arching backwards, with more severe clinical signs (convulsions, labored breathing) and death noted in dams at higher dose levels. In guideline studies, pyrethrum extract did not produce evidence of developmental toxicity, teratogenicity or sensitivity of the young in rats or rabbits following gavage administration in aqueous vehicle at maternally-toxic dose levels. At very high dose levels, which produced death in the does in the

rabbit range-finding study, serious effects including increased resorptions, increased post-implantation loss and decreased number of viable fetusus were noted. Developmental toxicity studies conducted with pyrethrum extract administered in oil vehicle were not identified; however, this was not a concern given the absence of developmental toxicity with the pyrethroids in general.

Available toxicology data regarding the potential for pyrethrum extract or the pyrethrins to induce endocrine toxicity are limited. However, there is evidence in oral studies conducted in rats that pyrethrum extract is associated with altered serum thyroid hormone levels (T3, T4, TSH) and histopathology in the thyroid.

The results of studies conducted on laboratory animals with pyrethrum extract or individual pyrethrin compounds are summarized in Appendix I, Table 1. The toxicology reference values used in the human health risk assessment are summarized in Appendix II, Table 2.

Pest Control Products Act hazard characterization

For assessing risks from potential residues in food or from products used in or around the home or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to take into account the completeness of the data with respect to the exposure of, and toxicity to, infants and children as well as potential pre- and post-natal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicology database for the assessment of risk to infants and children, the database contains the standard complement of required studies including oral developmental toxicity studies in rats and rabbits and a dietary multi-generation reproductive toxicity study in rats.

With respect to concerns relevant to the assessment of risk to infants and children, there was no evidence of increased sensitivity in rat or rabbit fetuses to in utero exposure in guideline oral developmental toxicity studies, while serious effects in the young (resorptions) were noted only at the highest tested dose level in a range-finding developmental toxicity study conducted in rabbits, in the presence of significant maternal toxicity. There was marginal evidence of sensitivity of the young in a dietary multi-generation reproductive toxicity study in rats, with effects in offspring (slight decrease in body weight) observed in the absence of maternal toxicity.

Young animals have incomplete maturation of enzyme systems that detoxify the pyrethroids (and pyrethrum extract/the pyrethrins) and thus may be more sensitive due to higher and prolonged brain concentrations, compared to adults (PMRA# 2007551). The database lacks additional information to fully characterize the potential for juvenile sensitivity to the neurotoxic effects of pyrethroids (and pyrethrum extract/the pyrethrins). Thus, an adequate assessment of sensitivity of the young is currently not available, and residual uncertainty remains concerning sensitivity of the young to potential neurotoxic effects of the pyrethroids and pyrethrum extract/the pyrethrins.

Recently, the results of work undertaken by the CAPHRA to address potential sensitivity of the young were submitted to the PMRA. Until these data are evaluated, this residual uncertainty is reflected in the form of a database uncertainty factor of threefold in the risk assessment. Since these concerns were addressed with a database uncertainty factor, the PCPA factor was reduced to onefold.

3.2 Dietary exposure and risk assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue may be ingested with the daily diet. Exposure to pyrethrins from potentially treated imported foods is also included in the assessment. Dietary exposure assessments are age-specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when exposure exceeds 100% of the reference dose. PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute, chronic and cancer risk assessment procedures.

Canadian maximum residue limits (MRLs) are established for pyrethrins for a range of plant and animal commodities. Residues in all other agricultural commodities, including those approved for treatment in Canada but without specific MRLs, are regulated under Subsection B.15.002 (1) of the Food and Drugs Regulations, which requires that residues do not exceed 0.1ppm. A complete list of MRLs specified in Canada can be found on the PMRA's MRL Database, an online query application that allows users to search for specified MRLs, regulated under the *Pest Control Products Act*, both for pesticides or food commodities.

The acute, chronic, and cancer dietary exposure and risk assessments for pyrethrins considered the registered food uses identified in the use information tables (Appendix I). Specifically, greenhouse peppers, blueberry, grape, raspberry, herbs, spices, pears, pinto, snap and wax beans, tomato, stored grains, the direct treatment of livestock, and the use in food handling establishments. Potential residues on foods imported to Canada were also considered. Sufficient information was available to assess the dietary exposure and risk to pyrethrins for the uses considered in the re-evaluation. Acute and chronic dietary exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™, Version 4.02, 05-10-c) program, which incorporates consumption data from the National Health and Nutrition Examination Survey, What We Eat in America (NHANES/ WWEIA) 2005-2010 available through the Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics (NCHS). Further details on the consumption data are available in Science Policy Note SPN 2014-01, *General Exposure Factor Inputs for Dietary, Occupational and Residential Exposure Assessments*.

For more information on dietary risk estimates and the residue chemistry information used in the dietary assessment, see Appendix III and IV.

3.2.1 Acute reference dose (ARfD)

To estimate acute dietary risk, the No-Observed-Adverse-Effect-Level (NOAEL) of 20 mg/kg bw in the acute oral neurotoxicity study conducted with pyrethrum extract was selected, based on fine tremors in adult female rats on the day of dosing at the LOAEL of 63 mg/kg bw. This endpoint was considered appropriate since the study was conducted by a relevant route and was of appropriate duration of exposure. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. Residual uncertainty regarding potential sensitivity of the young to neurotoxic effects was addressed through the application of a threefold database uncertainty factor. As discussed in the *Pest Control Products Act* Hazard Characterization Section, the PCPA factor was reduced to onefold. The resulting composite assessment factor (CAF) is 300.

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{20 \text{ mg/kg bw}}{300} = 0.07 \text{ mg/kg bw}$$

3.2.2 Acute dietary exposure and risk assessment

The acute dietary risk was calculated considering the highest ingestion of pyrethrins that would be likely on any one day, and using food and drinking water consumption and food and drinking water residue values. The expected intake of residues is compared to the acute reference dose (ARfD), which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, the acute dietary exposure is acceptable.

Acute dietary exposure and risk assessments for food and drinking water were conducted for all population subgroups. The acute analysis was conducted using available monitoring data and the highest average residue values taken from existing field trials. Where no monitoring data or field trials were available, MRLs and tolerances were used. Drinking water contribution to the exposure was accounted for by direct incorporation of the appropriate estimated environmental concentration (EEC), obtained from water modelling (see Section 3.3), into DEEM. Experimental and default processing factors were used for the estimation of residues in processed commodities.

The acute dietary (food and drinking water) exposure estimates, at the 95th percentile, ranged from 23% for adults older than 50 years of age to 96% of the ARfD for all infants, with cereal grains as the primary source of exposure. As noted below, cancellation of the use on stored cereal grains is a proposed mitigation measure to address chronic and cancer risks that are not acceptable. When the use on stored cereal grain is removed from the assessment, the acute dietary risks are less than or equal to 33% of the ARfD for all population subgroups and were shown to be acceptable.

3.2.3 Acceptable daily intake (ADI)

To estimate risk following repeated dietary exposure, the NOAEL of 4.4 mg/kg bw/day in the rat 2-year dietary toxicity study conducted with pyrethrum extract was selected, based on thyroid follicular cell hyperplasia in males and bile duct hyperplasia in females at the LOAELs of 43 and 56 mg/kg bw/day, respectively. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. Residual uncertainty regarding potential sensitivity of the young to neurotoxic effects was addressed through the application of a 3-fold database uncertainty factor. As discussed in the *Pest Control Products Act* Hazard Characterization section, the PCPA factor was reduced to onefold. The resulting CAF is 300.

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{4.4 \text{ mg/kg bw/day}}{300} = 0.01 \text{ mg/kg bw/day}$$

The acceptable daily intake (ADI) provides a margin of 640 to the NOAEL for offspring body weight effects (6.4 mg/kg bw/day) in the dietary multi-generation reproductive toxicity study in rats and a margin of greater than 83 000 to the dose associated with an equivocal increase in lung tumours in female mice in the 78-week dietary study (834 mg/kg bw/day). The ADI provides a margin of 17 300 to the dose associated with an increase in hepatocellular tumours in female rats in the 104-week dietary study (173 mg/kg bw/day), and a margin of 4300 to the dose associated with an increase in thyroid tumours in rats in the 104-week dietary study (43 mg/kg bw/day).

3.2.4 Chronic dietary exposure and risk assessment (cancer and non-cancer)

The chronic dietary risk from food and drinking water was calculated using the average consumption of different foods and drinking water and the average residue values on those foods and in drinking water. The estimated exposure was then compared to the ADI. When the estimated exposure is less than the ADI, the chronic dietary exposure is acceptable.

The chronic assessment was conducted using residue values taken from field trials and monitoring data. Where such data were not available, MRLs and tolerances were used to assess exposure levels. Refinements such as percent crop treated in food handling establishments and statistical import and domestic production were used in the risk assessment. Drinking water contribution to the exposure was accounted for by direct incorporation of the appropriate estimated environmental concentration (EEC), obtained from water modelling (see Section 3.3), into DEEM. Experimental and default processing factors were used for the estimation of residues in processed commodities.

The chronic dietary exposure estimates from food and drinking water ranged from 66% for adults older than 50 years of age to 252% of the ADI for all infants, with cereal grains as the primary source of exposure. In order to mitigate the chronic dietary risks, the use of pyrethrins on stored grains is proposed for cancellation. In addition, the established MRL of 3 ppm on raw cereals is proposed for revocation. When the use on stored cereal grain is removed from the assessment, the chronic dietary risks are less than or equal to 70% of the ADI for all population subgroups and were shown to be acceptable.

3.2.5 Cancer assessment

There is evidence of increased hepatocellular adenomas in female rats, and increased thyroid follicular cell adenomas in male and female rats following chronic oral exposure. A mode of action was proposed for each tumour type. The proposed MOAs were deemed plausible, despite some limitations, and the overall weight of evidence was sufficient to support a threshold-based mechanism for these tumours in rats. The ADI and selected toxicology reference values for residential and occupational risk assessment provide sufficient margins to the dose levels at which theses tumours were observed.

As previously discussed, the evidence for increased incidences of lung adenomas and combined adenomas/carcinomas in female mice was deemed equivocal; adequate margins to the dose levels at which these tumours were present are provided, based on the toxicology reference values selected for the non-cancer risk assessment.

3.2.6 Cancer dietary exposure and risk assessment

As noted in Section 3.2.5, the selected toxicology reference values are protective of the observed tumours. As the acute and chronic dietary risk assessments were acceptable when the proposed mitigation is considered, the dietary cancer risks are also acceptable.

3.3 Exposure from drinking water

Residues of pyrethrins in potential drinking water sources were estimated from modelling, as described below.

3.3.1 Concentrations in drinking water

Estimated environmental concentrations (EECs) were calculated using the Pesticide Water Calculator model (PWC, version 1.52). Modelling for surface water used a standard Level 1 scenario, a small reservoir adjacent to an agricultural field. EECs in groundwater were calculated by selecting the highest EEC from a set of standard scenarios representing different regions of Canada. The modelling used initial application dates between April and August. The surface water scenario was run for 50 years, while groundwater scenarios were run for 100 years

The daily and yearly ground water EEC of 1.7 and 0.19 µg a.i./L, respectively, was used in the acute and chronic exposure assessment.

Table 1 Level 1 estimated environmental concentrations of pyrethrins in potential sources of drinking water

Use pattern	Groundwater (µg a.i./L)		Surface water (µg a.i./L)	
	Daily[a]	Yearly[b]	Daily[c]	Yearly[d]
10 × 59 g a.i./ha at 7-day interval	0	0	1.7	0.19

a 90th percentile of daily average concentrations
b 90th percentile of 365-day moving average concentrations
c 90th percentile of the peak concentrations from each year
d 90th percentile of yearly average concentrations

3.3.2 Drinking water exposure and risk assessment

Drinking water exposure estimates were combined with food exposure estimates, with EEC point estimates incorporated directly in the dietary (food and drinking water) assessments. Please refer to Sections 3.2.2 and 3.2.4 for details.

3.4 Occupational and residential risk assessment

Occupational and residential risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

As noted in Section 3.2.5, the toxicology reference values selected for the occupational and residential risk assessment are protective of cancer risks, provided the target MOEs are met.

3.4.1 Toxicology reference values for residential and occupational exposure

3.4.1.1 Short-, itermediate-, and long-term dermal

For short-, intermediate- and long-term dermal occupational and residential risk assessment, a NOAEL of 1000 mg/kg bw/day was selected based on the absence of systemic effects at the limit dose in a 21-day dermal toxicity study in rabbits conducted with pyrethrum extract (in corn oil). The dermal study NOAEL is considered protective of the pup body weight effects in the rat dietary reproductive toxicity study, given the high degree of conservatism in the offspring NOAEL, as detailed previously. A target MOE of 300 was selected, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, in addition to a threefold database uncertainty factor to address the residual uncertainty related to potential sensitivity of the young to neurotoxic effects. This additional factor was also considered sufficient to address any potential concerns regarding durational effects for the long-term dermal assessment, given that a short-term study was selected. For residential scenarios, the PCPA factor was reduced to onefold as discussed in the *Pest Control Prodcuts Act* Hazard Characterization Section. The selection of this study and target MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed women.

3.4.1.2 Short-term inhalation

For short-term inhalation occupational and residential risk assessment, the 13-week (whole-body) inhalation toxicity study in rats was selected in which a LOAEL of 2.6 mg/kg bw/day (0.01 mg/L) for pyrethrum extract aerosol was derived based on laryngeal histopathology in male and female rats at the lowest administered concentration. A target MOE of 300 was selected, including uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, in addition to a threefold database uncertainty factor to address residual uncertainty related to potential sensitivity of the young to neurotoxic effects and lack of a NOAEL in the

inhalation study. A separate threefold uncertainty factor for lack of a NOAEL in the critical study was considered overly conservative, given that the endpoint was derived from a 13-week inhalation study (typically considered an intermediate-term duration exposure), and that lesion development and progression are generally duration-dependent for portal of entry effects. For residential scenarios, the PCPA factor was reduced to onefold as discussed in the *Pest Control Prodcuts Act* Hazard Characterization Section. The selection of this study and target MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed women.

3.4.1.3 Intermediate- and long-term inhalation

For intermediate- and long-term inhalation occupational and residential risk assessment, the 13-week (whole-body) inhalation toxicity study in rats was selected in which a LOAEL of 2.6 mg/kg bw/day (0.01 mg/L) for pyrethrum extract aerosol was derived based on laryngeal histopathology in male and female rats at the lowest administered concentration. A target MOE of 1000 was selected, including uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, a threefold database uncertainty factor to address the residual uncertainty related to potential sensitivity of the young to neurotoxic effects and lack of a NOAEL, and a threefold uncertainty factor for potential increased toxicity with increased duration of exposure for portal of entry effects. For residential scenarios, the PCPA factor was reduced to 1-fold as discussed in the *Pest Control Prodcuts Act* Hazard Characterization Section. The selection of this study and target MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed women.

3.4.1.4 Non-dietary incidental oral ingestion

For the assessment of short- and intermediate-term non-dietary incidental oral ingestion in children, the offspring NOAEL of 6.4 mg/kg bw/day in the dietary reproductive toxicity study in rats was selected, based on decreased pup body weight during the lactation period at the LOAEL of 65 mg/kg bw/day. A target MOE of 300 was selected, which includes 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a threefold database uncertainty factor to address the residual uncertainty related to potential sensitivity of the young to neurotoxic effects. The PCPA factor was reduced to onefold, as discussed in the *Pest Control Prodcuts Act* Hazard Characterization Section.

For the assessment of long-term non-dietary incidental oral ingestion in children, the NOAEL of 4.4 mg/kg bw/day in the rat 2-year dietary toxicity study with pyrethrum extract was selected, based on thyroid follicular cell hyperplasia in males and bile duct hyperplasia in females at the LOAEL of 43 and 56 mg/kg bw/day, respectively. This NOAEL is considered critical for risk assessment purposes since it is the lowest NOAEL in oral repeat-dose toxicity studies and is protective of toxicological effects in the young.

A target MOE of 300 was selected which includes standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, in addition to a threefold database uncertainty factor to address the residual uncertainty related to potential sensitivity of the young to neurotoxic effects. The PCPA factor was reduced to onefold as discussed in the *Pest Control Prodcuts Act* Hazard Characterization Section.

3.4.1.5 Dermal absorption

A dermal absorption value is not required since the toxicology point of departure was derived from a dermal toxicity study.

3.4.2 Non-occupational exposure and risk assessments (cancer and non-cancer)

Non-occupational (residential) risk assessment involves estimating risks to the general population, including adults, youth, and children, during or after pesticide application.

The United States Environmental Protection Agency (USEPA) has generated standard default assumptions for developing residential exposure assessments for both applicator and postapplication exposures when chemical- and/or site-specific field data are limited. The assumptions and algorithms may be used in the absence of, or as a supplement to, chemical- and/or site-specific data, and generally result in high-end estimates of exposure. These assumptions and algorithms relevant to the pyrethrins re-evaluation are outlined in the USEPA Standard Operating Procedures (SOP) for Residential Pesticide Exposure Assessments (2012) in the following sections:

- Section 3: Lawns and Turf
- Section 4: Gardens and Trees
- Section 5: Outdoor Fogging/Misting Systems
- Section 7: Indoor Environments
- Section 8: Treated Pets

3.4.2.1 Residential applicator exposure

A residential applicator is an individual (≥16 years old) who applies a domestic-class product in and around the home or directly to animals. Residential applicators are assumed to be wearing shorts, short-sleeve shirts, shoes, and socks during application. The residential applicator has the potential for short-term exposure (1–30 days) when applying products containing pyrethrins.

Based on the use pattern assessed, the major scenarios identified were:

- Applying liquid formulations using a hose-end sprayer, manually-pressurized handwand, backpack, and sprinkler can to lawns, turf, gardens, and trees
- Applying aerosol formulations to lawns, turf, gardens, and trees (includes nest spray), indoor environments (includes bed bugs), and pets/livestock
- Applying ready to use (RTU) formulations using a trigger-spray bottle and hose-end sprayer to lawns, turf, gardens, and trees (includes nest sprays)

- Applying RTU formulations using a trigger-spray bottle to indoor environments (includes bed bugs)
- Applying dust formulations using a bulb duster, plunger duster, shaker can, hand crank duster, and electric/power duster to gardens, trees, and indoor environments (includes bed bugs)
- Applying aerosol formulations as an outdoor aerosol space spray
- Applying solid (coil) formulations to outdoor areas
- Applying liquid formulations using a manually-pressurized handwand and backpack to indoor environments
- Applying liquid formulations as a mechanically-pressurized handheld sprayer for mists, aerosols, and fogs to indoor and outdoor areas
- Applying liquid formulations using a cloth/wipe-on to livestock
- Applying aerosol formulations using a cloth/wipe-on to livestock
- Applying RTU formulations of shampoo, trigger-spray bottle, and ear drops to pets
- Applying RTU formulations using a trigger-spray bottle or paste to livestock
- Loading aerosol products into an automatic dispenser (metered release sprays)
- Applying aerosol products as a total release fogger

Calculated MOEs for residential handlers exceeded target MOEs for both dermal and inhalation exposures, and therefore risks are not of concern. There are no data available to assess indoor or outdoor application using a mechanically-pressurized handheld sprayer for mists, aerosols, and fogs for residential applicators. Label directions are proposed to prohibit application using this type of equipment.

The results of the risk assessment are summarized in Appendix IV, Table 1.

3.4.2.2 Residential postapplication exposure and risk assessments (cancer and non-cancer)

Residential postapplication exposure occurs when an individual is exposed through dermal, inhalation, and/or incidental oral (non-dietary ingestion) routes as a result of being in a residential environment or by contacting a treated animal that has been previously treated with a pesticide. For pyrethrins, the area or animal could have been treated by a residential applicator using a domestic-class product or by a commercial applicator hired to treat the residential area or animal.

While exposure may occur for people of all ages, adults (>16 years old), youth (11<16 years old), and children (6<11 years old, 3<6 years old, and 1 <2 years old) have been chosen as the index lifestages to assess, based on behavioral characteristics and the quality of the available data. For many scenarios it is assumed that younger children (in other words, 1 <2 years old) would have higher exposure in these areas when playing or engaging in the types of activities associated with this lifestage (for example, crawling or mouthing) than would older children (in other words, >6 years old). For these scenarios, children 2 to <11 years were not assessed separately because their exposure is expected to be lower.

Due to seasonality of most pests listed on the label, most postapplication exposure is expected to be short- to intermediate-term in duration. The following scenarios were assessed for short- to

intermediate-term postapplication exposure for residential uses of products containing pyrethrins:

- Adults, youth (11<16 years), and children (1<2 years) dermal exposure resulting from activities on lawns and turf.
- Children (1<2 years) incidental oral exposure from treated lawns and turf.
- Adults and children (6<11 years) dermal exposure resulting from activities in gardens, trees, and indoor plants.
- Adults and children (1<2 years) dermal exposure resulting from mosquito abatement applications.
- Adults and children (1<2 years) dermal and inhalation exposure resulting from outdoor aerosol space sprays and burning coils.
- Adults and children (3<6 years old) dermal and inhalation exposure resulting from animal barn misting systems.
- Children (3<6 years old) incidental oral exposure from animal barn misting systems.
- Children (1<2 years) incidental oral exposure from outdoor aerosol space sprays.
- Adults and children (1<2 years) dermal and inhalation exposure resulting from activities indoors after indoor surface and space sprays (including total release foggers).
- Children (1<2 years old) incidental oral exposure resulting from indoor surface and space sprays (including total release foggers).
- Adults and children (1<2 years old) dermal exposure resulting from exposure to treated pets.
- Children (1<2 years old) incidental oral exposure from treated pets.

For treatment of bed bugs, there may be the potential for long-term exposure (>180 days). The following scenarios were assessed for long-term postapplication exposure for residential use of products containing pyrethrins for bed bugs.

- Adult and children (1<2 years old) dermal and inhalation exposure in indoor environments.
- Incidental oral (hand-to-mouth) exposure to children (1<2 years old) in indoor environments.

It was assumed that individuals would contact previously treated surfaces and pets on the same day the pesticide is applied.

Postapplication dermal exposure and risk assessment:

Postapplication dermal exposure can result from pesticide residue transfer to the skin of individuals who contact previously treated surfaces on lawns, gardens, trees, pets, and indoors, and during activities such as recreation, gardening, or housework.

For all indoor, outdoor, and pet postapplication scenarios, the dermal MOEs exceeded the target MOE, and therefore risks were found to be acceptable for all lifestages. The results of the risk assessment are summarized in Appendix V, Tables 2 and 3.

Postapplication inhalation exposure and risk assessment:

Inhalation is not considered to be a significant route of exposure for people entering treated areas following lawn, turf, garden, and tree applications due to the combination of the low vapour pressure of pyrethrins and the expected dilution in outdoor air. Postapplication inhalation exposure is expected to be low from exposure to treated pets due to the combination of a low vapour pressure and the small amounts of pesticide applied. Therefore, for these scenarios, a quantitative postapplication inhalation exposure assessment was not required.

Inhalation exposure during ground mosquito abatement application, as well as to outdoor aerosol space spray (OASS) and coil applications is expected to be short-term in duration. The inhalation MOEs for these scenarios exceeded the target MOE, and therefore risks were found to be acceptable for all lifestages.

For inhalation exposure in indoor environments, estimates of exposure are specified in the 2012 USEPA Residential SOPs for both aerosol and vapours. Aerosols are a spray of fine particles, typically present after space spray applications, which tend to settle out of the air after a certain period of time. Vapours occur when the pesticide volatilizes from a surface after application and can occur from all types of pesticide application. Postapplication inhalation exposure to vapours was determined to be minimal based on the low vapour pressure of pyrethrins and a quantitative postapplication inhalation exposure assessment was not required.

Exposure to indoor aerosols is expected to be short-term in duration. Aerosol space sprays are not used for bed bug treatment and therefore, a long-term inhalation exposure assessment was not required. For the indoor aerosol space spray (including total release foggers) postapplication scenario using both maximum and minimum domestic space spray rates, the calculated inhalation MOEs were below the target MOE and risks were not shown to be acceptable. As other risk mitigation measures are not available, this use will be proposed for cancellation.

For the indoor space spray (including total release foggers) postapplication scenario using maximum commercial space spray rates (area treated by commercial applicator), the calculated inhalation MOEs were below the target MOE. To mitigate risk, label directions are proposed to restrict the application rate with an accompanying re-entry interval in this scenario. Using this mitigation, risks were determined to be acceptable for space spray applications by commercial applicators.

For automatic dispenser (metered release sprays), exposure is expected to be intermediate-term in duration. Target MOEs were not met when using the defaults from the USEPA Residential SOPs (2012). A chemical-specific study (Selim, 2008) was used to refine the risk assessment and using this study, MOEs were greater than the target MOE, and therefore risks were shown to be acceptable.

The results of the postapplication inhalation risk assessment are summarized in Appendix V, Tables 4 and 5.

Incidental oral exposure and risk assessment:

Incidental oral exposure occurs when pesticide residues are transferred to the hands of children playing on treated lawns, indoor surfaces or with treated pets, and are subsequently ingested as a result of hand-to-mouth (HtM) transfer. Residues can also be transferred to objects in treated areas (for example, a child's toy) and subsequently ingested as a result of object-to-mouth (OtM) transfer. Soil can also be ingested while playing on treated lawns as a result of normal mouthing activities. There is potential for short-term exposure for all scenarios except for automatic dispenser (metered release) application scenarios, where there is potential for intermediate-term exposure. Long-term exposure was also assessed for bed bug applications, as it is expected that treatment could occur for most of the year.

A postapplication incidental oral assessment for gardens, trees, and indoor plants is not required for young children (1<2 years). The extent to which young children engage in the types of activities associated with these areas (for example, gardening or contacting treated ornamental plants) or utilize these areas for prolonged periods of play is low; therefore, significant incidental oral exposure is not expected.

Incidental oral exposures from indoor hard surfaces or carpet applications are considered to be protective of mattress applications, as the use of a protection factor for sheets on a mattress and the replenishment interval for hand-to-mouth activity is assumed to be less while a child is sleeping than while they are awake. As such, incidental oral exposure from mattresses was not quantitatively assessed.

For incidental oral exposure, calculated MOEs exceeded the target MOE and therefore risks were shown to be acceptable. Short- and intermediate-term incidental oral exposure estimates are presented in Appendix V, Tables 6–8. Long-term incidental oral exposure estimates are presented in Appendix V, Tables 9 and 10.

3.4.3 Occupational exposure and risk assessments (cancer and non-cancer)

There is potential for exposure to pyrethrins in occupational scenarios to workers handling pyrethrins products during the application processes, to workers entering treated areas, and to workers contacting animals previously treated with pyrethrins.

3.4.3.1 Occupational applicator exposure and risk assessment

Workers applying pyrethrins have the potential for short-, intermediate-, and long-term durations of exposure. Based on typical use patterns, the major scenarios identified were:

- Mixing and loading of liquids
- Applying liquids by airblast
- Applying liquids by groundboom
- Applying liquids by automated fogger in greenhouses
- Mixing, loading, and applying liquids by mechanically pressurized handgun
- Mixing, loading, and applying liquids by manually pressurized handwand
- Mixing, loading, and applying liquids by backpack sprayer

- Applying liquids by handheld airblast/mistblower
- Applying liquids by truck-mounted sprayer (fogger)
- Applying liquids and pressurized products by cloth (spraying on cloth and wiping on animal; spraying on animal and wiping with cloth)
- Applying liquids by mechanically pressurized handheld sprayer for mists, aerosols, and fogs
- Applying liquids by trigger-pump sprayer
- Applying liquids by hose-end sprayer
- Applying liquids by metered release devices
- Applying pressurized products by aerosol
- Applying pressurized products by total release fogger
- Applying pressurized products using a machine that produces mist/fog
- Applying pressurized products by metered release devices
- Applying dusts using bulbous duster, plunger duster, hand-crank duster, electric/power duster, and shaker can
- Commercial applicator re-entering site to move/adjust total release fogger or automated fogger during application

The exposure estimates for mixer/loaders and applicators are based on different levels of personal protective equipment (PPE) and engineering controls:

> Baseline PPE - long pants, long-sleeved shirt and chemical-resistant gloves
>
> Maximum-Level PPE - chemical-resistant coveralls with a chemical-resistant hood over a long-sleeved shirt, long pants, socks and shoes, chemical-resistant gloves, and a respirator
>
> Dust Mask - a NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested
>
> Respirator - a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides

Dermal and inhalation exposures for occupational applicators were estimated using data from the Pesticide Handlers Exposure Database (PHED), the Agricultural Handler Exposure Task Force (AHETF), the Outdoor Residential Exposure Task Force (ORETF), USEPA Dust Unit Exposures (USEPA, 2018), Krolski (2014), Thouvenin (2015), and Testman (2015).

The PHED version 1.1 is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of personal protective equipment. The AHETF was formed in 2001 with the objective of providing more up-to-date generic exposure data to replace the data currently being used in the Pesticide Handlers Exposure Database Version 1.1 (PHED). ORETF data were used for the hose-end sprayer, low pressure nozzle gun sprayer (connected to truck), garden pump duster, and trigger-

pump sprayer scenarios. The shaker can scenario from the USEPA dust unit exposures was used to address exposure from shaker cans, electric power, and hand crank dusters.

A passive dosimetry study was submitted to the PMRA that monitored exposure of pest control operators (PCOs) applying liquid products indoors as a surface spray using a manually pressurized handwand (Krolski, 2014). This study was reviewed by the PMRA and calculated dermal and inhalation unit exposures were determined to be acceptable for assessing PCO applicator exposure when using this type of equipment.

Two worker exposure studies were submitted to the PMRA that monitored workers when applying pesticides using application equipment representative of handheld airblast/mistblowers (HH AB/MB). One study (Thouvenin, 2015) monitored dermal exposure, while the other study (Testman, 2015) monitored inhalation exposure. These studies were reviewed by the PMRA and the calculated dermal and inhalation unit exposures were determined to be acceptable for assessing applicator exposure when using this type of equipment.

Inhalation exposures were based on light inhalation rates (17 L/min) except for backpack and handheld airblast/mistblower applicator scenarios, which are based on moderate inhalation rates (27 L/min).

For the commercial agricultural and non-agriculture/structural scenarios, the calculated dermal and inhalation MOEs are greater than the target MOE. Therefore, risks were shown to be acceptable for all scenarios, provided the proposed mitigation measures are implemented.

The results of the risk assessment are summarized in Appendix V, Tables 11–14.

3.4.3.2 Occupational postapplication exposure and risk assessment (cancer and non-cancer)

Agricultural sites

The postapplication occupational risk assessment considered exposures to workers who enter treated sites to conduct agronomic activities involving foliar contact (for example, scouting). Based on the registered use pattern, there is potential for short- (<30 days) to intermediate-term (30<180 days) postapplication exposure to pyrethrins residues for workers.

Potential dermal exposure to postapplication workers was estimated using updated activity-specific transfer coefficients (TCs) from the Agricultural Re-entry Task Force (ARTF) to estimate postapplication exposure resulting from contact with treated foliage at various times after application. A TC is a factor that relates worker exposure to dislodgeable residues. TCs are specific to a given crop and activity combination, for example, hand harvesting apples or scouting late season corn, and reflect standard clothing worn by adult workers. Postapplication exposure activities include, but are not limited to, scouting and hand weeding.

Dislodgeable foliar residue (DFR) and turf transferrable residues (TTR) refer to the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant or turf.

There were no chemical specific dislodgeable foliar residue (DFR) or turf transferable residue (TTR) studies submitted to the PMRA for the re-evaluation of pyrethrins; therefore the following defaults were used:

- A default peak value of 25% of the application rate with a dissipation rate of 10% was used for DFR for outdoor scenarios
- A default peak value of 25% was used with a default daily dissipation rate of 0% was used for DFR for greenhouse pepper crops
- A default peak value of 1% of the application rate with a dissipation rate of 10% was used for TTR

Exposure would be predominantly dermal for workers performing postapplication activities in crops treated with a foliar spray. Based on the vapour pressure of pyrethrins, inhalation exposure is likely to be acceptable provided that the minimum 12 hour restricted-entry interval (REI) is followed.

For agricultural workers entering a treated site, REIs are calculated to determine the minimum length of time required before workers can enter after application to perform tasks involving hand labour. An REI is the duration of time that must elapse before residues decline to a point where risks are shown to be acceptable for postapplication worker activities (in the case of pyrethrins, performance of a specific activity that results in exposures above the target MOE of 300 is considered to be acceptable).

The calculated MOEs for postapplication exposure in agricultural sites are greater than the target MOE, and therefore were shown to be acceptable for all uses provided a 12 hour REI is followed. The results of the risk assessment are summarized in Appendix V, Tables 15.

Non-agricultural/structural sites

There is potential exposure to workers entering treated livestock housing, including poultry houses, commercial or residential sites.

Similar to agricultural scenarios, postapplication inhalation exposure is not expected to be of concern due to the low vapour pressure of pyrethrins, and assuming re-entry does not occur until residues have deposited or dried.

A quantitative dermal assessment for postapplication workers in non-agricultural/structural scenarios was not conducted. It was assumed that risks to postapplication workers in these scenarios would be similar to or less than residential postapplication risks, since time spent in residential areas is assumed to be longer than time spent working. No risks of concern were identified for residential postapplication scenarios for adults, provided the recommended mitigation measures are implemented. This assumption is unlikely to underestimate occupational postapplication exposure.

Animal applications (livestock and pets):

Similar to other scenarios, dermal exposure is the primary route of concern following applications to livestock and pets, provided that exposure would occur after residues have dried.

A quantitative postapplication risk assessment was not conducted for livestock uses as the level of postapplication interaction with the animals is expected to be minimal.

For veterinarians or workers handling treated pets, a separate quantitative assessment was not conducted. It was assumed that risks to postapplication workers would be similar to or less than the risks for residential postapplication risks, due to the longer exposure duration considered in the residential scenario. The residential assessment, which showed acceptable risks, is discussed in Section 3.4.2.

3.5 Aggregate risk assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from dietary (food and drinking water), residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation). A major consideration is the likelihood of co-occurrence of exposures and durations of exposures. Additionally, only exposures from routes that share common toxicology points of departure can be aggregated.

3.5.1 Toxicology reference values for aggregate risk assessment

For short- and intermediate-term oral and inhalation aggregate risk assessment in all populations, endpoints related to neurotoxicity were selected. It was not necessary to aggregate exposure via the dermal route owing to the absence of neurotoxic effects at the limit dose in a 21-day dermal toxicity study conducted in rabbits with pyrethrum extract (in corn oil). For the oral route, the NOAEL of 20 mg/kg bw in the acute oral neurotoxicity study conducted with pyrethrum extract (in corn oil) was selected, based on fine tremors in female rats at the LOAEL of 63 mg/kg bw. For the inhalation route, the point of departure of 8.1 mg/kg bw/day (0.03 mg/L) in the 13-week inhalation toxicity study in rats was selected, based on tremors in females at 27 mg/kg bw/day (0.1 mg/L). A target MOE of 300 was derived for the oral and inhalation aggregate risk assessments, which included uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, in addition to a onefold database uncertainty factor to address residual uncertainty related to potential sensitivity of the young to neurotoxic effects. As discussed in the *Pest Control Products Act* Hazard Characterization Section, the PCPA factor was reduced to onefold.

For the assessment of long-term oral aggregate exposure via the diet, drinking water and non-dietary incidental oral ingestion, the NOAEL of 4.4 mg/kg bw/day in the rat 2-year dietary toxicity study with pyrethrum extract was selected, based on thyroid follicular cell hyperplasia in males and bile duct hyperplasia in females at the LOAEL of 43 and 56 mg/kg bw/day, respectively. This NOAEL is considered critical for risk assessment purposes since it is the lowest NOAEL in oral repeat-dose toxicity studies, and is protective for toxicological effects in the young. A target MOE of 300 was selected, which includes standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, in addition to a

threefold database uncertainty factor for concerns related to sensitivity of the young. The PCPA factor was reduced to onefold as discussed in the *Pest Control Products Act* Hazard Characterization Section. It was not necessary to aggregate exposure via the inhalation route since this route is not relevant to the exposure scenario. Also, it was not necessary to aggregate exposure via the dermal route owing to the absence of systemic toxicity at the limit dose in the 21-day rabbit dermal toxicity study.

3.5.2 Aggregate risk assessment

For short- and intermediate-term aggregate risk, oral and inhalation routes of exposure are the most relevant as it was not necessary to aggregate exposure via the dermal route due the absence of a common toxicology endpoint via this route (see Section 3.5.1). However, for most residential scenarios, dermal exposure was the predominant route for adults, with both oral and dermal routes predominant for children. There were limited scenarios with co-occurrence of oral or inhalation exposures (for example, outdoor aerosol space sprays, mosquito abatement, and indoor environments). Aggregation with dietary exposure and residential incidental oral or inhalation exposures was conducted where appropriate.

All residential postapplication scenarios were considered to be short- or intermediate-term exposure with the exception of indoor environments, which is also considered long-term exposure for bed bug scenarios. Incidental oral exposure is expected in children that are primarily 1<2 years of age, except for the animal barn misting systems scenario, which considered incidental oral exposure in children 3<6 years of age. For the long-term aggregate scenario (bed bugs), the only lifestage considered was children 1<2 years of age and the only scenario aggregated was oral (incidental oral + chronic dietary). Long-term inhalation exposure to adults and children is not expected, and it was not necessary to aggregate exposure via the dermal route as there was no evidence of systemic toxicity via this route.

It was considered highly unlikely that a homeowner would be exposed to peak residues of pyrethrins from different residential scenarios (for example, lawns, gardens, indoors, and pets) on the same day. It was considered highly unlikely that a homeowner would apply (or be exposed to) pyrethrins from an OASS application on the same day as exposure to pyrethrins from a coil or an animal barn misting system. Each of those scenarios were aggregated with oral exposure separately.

The highest exposure (inhalation and/or incidental oral (hand-to-mouth or object-to-mouth)) from each scenario was used to assess aggregate exposure.

The results of the aggregate risk assessment are summarized in Appendix VI, Tables 1 and 2. All scenarios had MOEs which exceeded the target MOEs, and therefore risks were shown to be acceptable.

3.6 Cumulative risk assessment

The *Pest Control Products Act* requires that Health Canada consider the cumulative exposure of pest control products that have a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity was undertaken for pyrethrum extract and the pyrethrins. Pyrethrum extract and the pyrethrins belong to a group of chemicals classified as the pyrethroid/pyrethrins group that have a common mechanism of toxicity wherein they possess the ability to interact with voltage-gated sodium channels ultimately leading to neurotoxicity. Upon completion of the re-evaluation of the individual chemicals in the pyrethroid/pyrethrins group, cumulative risk will be assessed as a separate exercise, incorporating all relevant members of the common mechanism group(s).

4.0 Environmental assessment

4.1 Fate and behaviour in the environment

Pyrethrins are a mixture of substances consisting of pyrethrins I (pyrethrin I, cinerin I and jasmolin I) and pyrethrins II (pyrethrin II, cinerin II and jasmolin II). Pyrethrins are not soluble in water and not expected to volatilize and enter the atmosphere from water surfaces or moist soil. Available information suggest the fate characteristics of pyrethrin I can be used to characterize the fate of pyrethrins.

A summary of the data on environmental fate and behaviour of pyrethrins is presented in Appendix VII, Table 1.

Behaviour in soil

In aerobic soil, microbial degradation causes pyrethrins to break down rapidly, with a half-life of less than 5 days depending on the soil type, forming a number of minor transformation products. In field studies, pyrethrins are non-persistent in soil with a reported half-life of <1 day. No major transformation products were identified in soil studies, with chrysanthemic acid being formed in small amounts (<10% of the applied pyrethrins). On soil surfaces, sunlight causes rapid breakdown of pyrethrins (<13 hours).

Pyrethrins have a high binding affinity for soil. Adsorption/desorption studies, the criteria of Cohen et al. (1984) and the groundwater ubiquity score (GUS) all indicate that pyrethrins should be immobile in soil, regardless of soil type. Considering the non-persistent nature and adsorption to soil particles, pyrethrins are expected to have a low potential to leach to groundwater.

Behaviour in water

Pyrethrins are not persistent in aerobic water. Microbes break down pyrethrins in water bodies in <8 hours and breakdown occurs more rapidly in shallow water bodies from exposure to sunlight (half-life of <12 hours). In aerobic water systems, pyrethrins partition to aquatic sediments.

One major transformation product, chrysanthemic acid, is soluble in water and tends to stay in the water rather than partition to sediment. Some removal of pyrethrins is expected through partitioning to sediment. In anaerobic aquatic systems, pyrethrins are slightly to moderately persistent (half-life of 86 days).

Behaviour in air

Pyrethrins have vapour pressures ranging from 0.025 (jasmolin II) to 2.7 mPa (pyrethrin I) and overall are classified as having low to intermediate volatility. According to their Henry's law constant (1/H = 5.59E+02) pyrethrins are expected to be slightly volatile from water and moist surfaces. This conclusion is supported by laboratory data where limited volatilization of pyrethrin I from moist soil was observed.

Bioaccumulation

Log K_{ow} values (5.9 for pyrethrin I and 4.3 for pyrethrin II) indicate pyrethrins may have the potential to bioaccumulate, however a bioaccumulation study indicates pyrethrins are rapidly eliminated from fish tissue. As such, pyrethrins are not expected to bioaccumulate.

4.2 Environmental risk characterization

A summary of ecotoxicity data for pyrethrins is presented in Appendix VII, Table 2.

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 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. The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species.

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, 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.

The environmental risk assessment was conducted based on the maximum annual application rates for each application method. For greenhouse uses, terrestrial and aquatic environmental exposure is not expected outside of the greenhouse and therefore risks to pollinators and non-target arthropods are expected to be limited to those found inside the treated greenhouse.

4.2.1 Risks to terrestrial organisms

Results of the terrestrial risk assessment are presented in Appendix VII, Tables 3 and 4.

Toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can potentially be exposed. Toxicity information was available for honeybees, beneficial insects, earthworms, birds and terrestrial plants. For acute toxicity studies, an uncertainty factor of 1/10 the EC_{50} (LC_{50}) was applied to toxicity values for terrestrial invertebrates, birds and mammals when calculating risk quotients. Uncertainty factors were not applied to chronic NOEC endpoints. As there are currently over 400 products that contain pyrethrins, risks to non-target organisms were assessed according to application method.

Risks to terrestrial organisms from commercial groundboom and airblast applications

The screening level risk assessment for groundboom and airblast applications indicated acceptable risk to birds, mammals and terrestrial plants. Potential risks were identified at the screening level for earthworms, pollinators and non-target beneficial arthropods.

Although the screening level risk assessment identified risks to earthworms from pyrethrins, colonization from surrounding untreated areas is expected and effects at the population level are not expected. No further risk characterization was performed.

Risks to pollinators could not be further characterized as data on pollen and nectar residue levels and/or higher tier studies were not available. Pollinators are potentially at risk from groundboom or airblast application of pesticides when plants are in bloom and pollinators are visiting flowers. These risks can be mitigated with restrictions on application timing. Pollinator exposure to pyrethrins is expected to be higher for orchard crops (pear), berry crops and certain herbs. Low to moderate pollinator exposure to pyrethrins is expected for tomatoes, fruiting vegetable (beans), spices, certain herbs and grape.

Risks to non-target beneficial arthropods were further characterized using more realistic exposure estimates, which considered spray drift for off-field exposure and foliar interception of spray deposition for on-field exposure. The results of the refined risk assessment are presented in Appendix VI, Table 4. To refine the in-field exposure estimate, harmonized foliar deposition fractions, which are crop and growth phase-specific, were applied. Refined in-field EECs for foliar-dwellers = cumulative application rate × Fraction intercepted. To refine the off-field exposure estimate, a vegetation distribution factor of 0.10 was applied, since the drift values overestimate drift to the lower or interior portions of a three-dimensional habitat structure. Most

of the drift would be intercepted by the top or side portions of the habitat structure. Refined off-field EEC = off-field EEC × vegetation distribution factor of 0.10. Using these exposure refinements, risks from pyrethrins to non-target beneficial arthropods are considered acceptable for ground boom applications and early season airblast applications. Potential risks were identified on-field for late-season airblast applications (RQ = 3.44). Considering off-field risks from late season airblast applications are negligible, it can be expected that off-field arthropod populations will recolonize on-field treatment areas following application. Hazard statements are proposed for product labels.

Risks to terrestrial organisms from ULV/fogging applications

The screening level risk assessment, which conservatively assumes all of the applied pyrethrins from truck-mounted ULV/fogging applications are deposited to soil, water and plant surfaces, indicates potential risk to pollinators and beneficial arthropods. Deposition from the ULV/fogging spray cloud is expected to be less than 100%, as the objective of this application method is to have the spray cloud spread and disperse from the point of application. Risks are considered acceptable given in-field pollinators and non-target arthropods are normally subject to an overall reduction in insect numbers from agricultural practices, including, but not limited to, the application of pesticides. It is expected that off-field populations would act as a natural reservoir for immigration, emigration and reproduction of beneficial arthropod populations on-field. Hazard statements are proposed for product labels. ULV applications are typically made after sundown when pollinators are not active. In addition, product labels will direct users to the Health Canada's document, *Protecting Pollinators during Pesticide Spraying - Best Management Practices*, which provides comprehensive guidance on protecting pollinators.

Risk to terrestrial organisms from domestic uses

Registered domestic outdoor uses include ornamentals, lawns and groundcovers, with a maximum single application rate of 140 g a.i./ha. The maximum number of applications are not specified on registered labels, but a minimum application interval of 10 days is specified. As a result, for the screening level risk assessment, the maximum possible number of yearly applications was assumed to be 36. The calculated risk quotients indicate risks are acceptable for birds but potential risks were identified for small and medium wild mammals. Given the limited and localised outdoor areas of use for domestic applications and the conservatisms used in the risk assessment, risks are not expected. Label statements to inform users of the potential risk to small wild mammals are proposed.

4.2.2 Risks to aquatic organisms

Results of the aquatic risk assessment are presented in Appendix VII, Tables 3 and 4.

Toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of aquatic species that can be potentially exposed following application of pyrethrins. Toxicity information was available for freshwater and marine invertebrates, algae and fish. For acute toxicity studies, an uncertainty factor of 1/2 EC_{50} (LC_{50}) was applied for aquatic plants and invertebrates. An uncertainty factor of 1/10 the EC_{50} (LC_{50}) was applied for fish species. No uncertainty factors were applied to chronic NOEC endpoints. For groups where potential risks

were identified at the screening level, further characterization was done to determine risk resulting from spray drift and run-off separately. As there are currently over 400 products that contain pyrethrins, risks to non-target organisms were assessed according to application method.

Risks to aquatic organisms from commercial groundboom and airblast applications

The screening level risk assessment for aquatic organisms was based on the highest maximum cumulative application rate for groundboom and airblast applications (8 applications of 60 g a.i./ha with a minimum of 7-day intervals and a maximum aerobic aquatic biotransformation DT_{50} of 7.84 days for the total system). When calculating screening level risk to all aquatic organisms except amphibians, exposure estimates are calculated for an 80-cm water depth. For amphibians, exposure levels are calculated using a 15-cm water depth. Risks were found to be acceptable for freshwater plants and freshwater and marine algae. Potential risks of concern were identified for freshwater invertebrates, fish and amphibians, as well as marine fish and invertebrates.

Further characterization of risks was done looking at the percentage of spray drift expected from the different application methods (Appendix VII, Table 4). Risks to aquatic organisms from pyrethrins are acceptable for groundboom and airblast applications when mitigation, in the form of spray buffer zones, are employed (4–50m).

Further characterization for run-off was done by estimating EECs through water modelling. Model inputs are presented in Appendix VII, Table 5.

For the ecological risk assessment, run-off into a permanent water body is represented by a 10 hectare field adjacent to a one-hectare water body with a depth of 80 cm. The model is run for 50 years and calculates the amount of pesticide entering the water body through run-off, taking into consideration the degradation of the pesticide in water and sediment. Deposition of pesticide on the water body due to spray drift is not considered in the model. Depending on the type of endpoint being considered, predicted concentrations of pyrethrins in water used in the further characterization of risk to aquatic organisms included the peak run-off EEC (0.00036 mg a.i./L), the 24-hr EEC (0.00064 mg a.i./L) and the 21-d EEC (0.00014 mg a.i./L) (Appendix VI, Table 6).

A summary of the results of the refined risk assessment for run-off is presented in Appendix VII, Table 7. Risks were acceptable or slightly exceeded the level of concern for fresh water organisms. Risk quotients for marine organisms were <36. In the marine environment, concentrations are not expected to persist due to mixing and tides.

Water monitoring data from Canada (Appendix VIII) indicates pyrethrins were not detected in the limited number of samples analyzed.

Given the conservatisms in the risk assessment, risks to populations of aquatic organisms are not expected from the use of pyrethrins. Standard run-off label statements are proposed.

Risks to aquatic organisms from ULV/fogging applications

The screening level risk assessment conservatively assumes all of the applied pyrethrins from truck-mounted ULV/fogging applications are deposited directly onto a water surface. The highest cumulative application rate of 75.86 g a.i./ha (35 g a.i./ha, 26 applications per season, 7-day intervals, aerobic aquatic biotransformation DT_{50} of 7.84 days for the total system). When calculating screening level risk to all aquatic organisms except amphibians, exposure estimates are calculated for an 80-cm water depth. For amphibians, exposure levels are calculated using a 15-cm water depth. Risks were acceptable for freshwater aquatic plants and freshwater and marine algae. Potential risks were identified for freshwater and marine invertebrates and fish as well as amphibians.

Deposition from the ULV/fogging spray cloud is expected to be less than 100%, as the objective of this application method is to have the spray cloud spread and disperse from the point of application. The risk assessment conducted using EECs modelled for ground boom and airblast application methods are expected to be protective of ULV/fogging uses. Risks to aquatic organisms associated with ULV/fogging applications are considered acceptable.

Risks to aquatic organisms from domestic uses

Registered domestic uses on outdoor sites (ornamentals, lawns and groundcovers) have maximum single application rates of 140 g a.i./ha. The number of applications per year is not specified on registered labels, but a minimum application interval of 10 days is specified. As a result, the maximum number of yearly applications was assumed to be 36. At the screening level, risks from pyrethrins were acceptable for freshwater algae and diatoms, freshwater vascular plants, cyanobacteria and marine diatoms. Potential risks of concern were identified for freshwater invertebrates and fish, amphibians, marine fish, oysters and crustaceans.

Given the limited and localised outdoor areas of use for domestic applications of pyrethrins and the conservatisms used in the risk assessment, risks to aquatic organisms from domestic uses are considered acceptable. Label statements are proposed to inform users of the potential risk.

5.0 Value assessment

Pyrethrins are naturally-occurring contact insecticides derived from the flowers of Chrysanthemum. They are non-persistent and act on the nervous system of the insect. They are one of the few insecticides permitted for use in organic crop production, and based on their broad-spectrum of activity, are valued by organic growers.

Pyrethrins and pyrethroids are a component of a successful integrated pest management program to control domestic pests, such as bed bugs, cockroaches, fleas, and indoor ants. Since the majority of commercial products used to control these pests contain both piperonyl butoxide and pyrethrins or pyrethroids, retaining piperonyl butoxide will maintain effective pest control options for pest control operators. One exception is the label claim related to killing lice on mattresses, bedding, furniture, and garments. Lice die in the absence of a host; therefore, infestations on mattresses, bedding, furniture, and garments would cease on their own or in conjunction with cultural control strategies (for example, laundry for garments and vacuuming).

There is little to no value in treating various lice species when off the host; therefore, these claims are proposed for cancellation.

6.0 Pest control product policy considerations

6.1 Toxic substances mnagement 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, that is, 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, pyrethrins and their transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-031 and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that pyrethrins and their transformation products do not meet all o the TSMP Track 1 criteria.

The TSMP assessment is presented in Appendix VII, Table 8.

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 Notice of Intent NOI2005-01[7] and is based on existing policies and regulations, including the Toxic Substances Management Policy[8] and Formulants Policy,[9] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol).

The active ingredient pyrethrins do not contain any formulants of health or environmental concern identified in the *Canada Gazette*. However, the end-use products do contain aromatic petroleum distillates. Therefore, the labels for the relevant end-use products will include the statement: “This product contains aromatic petroleum distillates that are toxic to aquatic organisms.”

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6 SI/2005-114, last amended on June 25, 2008. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

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

8 DIR99-03, *The Pest Management Regulatory Agency’s Strategy for Implementing the Toxic Substances Management Policy*.

9 - DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

The PMRA has reached the conclusion that pyrethrins and associated end-use products do not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

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

7.0 Incident reports

7.1 Health incident reports

As of 14 November 2019, the PMRA had received 281 human incidents and 1200 domestic animal incidents involving pyrethrins. In most of these incidents, the reported pyrethrins product was co-formulated with piperonyl butoxide and/or other active ingredients (for example, synthetic pyrethroids, MGK-264, s-methoprene). Pyrethrins incidents most commonly involved products for use on companion animals (1122 reports) followed by products for use at residential sites (359 reports).

7.1.1 Incidents involving pyrethrins products for use on companion animals

There were 26 human incidents involving pyrethrins products for use on companion animals. People were exposed either when treating their pets or after coming in contact with a treated pet. Reported effects in people following exposure were mainly minor in severity and included signs such as tingling skin, skin or eye irritation, dizziness or headache. Given the low number of human incidents over a 12-year period, no specific human health concerns were identified.

All other incidents involving pyrethrins products for use on companion animals involved cats or dogs (1096 reports) mainly treated with animal spray or shampoo products for the control of fleas and ticks. In general, animal incidents involving pyrethrins sprays were reported more often when compared to incidents involving pyrethrins shampoos, and incidents involving cats were more frequently reported than those involving dogs.

In most Canadian animal incidents involving pyrethrins sprays or shampoos, there was no apparent misuse outlined in the incident report. The symptoms reported in pets following use of the product types were frequently minor in severity and involved signs such as lethargy, anorexia, vomiting, drooling or itchy skin. Incidents that were more serious in nature (classified as moderate) were reported in both cats and dogs. The signs reported in animals included neuromuscular effects such as tremor, ataxia, muscle twitching or convulsions. Life-threatening effects including death were reported primarily in cats (25 animals). The observed patterns indicate that cats appear to be sensitive to the effects of pyrethrins sprays or shampoos; however, the potential for life-threatening effects including death is considered low given the few serious incidents reported over a 12 year period. In addition, no consistent patterns were noted in the incident reports. The patterns reported in Canadian incidents were similar to that noted in the serious incidents involving pyrethrins sprays and/or shampoos that occurred in the United States.

Overall, the incident reports involving co-formulated pyrethrins spray or shampoo products for use on companion animals point to a concern of adverse effects in cats and dogs even when the

products are used according to label directions. It is therefore proposed that the labels of all pyrethrins spray and shampoo products be updated to inform the consumer of possible side effects that may be expected in their pets following the use of these products. The proposed recommendations are similar to those outlined in the 2019 PMRA Guidance Document, *Label Improvements for Spot-on Pesticides Used on Companion Animals*. In addition, the product labels should be amended to reflect the statements outlined in DIR2002-01, *Canadian Label Improvement for Pesticides used on Companion Animals*, in order to address the deficiencies and/or inconsistencies noted in the precautionary and use direction statements across the various registered products.

7.1.2 Incidents involving pyrethrins products for use at residential sites

Human incidents involving pyrethrins (257 reports) were mainly associated with domestic class products that were frequently formulated as pressurized sprays (includes foggers). The reported exposure scenarios in people include inhaling the product mist when applying the product in enclosed areas, entering treated areas, living/working in treated areas, coming in contact with product residues on treated surfaces or sleeping on treated beds.

The signs reported in people following exposure to a pyrethrins product were mainly minor in severity and included cough, nasal congestion, respiratory irritation, tingling mouth, irritated eye or nausea. There were 2 serious Canadian and 10 serious American incidents that were considered to be related to the reported pyrethrins product. In the two major Canadian incidents, the reported pyrethrins product was not used according to the label directions. Reported effects in the two individuals involved either respiratory irritation for a period of over six months or signs of pneumonia and collapsed lung. In the serious American incidents, people were exposed either when using pyrethrins products or living in treated areas. Reported effects in people included respiratory distress, seizures, muscle weakness, swollen mouth, burns, chest discomfort or irregular heartbeat. In one American incident involving death, a person with a pre-existing chronic respiratory condition experienced cardiac arrest after remaining in a home during treatment with pyrethrins pesticide fogger. In this incident, the product label directions requiring individuals to vacate the premises during treatment were not followed.

Incidents involving domestic animals (102 reports) were associated with various domestic class pyrethrins products (for example, indoor/outdoor sprays, foggers, carpet powders) that were used in and around the home according to the label directions. Animal types reported in incidents frequently involved dogs followed by cats. Exposure of animals to the pyrethrins product occurred either when licking a treated area or coming in contact with a treated area. The symptoms reported in animals were mainly minor or moderate in severity and included symptoms such as vomiting, anorexia, lethargy or ataxia. Serious animal incidents (classified as major or death) involving pyrethrins products used at residential sites mainly occurred in the United States. The incidents involved various animal types such as snakes, cats, dogs or fish and the symptoms included convulsions, ataxia, vomiting, anorexia, lethargy, diarrhea or death.

Overall, the review of human and domestic animal incidents involving co-formulated pyrethrins products for use at residential sites indicates a potential for incidental oral and/or dermal exposure of people and animals to pyrethrins products even when products are used according to

the label directions. The current label language on pyrethrins products that were most frequently reported in incidents was found to be somewhat vague and non-specific.

Label amendments as outlined in the Guidance Document (PMRA Guidance Document *Structural Pest Control Products: Label Updates*) are therefore proposed for all domestic class pyrethrins products for use at residential sites in order to minimize the likelihood of exposure of people and animals following product use.

7.2 Environmental incident reports

7.2.1 Canadian incident reports

As of 28 June 2019, 31 environment incidents involving pyrethrins products were submitted to the PMRA. The incidents were classified as either minor (30 reports) or moderate (1 report). The incidents involved effects on herbaceous plants (25 incidents), trees or shrubs (4 incidents), ladybugs (1 incident), and songbirds (1 incident).

Environment incidents with pyrethrins products co-formulated with piperonyl butoxide frequently occurred at residential sites. Scotts Ecosense Bug-B-Gon Ready to Use Insecticide (PCP Reg. No. 28379) was commonly reported in incidents (20 reports), with the product being applied to either lawns, various types of plants (tomato, beans, ornamentals, marijuana etc.) or fruit trees. Damage reported in plants included visible injury, leaf discoloration or plant mortality. One minor incident involved the death of 900 ladybugs that were exposed to a plant(s) some time after treatment with a pyrethrins product co-formulated with piperonyl butoxide. In addition to the above incidents, there was 1 minor incident involving barn swallows (song bird). In this incident, a pyrethrins product co-formulated with piperonyl butoxide was applied to horses in a barn. Sometime following application, the caller reported finding 3–4 dead barn swallows in a barn stall.

7.2.2 United States environmental incidents

The United States EIIS (Ecological Incident Information System) database was queried for environment incidents involving pyrethrins that occurred in the United States. As of October 2015, there were 22 incidents involving pyrethrins. Most pyrethrins incidents involved plants (25 reports). Most these incidents were assigned the certainty index of possible or higher (20 incidents). Other incidents involved aquatic organisms (2), plants (9) and terrestrial organisms (9). Aquatic organisms included fish, flounder, grass shrimp or fluke; plants included ornamentals, roses or sunflowers; and terrestrial organisms included honey-bees, bumble-bees, monarch butterflies or Canada goose. Exposure scenarios reported in incidents include direct treatment with a product containing piperonyl butoxide in agricultural or residential areas, product ingestion as well as drift/run-off from treated sites. Reported signs in plants following exposure was noted as plant damage and mortality. In terrestrial and aquatic organisms, mortality was noted following exposure.

In two incidents, fish mortality was reported in unknown fish species either following run-off from an intentional misuse of a pyrethrins product formulated as a dust or from exposure to a pyrethrins dip product that was applied to a dog.

Given the trends observed in the current and previous review of the environmental incident data, the following label statements are proposed for products containing pyrethrins and piperonyl butoxide in order to minimize the likelihood of plant damage or death.

- Do not wet plants to the point of run-off or drip.
- Before making widespread applications of this product, treat a limited number of plants and observe for plant damage over a 10-day period.

8.0 Conclusion of science evaluation

Health

Dietary risk

- To protect the general population the cancellation of the use of pyrethrins for stored grains is proposed. In addition, the MRL of 3 ppm on raw cereals is proposed for revocation.
- The enforcement residue definition for all commodities is currently expressed as:

  4-hydroxy-3-methyl-2-(2,4-pentadienyl)-2-cyclopenten-1-one 2,2-dimethyl-3-(2-methylpropenyl)cyclopropanecarboxylate and 4-hydroxy-3-methyl-2-(2,4-pentadienyl)-2-cyclopenten-1-one 1-methyl 3-carboxy-α,2,2-trimethylcyclopropaneacrylate ester

- It is proposed to revise the residue definition to:

  The sum of (1S)-2-methyl-4-oxo-3-(2Z)-2,4-pentadien-1-yl-2-cyclopenten-1-yl (1R,3R)-2,2-dimethyl-3-(2-methyl-1-propen-1-yl)cyclopropanecarboxylate and (1S)-2-methyl-4-oxo-3-(2Z)-2,4-pentadien-1-yl-2-cyclopenten-1-yl (1R,3R)-3-[(1E)-3-methoxy-2-methyl-3-oxo-1-propen-1-yl]-2,2-dimethylcyclopropanecarboxylate.

- A plant-back interval (PBI) of 12 months for all crops other than the ones for which pyrethrins is registered for use is proposed.

Occupational and residential exposure

Data are required to confirm that the application rates and use directions on current product labels are consistent with the rates used in the residential, bystander and occupational risk assessments.

In addition, although not required, the registrants and other stakeholders may submit information that may address uncertainties in the available information database of pyrethrins to support refinement of the risk assessment and, subsequently, change the proposed mitigation.

To protect residential applicators and those entering treated residential and commercial areas, the following measures are proposed:

Domestic-class products:

- Prohibit application using a mechanically-pressurized handheld sprayer for mists, aerosols, and fogs.
- Prohibit the use of total release foggers (cancel all domestic-class end-use products that have the "lock-valve" option).
- Prohibit the use of indoor aerosol space sprays (not including metered release devices).

Commercial-class products:

- Restrictions on applications to golf course greens, fairways, and tees.
- Restriction on amount applied as a space spray (not including metered release devices) in indoor residential sites.
- A 2 hour re-entry interval is required after indoor residential space spray (not including metered release devices) applications.

To protect commercial mixer/loader/applicators and those entering treated agricultural sites, the following measures are proposed:

Commercial-class agricultural products:

- For application to agricultural crops using a mechanically-pressurized handgun, wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides during mixing, loading, application, clean-up and repair.
- For application using handheld airblast/mistblower, wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, socks, chemical-resistant footwear, and a respirator with a NIOSH-approved organic-vapour removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
- When entering treated indoor areas prior to venting after application using a fogger (handheld airblast/mistblower or automatic fogger), wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, chemical-resistant footwear, socks, chemical-resistant gloves, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
- Restriction on the amount handled per day when applying using a handheld airblast/mistblower to 0.05 kg a.i. per person/day.
- A label statement requiring a 12 hour restricted-entry interval is proposed.

Commercial-class non-agricultural/structural products:

- For application using a mechanically-pressurized handgun, wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides during mixing, loading, application, clean-up and repair.
- For application using mechanically-pressurized handheld sprayer for mists, aerosols, and fogs, wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, socks, chemical-resistant footwear, and a respirator with a NIOSH-approved organic-vapour removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
- For mixing, loading, and application using dust formulations, wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and a NIOSH approved N95 (minimum) filtering facepiece respirator (dust mask).
- When entering treated indoor areas prior to venting after applying using a fogger (total release fogger, mechanically-pressurized handheld sprayer for mists, aerosols, and fogs, and automatic fogger), wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, chemical-resistant footwear, socks, chemical-resistant gloves, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
- Restriction on the amount handled per day when applying using mechanically-pressurized handheld sprayer for mists, aerosols, and fogs in indoor scenarios to 0.05 kg a.i. per person/day.

To protect bystanders from spray drift, a statement to promote best management practices to minimize human exposure from spray drift, or spray residues resulting from drift in non-target areas, is proposed.

Environment

To protect the environment, the following risk mitigation measures are proposed:

- Standard environmental hazard statements to inform users of the potential toxic effects on bees, beneficial insects, birds and aquatic organisms.

- Prohibition or restriction of application during crop blooming period to protect pollinators.

- Label directions to minimise spray drift to reduce risk to beneficial insects living in habitats adjacent to the application site.

- Spray buffer zones for non-target aquatic habitats.

- Precautionary statements for sites with characteristics that may be conducive to run-off and when heavy rain is forecasted, in order to reduce the potential for run-off of pyrethrins to adjacent aquatic habitats.

Value

- Pyrethrins control a broad spectrum of insect pests on a wide variety of sites, including commercial and domestic agricultural and structural sites.

- They are important to pest control operators and the general public for the treatment of cockroaches, fleas, indoor ants, and notably bed bugs, where they are an essential component of a successful integrated pest management program. Pyrethrins do not have value in treating various lice species when off the host.

Uses not included in the assessment and proposed for cancellation due to lack of data:

- The following crops appear on domestic product labels but were not assessed:
    - Apple tree, "fruit" tree (except pear)
    - Outdoor and greenhouse applications to asparagus, beets, broccoli, Brussels sprout, cabbage, carrots, cauliflower, celery, cole crops, collards, cranberries, cucumbers, eggplant, kale, lettuce, mustard green, onion, pea, potato, radish, spinach, squash, turnip, "vegetables" (except crops specifically identified on commercial class pyrethrins labels), and vine products
    - Outdoor application to peppers
    - Greenhouse application to beans, herbs, tomatoes, "Greenhouse plantings" (except peppers)

List of abbreviations

1-ABT	1-Aminobenzotriazole
ABMS	animal barn misting system
AC	air concentration
AD	administered dose
ADI	acceptable daily intake
a.i.	active ingredient
AHETF	Agricultural Handlers Exposure Task Force
AHPD	amount handled per day
ALT	alanine transaminase
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
AST	aspartate aminotransferase
ATPD	area treated per day
BFC-O-debenzylase	7-benzyloxy-4-trifluoromethylcoumarin-O-debenzylase
bw	body weight
bwg	body weight gain
C	control
C_o	initial concentration
CAF	composite assessment factor
CAPHRA	Council for Advancement of Pyrethroid Human Risk Assessment
CAR	constitutive androstane receptor
CC	crack and crevice
CCTM	candles, coils, torches, mats
CDC	Centers for Disease Control
CDCA	chrysanthemum dicarboxylic acid
cm	centimetre
cm^2/hr	centimetre squared per hour
CR	chemical resistant
CYP	cytochrome P450
DA	dermal absorption
DACO	data code
DEEM	Dietary Exposure Evaluation Model
DFR	dislodgeable foliar residue
DMSO	dimethyl sulfoxide
DNT	developmental neurotoxicity
DR	deposited residue
DU	dust
EC	emulsifiable concentrate
EEC	estimated environmental concentrations
ET	exposure time
Fc	food consumption
F_1	first filial generation
F_2	second filial generation
FOB	functional observational battery
g	gram(s)
GC-ECD	gas chromatography with electron capture detector

GLC-ECD	gas-liquid chromatography with electron capture detector
GD	gestation day
GJIC	Gap-Junction Intercellular Communication
ha	hectare
Hct	hematocrit
HED	Health Evaluation Directorate
Hgb	hemoglobin
HH AB/MB	handheld airblast/mistblower
HPLC-UV	high performance liquid chromatography with ultraviolet detector
hr	hour(s)
HtM	hand-to-mouth
IR	inhalation rate
iv	intravenous
kg	kilogram(s)
L	liter(s)
LC-MS/MS	liquid chromatography with mass spectrometry
LC_{50}	concentration estimated to be lethal to 50% of the test population
LD_{50}	dose estimated to be lethal to 50% of the test population
LOAEL	Lowest-Observed-Adverse-Effect-Level
m	meter(s)
m^2	meter squared
m^3	meter cubed
MAS	maximum average score
max	maximum
mg	milligram(s)
min	minute
MIS	mean irritation score
M/L/A	mixer/loader/applicator
MOA	mode of action
MOE	margin of exposure
MPHG	mechanically pressurized handgun
MPHW	manually pressurized handwand
MPHS	mechanically pressurized handheld sprayer for mists, aerosols, and fogs
MRL	maximum residue limits
MRM	multiresidue analytical methods
mRNA	messenger RNA
n/a	not available
NAFTA	North American Free Trade Agreement
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
NIOSH	National Institute for Occupational Safety and Health
NOAEL	No-Observed-Adverse-Effect-Level
OASS	outdoor aerosol space spray
ORETF	Outdoor Residential Exposure Task Force
OtM	object-to-mouth
PB	phenobarbital
PBI	plant-back interval
PBU	piperonyl butoxide

PCNA	proliferating cell nuclear antigen
PCO	pest control operator
PHED	Pesticide Handler Exposure Database
PHI	pre-harvest interval
PMRA	Pest Management Regulatory Agency
PND	post-natal day
PP	pressurized products
PPAR (α, γ)	peroxisome proliferator-activated receptors
PPE	personal protection equipment
ppm	parts per million
PWC	pesticide water calculator
PYR	pyrethrins
RBC	red blood cells
REI	restricted-entry interval
rel	relative
RfD	reference dose
rT3	reverse triiodothyronine
RTU	ready-to-use
RXRα	retinoid X receptor - α
SOP	standard operating procedure
SN	solution
TC	transfer co-efficient
TSH	thyroid stimulating hormone
T3	triiodothyronine
T4	thyroxine
TR	transferable residue
TTR	turf transferable residue
UDPGT	uridine diphosphate glucuronyltransferase
µg	microgram(s)
ULV	ultra low volume
USEPA	United States Environmental Protection Agency
WBC	white blood cell
wt	weight
♂	males
♀	females
↑	increased
↓	decreased

Appendix I Summary of the registered uses of pyrethrins at the basis of the risk assessment

Table 1.1 Summary of use information – commercial agriculture

Use-site category	Site/crop	Application equipment	Formulation	Max canadian label rate	Spray volume	No. apps/year	Min interval between apps (days)	REI (days)
5	Greenhouse Peppers	Ground (MPHG, Backpack, MPHW, HH AB/MB), Automated Fogger	SN	59 g a.i./ha (0.09 g a.i./L)	625 L/ha	10	7	0.5
13	Pastures [a]	Truck mounted fogger	SN, EC	3 g a.i./ha	n/a	25 (USEPA RED)	1	0.5
14	Blueberry and Raspberry	Ground (GB, Airblast, MPHG, Backpack, MPHW, HH AB/MB)	EC	60 g a.i./ha (0.2 g a.i./L)	300 – 1000 L/ha	8	7	0.5
14	Grape	Ground (Airblast, MPHG, Backpack, MPHW, HH AB/MB)	EC	60 g a.i./ha (0.2 g a.i./L)	300 – 1000 L/ha	8	7	0.5
14	Herbs and Spices (Crop Group 19)	Ground (GB, MPHG, Backpack, MPHW)	SN	59.52 g a.i./ha (0.09 g a.i./L)	625 L/ha	8	7	0.5
14	Pear Orchards	Ground (Airblast, HH AB/MB)	SN	59 g a.i./ha (0.15 g a.i./L)	400 – 1500 L/ha	10	7	0.5
14	Bean (Pinto, Snap, Wax), Field Tomato	Ground (GB, MPHG, Backpack, MPHW)	EC	60 g a.i./ha (0.4 g a.i./L)	135 – 140 L/ha	8	7	0.5
27	Roses (outdoor)	Ground (GB, Airblast, MPHG, Backpack, MPHW, HH AB/MB)	EC	60 g a.i./ha (0.6 g a.i./L)	100 – 1000 L/ha	8	7	0.5
27	Outdoor Ornamentals	Ground (GB, Airblast, HH AB/MB, MPHG, Backpack, MPHW)	SN, EC	75 g a.i./ha (0.75 g a.i./L)	100 L/ha	10	7	0.5
		Aerosol (RTU)	PP	75 g a.i./ha	n/a	NS (10) [b]	NS (7) [b]	NS
27	Ornamental Trees, Ornamental Shrubs	Ground (GB, Airblast, HH AB/MB, MPHG, Backpack, MPHW)	SN	59 g a.i./ha (0.6 g a.i./L)	100 L/ha	10	7	0.5
8, 9, 24 [c]	Beef/Dairy Cattle, Hogs/Swine, Horses, Mules, Ponies	Handheld sprayers (MPHW, Backpack, MPHG, HH AB/MB), RTU Spray Container, Cloth	SN, EC	0.13 g a.i./animal	n/a	180	1	n/a
	Poultry	Handheld sprayers (MPHW, Backpack, MPHG, HH AB/MB)	SN	0.02 g a.i./animal [d]				
	Beef Cattle, Dairy Cattle, Hogs/Swine, Horses, Mules, Goats	Pressurized Spray Container, Cloth	PP	0.136 g a.i./animal	n/a	180	1	n/a
8, 9	Sheep	Pressurized Spray Container	PP	0.136 g a.i./animal	n/a	36	10	n/a
8	Poultry [e]	Pressurized Spray Container	PP	0.0033 g a.i./m^3	n/a	36	10	n/a

REI = restricted-entry interval; GB = groundboom; MPHW = manually pressurized handwand, MPHG = mechanically pressurized handgun; HH AB/MB = handheld airblast/mistblower; RTU = ready to use; SN = solution; EC = emulsifiable concentrate; PP = pressurized product; Max = maximum; No. = Number; Apps = applications; Min = minimum; n/a = not applicable; NS = not stated.

[a] USEPA (RED) indicates a max rate of 8.97 g a.i./ha/day with a yearly maximum of 224.17 g a.i./ha/year. Maximum Canadian label rate is 3.0 g a.i./ha. Canadian labels are silent concerning maximum

number of applications; applications were calculated by extrapolating maximum number of applications per year from USEPA RED. Labels indicate that all products are to be used on truck-mounted sprayers as a mosquitocide.
[b] Application timing information was not stated. Number of applications per year and application interval from application of liquid to outdoor ornamentals used.
[c] Minimum and maximum rates included on currently registered product labels were used.
[d] Minimum rate from PCP# 1268 was used in the risk assessment on poultry as labels indicate the maximum rate is used to treat an adult cow.
[e] is expressed in cubic metre and not per animal since the product is applied as a mist over the birds.

Table 1.2 Summary of use information – commercial application to structural areas (commercial and residential)

Use-site category	USEPA site description from master label	Formulation	Application method as per canadian label	Application equipment listed used for risk assessment	Max canadian label rate [a]	Max US master label rate	Max number of apps/year	Min interval between apps (days)
12	Post-harvest application to stored grains	EC	Surface spray	Stationary Fogger, MPHS	0.165 g a.i./m^2	0.244 g a.i./m^2	6	2nd app: 14 days then every 30 days until early fall
3, 20	Commercial Indoor Sites and Agricultural Premises	SN, EC	Space Spray (includes nest spray), Space spray (fog)	Stationary Fogger, MPHS	0.0497 g a.i./m^3	0.128 g a.i./m^3	12 [365]	30 [1]
			Surface, Crack and Crevice Spray	PCO MPHW, Trigger-pump Sprayer	0.28 g a.i./m^2	1.074 g/m^2		
		PP	Space Spray (includes nest spray)	Aerosol Can (RTU)	0.016 g a.i./m^3 (0.01 kg a.i./can)	0.128 g a.i./m^3	NS [365]	NS [1]
			Surface, Spot, Crack and Crevice		0.1014 g a.i./m^2 (0.01 kg a.i./can)	1.074 g/m^2		
			Battery Operated Dispenser	Automatic Dispenser	0.024 g a.i./m^3	0.08 g a.i./m^3/day	12 dispensers/year	Released every 7.5 min
		DU	Crack and Crevice, Dust-on	Plunger Duster, Bulbous Duster, Hand Crank Duster, Electric/Power Duster, Shaker Can	0.06 g a.i./m^2	1.074 g/m^2	NS	NS
13, 16, 25	Commercial Mosquito Abatement	SN, EC	Fogging Spray	Truck-mounted Fogger, Stationary Fogger, MPHS	2.95 g a.i./ha	2.802 g a.i./ha	NS [365]	NS [1]
		PP	Broadcast Spray	Aerosol Can (RTU)	2.88 g a.i./ha (0.0055 kg a.i./can)	2.802 g a.i./ha	NS	NS
			Fogging Spray	MPHS	35 g a.i./ha	2.802 g a.i./ha	NS [26]	NS [7]
16, 20, 25, 27, 30	Commercial and Residential	SN, EC	Broadcast, Surface, Perimeter Spray (includes nests)	MPHW, Backpack, MPHG, Stationary Fogger, MPHS, Hose-end Sprayer	0.046 g a.i./m^2	1.074 g a.i./m^2	8 [365]	7 [1]

Use-site category	USEPA site description from master label	Formulation	Application method as per canadian label	Application equipment listed used for risk assessment	Max canadian label rate [a]	Max US master label rate	Max number of apps/year	Min interval between apps (days)
20, 25, 27	Outdoor Sites	PP	Broadcast, Surface Spray (includes nest)	Aerosol Can (RTU)	0.0075 g a.i./m^2 (0.01 kg a.i./can)	0.037 g a.i./m2	NS [52]	NS [7]
20	Residential Indoor Sites	SN, EC	Space Spray	MPHS, Stationary Fogger	0.0246 g a.i./m^3	0.053 g a.i./m^3	NS [365]	NS [1]
20, 25, 26, 28			Broadcast, Surface, Spot and Crack and Crevice Spray	PCO MPHW, Trigger-pump Sprayer	0.1336 g a.i./m^2	1.074 g a.i./m^2		
26			Bed Bug Treatment (bed, mattress, surroundings)	PCO MPHW, Trigger-pump Sprayer	n/a (0.1336 g a.i./m^2) [b]	n/a	NS [52]	NS [7]
20		PP	Space Spray (includes nests)	Aerosol Can (RTU)	0.016 g a.i./m^3 (0.00214 g a.i./m^3) [c] (0.01 kg a.i./can)	0.053 g a.i./m^3	NS [365]	NS [1]
20, 26			Broadcast, Surface, Crack and Crevice (includes bed bug treatment)		0.077 g a.i./m^2 (0.01 kg a.i./can)	1.074 g a.i./m^2	NS [365]	NS [1]
20			Battery Operated Sprayer	Automatic dispensers	0.0006 g a.i./m^3	0.08 g a.i./m^3/day	12 dispensers/year	Released every 7.5 min
20, 26		DU	Dust-on, Bed Bug Treatment	Plunger Duster, Bulbous Duster, Hand Crank Duster, Electric/Power Duster, Shaker Can	0.06 g a.i./m^2 (0.004 kg a.i./can)	1.074 g a.i./m^2	NS	NS
20			Wasp/Hornet Nest		0.02 g a.i./nest (0.004 kg a.i./can)	1.074 g a.i./m^2	NS	NS

SN = solution; EC = emulsifiable concentrate; DU = dust/powder; PP = pressurized product; NS = not stated; RTU = ready-to-use; MPHG = mechanically pressurized handgun; MPHW = manually pressurized handwand; MPHS = mechanically-pressurized handheld sprayer for mists, aerosols, and fogs; Max = maximum; Min = minimum; apps = applications; PCO = Pest Control Operator
Information from registrants in square brackets – not on end-use product labels

[a] Information in brackets calculated using maximum can size and % guarantee and used for risk assessment.

[b] Rate not stated – scenario assessed with maximum registered rate of 0.1336 g a.i./m^2 from indoor residential scenarios.

[c] Refined AR required for the risk assessment.

Table 1.3 Summary of use information - domestic agricultural use information

Use-site category	Site/crop [a]	Formulation	Application method	Application equipment	Max canadian label rate	Max US master label rate	Max apps/year	Min interval
5	Greenhouse Peppers	EC	Broadcast Spray	Trigger Sprayer, Hose-end Sprayer, Backpack, Hand sprayer	55 g a.i./ha	56 g a.i./ha	17	7
14	Herbs	EC	Broadcast Spray	Trigger Sprayer, Hose-end Sprayer, Backpack, Hand sprayer	55 g a.i./ha	56 g a.i./ha	17	7
14	Beans, Tomato, Grape	EC, SN	Broadcast Spray	Trigger Sprayer, Hose-end Sprayer, Backpack, Hand sprayer	55 g a.i./ha	56 g a.i./ha	17	7
		PP		Aerosol can	20 g a.i./ha		10	7
14	Beans	DU	Dust-on	Plunger Duster, Bulbous Duster, Hand Crank Duster, Electric/Power Duster, Shaker Can	65 g a.i./ha	NS	10	7
14	Fruit Trees (Pear)	EC, SN	Broadcast Spray	Trigger Sprayer, Hose-end Sprayer, Backpack, Hand sprayer	55 g a.i./ha	56 g a.i./ha	17	7
		PP	Broadcast Spray	Aerosol can	55 g a.i./ha	NS	17	7
8, 9, 24	Cattle, Livestock, Horses	SN	Direct Application	MPHW, Backpack, MPHG, Trigger-pump Sprayer, Cloth	0.12 g a.i./animal	NS	180	1
	Horses	PP		Aerosol Can	0.06 g a.i./animal			
	Horses and Ponies	PA		Ointment (using cloth)				

PP = pressurized product; SN = solution; EC = emulsifiable concentrate; PA = paste; DU = dust; NS = not stated; Max = maximum; Apps = applications; Min = minimum

[a] List of domestic agricultural products which were assessed. Any food crops appearing on domestic-class product labels that were not assessed under the commercial agriculture scenarios were also not assessed in the residential scenarios. Products with food uses co-formulated with PBU were not assessed as PBU has no data to assess dietary exposure.

The following crops appear on domestic product labels but were not assessed due to lack of data:

- Apple tree, "fruit" tree (except pear)
- Outdoor and greenhouse applications to asparagus, beets, broccoli, Brussels sprout, cabbage, carrots, cauliflower, celery, cole crops, collards, cranberries, cucumbers, eggplant, kale, lettuce, mustard green, onion, pea, potato, radish, spinach, squash, turnip, "vegetables" (except for those listed in the table above), and vine products
- Outdoor application to peppers
  Greenhouse application to beans, herbs, tomatoes, "Greenhouse plantings" (except peppers)

Table 1.4 Summary of use information - domestic structural use information

Use-site category	Site	Formulation	Application method	Application equipment for assessment	Canadian max appl. rate	American max rate (master label)	Max # apps/year	Min app interval
6, 20, 27, 28 30, 33	Outdoor grassy area, Lawn, Turf; Outdoor ornamentals, groundcovers, area around residential area, gardens; Domestic Greenhouse	DU	Dust container (RTU)	Bulb Duster, Plunger Duster, Shaker Can, Hand-crank Duster, Electric/Power Duster	NS (65 g a.i./ha) [a]	0.0098 g a.i./m^2	NS	7
		PP	Broadcast, Surface, Crack and Crevice, Spot, Nest Spray	Aerosol Can, Outdoor fogger	0.002 g a.i./m^2 (3.875 g a.i./can) (0.067 g a.i./nest)	0.0098 g a.i./m^2	20 (1 nest/day)	7
		SN, EC	Broadcast and Surface Spray	Hose-end sprayer	0.014 g a.i./m^2; 56 g/ha; 0.48 g a.i./L	0.0098 g a.i./m^2; 168.13 g a.i./ha	17 at lower rate, 9 at high rate	7 – 14
				MPHW, Backpack, Trigger-pump Sprayer			15	7
				Handheld Fogger	NS [b]	0.0098 g a.i./m^2	NS	NS
		SO	Coil	Coil	0.015 g a.i./hr	1% PYR	10/year	NS
20, 26	Indoor Environment (dwellings, garages, storage buildings, agricultural premises, etc)	DU	Dust-on (includes bed bug and nest treatment)	Bulb Duster, Plunger Duster, Shaker Can, Hand-crank Duster, Electric/Power Duster	0.06 g a.i./m^2 (0.01 kg a.i./kg dust) (0.01 kg a.i./can)	1.074 g a.i./m^2	NS	NS
		PP	Automated aerosol dispenser	Metered Release	0.19 g /170m^3/day (0.0011 g a.i./m^3)	0.08 g a.i./m^3/day	12 cartridges/year	Released every 7.5 minutes
			Space Spray – includes nests	Aerosol Can	0.0053 g a.i./m^3	0.053 g a.i./m^3	52	1
				MPHS (Total Release Fogger)	0.0014 g a.i./m^3 (13.6 g a.i./can) (25.77 µg a.i./cm^2) [c]		52	14
			Surface, CC, Spot Spray (includes bed bugs)	Aerosol Can	0.3 g a.i./m^2 (13.6 g a.i./can)	1.074 g a.i./m^2	52	1
		SN, EC	Space Spray (includes nests)	MPHW, Trigger-pump Sprayer	0.043 g a.i./30m^3 (38.9 g a.i./L) (38.9 g a.i./bottle) (25.77 µg/cm^2) [c]	0.053 g/m^3	52	7
				MPHS,	NS [b]	0.053	NS	NS

Use-site category	Site	Formulation	Application method	Application equipment for assessment	Canadian max appl. rate	American max rate (master label)	Max # apps/year	Min app interval
				Automatic Mister/Fogger		g/m^3		
			Surface (includes clothing and bed bugs), Crack and Crevice, Spot Spray	MPHW, Trigger-sprayer	0.3 g a.i./m^2 (38.9 g a.i./L) (38.9 g a.i./bottle)	1.074 g/m^2	52	1
				MPHS, Automatic Mister/Fogger	NS [b]	1.074 g/m^2	NS	NS
24	Pets (Cats, Dogs, Birds, Rabbits)	PP	Direct Application (Spray)	Aerosol Can	0.016 g a.i./kg body weight	0.3% PYR	16	3.5
			Direct Application (Shampoo)	Aerosol Can (Shampoo)				
		SN, EC	Direct Application (Spray)	Trigger-pump Sprayer	0.016 g a.i./kg body weight	0.3 % PYR	16	1
			Direct Application (Shampoo)	Shampoo	0.012 g a.i./kg body weight		16	14
			Direct Application (Ear drop)	Ear Drop	Max 15 drops [d]	1% PYR	NS	2/day
8, 9, 24	Agricultural Animals (Horses, ponies)	PA	Direct Application	Sponge	NS (0.12 g a.i./animal) [e]	4.19 g a.i./L	NS	1
		PP	Direct Application (Spray or wipe-on)	Aerosol Can, Sponge (for wipe-on)	0.066 g a.i./adult horse	4.19 g a.i./L	NS	1
		SN, EC	Direct Application	Sponge, Trigger-sprayer	0.167 g a.i./adult horse	4.19 g a.i./L	NS	1

PP = pressurized product; SN = solution; EC = emulsifiable concentrate; DU = dust; PA = paste; SO = solid; RTU = ready to use; MPHS = mechanically-pressurized handheld sprayer for mists, aerosols, and fogs; NS = not stated;Appl. = application; Max = maximum; Apps = applications; Min = minimum; PYR = pyrethrins; MPHW = manually pressurized handwand;

[a] Rate not stated. Registered rate of 65 g a.i./ha from domestic agriculture scenario used for risk assessment.

[b] Not assessed due to lack of data.

[c] Calculated using maximum can size, maximum guarantee, standards from USEPA RES SOP (2012).

[d] Information from product label.

[e] Rate from domestic agriculture labels.

Appendix II Toxicology

Table 1 Toxicology profile for pyrethrum extract

Note: Effects noted below are known or assumed to occur in both sexes unless otherwise noted: in such cases, sex-specific effects are separated by semi-colons. Effects on organ weights are known or assumed to reflect changes in both absolute weight and relative (to body weight) weight, unless otherwise noted.

Toxicokinetic and metabolism studies
Sprague-Dawley rats were dosed by gavage in corn oil with [cyclopropane-1-^{14}C] – pyrethrin I with either 1) a single dose of 10 mg/kg bw or 100/50 mg/kg bw (♂/♀), or 2) repeat-doses of 10 mg/kg bw/day unlabelled pyrethrin for up to 14 days followed by a single dose of 10 mg/kg bw [cyclopropane-1-^{14}C] pyrethrin I. Absorption was assessed in animals administered a single dose of 10 mg/kg bw only (PMRA# 1829317). **Absorption** **10 mg/kg bw (single-dose) (♂/♀):** Following a single low-dose, peak blood levels (T_{max}) were noted at 5-6 in ♂ and 6-8 hrs in ♀**;** the elimination $T_{1/2}$ in blood was 5.3/6.7 hrs and the Cmax was 1.1/2.4 ng equiv/mL. **Distribution (at 7 days post-dosing)** **10 mg/kg bw (♂/♀):** fat (0.19/0.35 ppm with single low-dose; 0.33/0.53 ppm with repeated low-dose) > ovaries, liver, blood, kidneys, prostate, pancreas (0.02 to 0.08 ppm) > plasma (<0.01 ppm) **100/50 mg/kg bw (single-dose) (♂/♀):** fat (2.8/2.1 ppm) > ovaries, liver, blood, kidneys, prostate, pancreas (0.1 to 0.5 ppm) > plasma (< 0.01 ppm) * radioactivity (dose-related) was detected in the brain in both sexes, irrespective of dosing regime (0.003 to 0.1 ppm) **Metabolism** Two metabolic pathways are proposed: 1) Oxidation of the methyl group of the cyclopropane side chain and subsequent oxidation of the double bond of the side chain on the cyclopentene ring. This yields carboxylic acid-type metabolites and dihydrodiol-type metabolites (including metabolite E), respectively. 2) Hydrolysis of the ester bond which yields CDCA. Pyrethrin 1 and five metabolites were identified in urine and faeces; one additional metabolite was identified in urine (in other words, glucuronic acid conjugate of metabolite E). In urine, metabolite C or chrysanthenic dicarboxylic acid (CDCA) was the major metabolite (11%–20% AD), followed by metabolite E (3%–10% AD), with <6% each of the other metabolites identified (in other words, metabolites A, B, D, F). Pyrethrin 1 was recovered in the urine of single low-dose females (7%), but was detected at very low levels (<1%) in males, or females administered other dosing regimes. In feces, the recovery of the parent compound ranged from 4.8% to 22% of the administered dose, with the highest recovery of parent compound noted in males exposed to a single high-dose. The major metabolites in feces were metabolite E (7%–15%) and CDCA (4%–8%), with smaller amounts (<5% each) of other metabolites detected. **Elimination (at 24 hrs or 7 days post-dosing)** **10 mg/kg bw (single dose):** After 24 hrs, elimination of the administered dose was 29%/33% (♂/♀) in urine and 28%/15% (♂/♀) in faeces. After 7 days, elimination of the administered dose was 42%/55% (♂/♀) in urine and 63%/50% (♂/♀) in faeces; 0.5%/0.4% (♂/♀) of the administered dose was recovered in the carcass.

Toxicokinetic and metabolism studies
100/50 mg/kg bw (single-dose): After 24 hrs, elimination of the administered dose was 23%/34% (♂/♀) in urine and 41%/23% (♂/♀) in faeces. After 7 days, elimination was 32%/49% (♂/♀) in urine, 71%/50% (♂/♀) in faeces; 0.9%/0.6% (♂/♀) of the administered dose was recovered in the carcass. **10 mg/kg bw/day (repeat-dose):** Elimination was 20%/30% (♂/♀) in urine and 0/1.0% (♂/♀) in faeces from 0 to 12 hrs, and 16% (♂/♀) in urine and 23% (♂/♀) in faeces from 12 to 24 hrs. After 7 days, elimination in ♂/♀ was 47%/57% in urine, 55%/52% in faeces and <0.6% in carcass, respectively. **Elimination (Preliminary Study)** Sprague-Dawley rats were administered a single dose of 10 mg/kg bw [cyclopropane-1-^{14}C] pyrethrin-I in corn oil by gavage (PMRA# 1284074). **10 mg/kg bw**: 0.21% of the administered dose was recovered in expired air after 24 hrs. **Elimination Vehicle Study (Supplemental)** Sprague-Dawley rats were orally administered a single dose of 100 mg/kg bw [^{14}C] pyrethrin I in corn oil, food slurry, or dimethyl sulfoxide (DMSO), or 4 × 400 mg/kg bw pyrethrin I in DMSO (dosed at 12 hour intervals, first 3 unlabelled, last labelled). Urine and faeces were examined for radioactivity after 3 days; urine was examined for CDCA content (PMRA# 1829315). **100 mg/kg bw (single-dose)**: With corn oil and DMSO vehicle, 84% to 86% of the administered dose was eliminated from the body, with 55% to 57% eliminated via faeces and 29% to 34% eliminated in urine. For food slurry, less of the administered dose was recovered (in other words, 66%) and the primary route of elimination was faeces. Regardless of the vehicle used, 11–13% of the administered dose was eliminated in urine as the CDCA metabolite. **400 mg/kg bw (repeat-dose):** 86% of the AD was eliminated (63% via faeces, 23% in urine). Approximately 5% of the administered dose was eliminated in urine as CDCA. Twitching, spasms, tremors were noted within 1.5 hrs after the first dose.
In vitro, mouse and rat liver microsomes incubated with each of the 6 pyrethrin compounds of pyrethrum extract for 1 hour, prior to isolation of metabolites (PMRA# 1829312). **Metabolism** The chrysanthemates (pyrethrin I, cinerin I, jasmolin I), were oxidized to 12 metabolites (including intermediary metabolites). Yielded 7, 8-epoxy derivatives, as well as 8', 9'-dihydrodiol, and 10', 11'- and 8', 11'-dihydrodiols derivatives. The pyrethrates (pyrethrin II, cinerin II, jasmolin II), were hydrolyzed and oxidated forming up to 8 metabolites, including intermediary ones. This included 8', 9'- or 10', 11'-epoxy-7'-ol metabolites (not observed with metabolism of chrysanthemates). Two major metabolic pathways were indicated, the first involving oxidation of the double bond and/or the methyl groups and the second involving hydrolysis of the ester bond. The chrysanthemates were metabolised mainly through oxidative processes, while the pyrethrates were metabolized through a combination of hydrolytic and oxidative processes. No significant differences were noted in rats versus mice.

Toxicokinetic and metabolism studies	
Acute toxicity studies	
Study/species	**Results/effects**
Acute Oral Toxicity - Gavage (pyrethrum extract) Sprague-Dawley Rat PMRA# 1521098	LD_{50} = 2140/700 mg/kg bw (♂/♀) (deionized water) **≥1410/355 mg/kg bw (♂/♀):** dark nasal or ocular staining, ruffled fur, tremors Pathology among animals found dead included yellow liquid in the stomach and lower gastrointestinal tract, gas in the lower gastrointestinal tract, empty stomach, clear/dark muzzle staining, yellow/dark genital staining and spongy and/or hemorrhagic lungs. **Moderate Acute Oral Toxicity**
Acute Oral Toxicity - Gavage (pyrethrum extract) Sprague-Dawley Rat PMRA# 1829226	LD_{50} = 2370/1030 mg/kg bw (♂/♀) (undiluted) **≥891/500 mg/kg bw (♂/♀):** hunched posture, ruffled fur, tremors, hyperactivity Pathology of animals found dead included muzzle/nasal/genital staining, hemorrhagic lungs and pink/yellow/tan liquid or material in the lower gastrointestinal tract. **Slight Acute Oral Toxicity**
Acute Dermal Toxicity (pyrethrum extract) New Zealand White Rabbit PMRA# 1521099	LD_{50} >2000 mg/kg bw (♂/♀) (undiluted) **Low Acute Dermal Toxicity**
Acute Inhalation Toxicity - Whole Body (pyrethrum extract aerosol) Sprague-Dawley Rat PMRA# 1521100	LC_{50} = 3.9/2.5 mg/L (♂/♀) (4-hrs; in acetone) **≥2.1 mg/L:** reddening of the lungs and nasal turbinates, lung edema; tremors (♀) **Low Acute Inhalation Toxicity**
Eye Irritation (pyrethrum extract) New Zealand White Rabbit PMRA# 1521101	MAS = 1.67 (undiluted) **Minimal Eye Irritation**
Dermal Irritation (pyrethrum extract) New Zealand White Rabbit PMRA# 1521102	MAS = 1.33 (undiluted) **Minimal Dermal Irritation**

Toxicokinetic and metabolism studies	
Skin Sensitization - Modified Buehler Assay (pyrethrum extract) Hartley Guinea-Pig PMRA# 1521103	Negative
Subchronic toxicity studies	
Study/species	**Results/effects**
13-Week Oral Toxicity - Diet (pyrethrum extract) CD-1 Mouse PMRA# 1829253	**Supplemental (range-finding study)** **≥150 mg/kg bw/day (♂):** ↑ mild liver congestion (♂) **≥433/506 mg/kg bw/day (♂/♀):** hepatocellular hypertrophy; ↓ rel testes wt (♂); ↑ liver wt (♀) **≥1429/1710 mg/kg bw/day (♂/♀):** mortality (day 2), tremors and ↑ activity (wk 1, wk 2); enlarged liver, liver necrosis, ↓ testes wt (♂); ↑ moderate to severe liver congestion (♀) All animals in the highest dose group died or were sacrificed *in extremis* by study day 10. Clinical observations included hunched posture, altered activity, ↓ defecation, cold to touch, scabbed area, exposed skin areas pale, labored breathing and pupils dilated. Due to early mortality, no other assessments were conducted in this group.
8-Week Oral Toxicity - Diet (pyrethrum extract) Beagle Dog PMRA# 1686695	**Supplemental (range-finding study)** **≥75 mg/kg bw/day (♂/♀)**: inappetence, thin appearance, ataxia, trembling, oily coat, impaired limb function, shallow breathing **150 mg/kg bw/day (♂/♀)**: mortality, ↓ bw, ↓ fc, anemia, alterations in electrolytes, ↑ ALT, ↑ AST
52-Week Oral Toxicity - Diet (pyrethrum extract) Beagle Dog PMRA# 1829281	**NOAEL = 13.7/14.2 mg/kg bw/day (♂/♀)** **LOAEL = 66/75 mg/kg bw/day (♂/♀),** based on ↑ liver wt; ↓ RBC, ↓ Hgb, ↓ Hct (♂); ↑ ALT (♀)
3-Week Dermal Toxicity (pyrethrum extract in corn oil) New Zealand White Rabbit PMRA# 1829246	**Systemic NOAEL not established (♂/♀)** **Systemic LOAEL >1000 mg/kg bw/day (♂/♀),** based on the absence of systemic effects at the limit dose **Dermal NOAEL = 300 mg/kg bw/day (♂/♀)** **Dermal LOAEL = 1000 mg/kg bw/day (♂/♀),** based on very slight well-defined erythema, ↑ desquamation
13-Week Inhalation Toxicity - Whole Body (pyrethrum extract aerosol)	**NOAEC not established (♂/♀)** **LOAEC = 0.01 mg/L (2.6/2.7 mg/kg bw/day) (♂/♀)**, based on histopathology in laryngeal mucosa: ↑ hypertrophy/hyperplasia in the

Toxicokinetic and metabolism studies	
CD Rat PMRA# 1829248, 1829250, 1829251, 1829257	seromucous glands, ↑ squamous/squamoid metaplasia/hyperplasia of pseudostratified columnar epithelium in the ventral seromucous glands,↑ hyperkeratosis in the squamous/squamoid epithelium in the ventral seromucous glands **≥0.03 mg/L (7.7 mg/kg bw/day) (♂):** matted coat **≥0.1 mg/L (26/27 mg/kg bw/day) (♂/♀):** ↓ bw, ↓ bwg; matted coat, transient tremors and lacrimation, labored breathing, dry rales, moist rales, ↑ rel kidney wt (♀) **0.36 mg/L or 90/94 mg/kg bw/day (♂/♀)**: hunched posture, hyperactivity, yellow anogenital stains, dried yellow material on face, ↓ Hgb, ↓ Hct, ↑ liver wt, ↑ lung wt, ↑ histopathological changes in larynx (eosinophilic material in lumen, hyperkeratosis of metaplastic epithelium, squamous/squamoid metaplasia/hyperplasia of cuboidal/columnar epithelium), ↑ changes in the nasal mucosa (inflammation, squamous cell hyperplasia, hyperkeratosis, squamous/squamoid metaplasia), hypertrophy/hyperplasia in the lung epithelium of the terminal bronchioles; mortality (day 15), labored breathing, dry rales, moist rales, transient lacrimation, ↓ RBC, ↓ total protein and globulin, discoloration in lungs, ↑ rel lung wt (♂); ↑ creatine, ↑ glucose, ↑ WBC (♀)
Neurotoxicity studies	
Study/species	**Results/effects**
Acute Oral Neurotoxicity - Gavage (pyrethrum extract in corn oil) CD Rat PMRA# 1829293	**NOAEL = 40/20 mg/kg bw (♂/♀)** **LOAEL = 125/63 mg/kg bw (♂/♀)**, based on ↓ motor activity day 1 (↓ rearing, ambulation, fine movements) (♂); fine tremors day 1 (♀) **400/200 mg/kg bw (♂/♀):** death day 1, clinical signs day 1 (tremors, urogenital wetness), alterations in FOB (coarse tremors, exaggerated startle response, decreased grip strength), ↑ body temperature, myelin/axonal degeneration in sciatic, peroneal and tibial nerves; fine tremors day 1 (♂); ↓ motor activity day 1 (↓ rearing, ambulation, fine movements), salivation (♀)

Toxicokinetic and metabolism studies	
Acute Oral Neurotoxicity - Gavage (pyrethrum extract in corn oil) CD Rat PMRA# 1829295	**Supplemental (range-finding study)** Phase I **≥50 mg/kg bw** (♀): tremors **≥200 mg/kg bw (**♂/♀**)**: tremors (♂); death (preceded by lying on stomachs, labored respiration, salivation, urine stains, and prostration) (♀) **≥1400 mg/kg bw** (♂): death (preceded by lying on stomach, labored respiration, salivation, urine stains, and prostration) Phase II **≥100 mg/kg bw (**♂/♀**)**: ↑ arousal (♂); tremors (♀) **≥150 mg/kg bw** (♀): altered gait **≥200 mg/kg bw** (♀): perinasal encrustation, hyperactivity **400 mg/kg bw** (♂): tremors, piloerection, perinasal encrustation, red extremities Time-to-peak effect for neurotoxicity was 3 to 5 hrs.
Chronic toxicity/carcinogenicity studies	
Study/species	**Results/effects**
78-Week Carcinogenicity - Diet (pyrethrum extract) CD-1 Mouse PMRA# 1829258, 1829259, 1829260, 1829261, 1829265, 1829285	**NOAEL = 13.8/16.6 mg/kg bw/day (**♂/♀**)** **LOAEL = 346/413 mg/kg bw/day (**♂/♀**)**, based on ↑ liver wt; vacuolar fatty change in the liver (♂); dark liver (♀) **686/834 mg/kg bw/day (**♂/♀**):** mortality (wk 1); ↑ dark brown pigment in liver (♂) There was an increased incidence of alveolar and bronchiolar tumours in ♀ rats receiving 0:0 (control 1:control 2), 13.8/16.6, 346/413 or 686/834 mg/kg bw/day (♂/♀) (original sections, except where specified): **↑ Alveolar/bronchiolar adenomas** 23%:27%, 25%, 22%, 28% (♂); 13%:6.6%, 18%, 8.3%, 32% (♀); 32%:28%, -, -, 37% (♀, re-sectioned control/high-dose) **↑ Alveolar/bronchiolar carcinomas** 0:0, 2%, 5%, 5% (♂); 2%:5%, 0, 3%, 3% (♀); 2%:5%, -,-, 3% (♀, re-sectioned control/high-dose) **↑ Combined alveolar/bronchiolar adenomas and carcinomas** 23%:27%, 27%, 27%, 33% (♂); 15%:12%, 18%, 12%, 35% (♀); 33%:33%, -, -, 40% (♀, re-sectioned control/high-dose) **Historical control data**: Adenoma – 16.7–31.7% (♂/♀) Carcinoma – 1.3–8% (♂) Carcinoma – 1.6–8% (♀) **Equivocal Evidence of Tumourigenicity**
104-Week Chronic Toxicity/ Carcinogenicity - Diet (pyrethrum extract)	**NOAEL = 4.4/5.4 mg/kg bw/day (**♂/♀**)** **LOAEL = 43/56 mg/kg bw/day (**♂/♀**),** based on ↑ thyroid follicular cell hyperplasia (♂); ↑ bile duct hyperplasia (♀) **130/173 mg/kg bw/day** (♂/♀**):** ↓ bw, ↓ bwg, ↓ fc, ↓ adrenal wt, ↑ rel

Toxicokinetic and metabolism studies	
Sprague-Dawley Rat PMRA# 1829269, 1829272, 1829273, 1829274, 1829275, 1829276, 1829277, 1829280	liver wt; ↑ AST and ALT, spongiosis hepatis (♂); ↑ thyroid follicular cell hyperplasia (♀) There was an increased incidence of thyroid follicular cell adenomas in both sexes. The incidence in ♂ receiving 0:0 (control 1:control 2), 4.4/5.4, 43/56 or 130/173 mg/kg bw/day was 3%:2%, 6.6%, 10% or 8.3%, respectively. The incidence in control 1:control 2, low-, mid- or high-dose ♀, respectively, was 0:2%, 3%, 5% or 8.3%. There was an increase in the combined incidence of thyroid follicular cell adenomas and carcinomas in both sexes. The incidence in 0:0 (control 1:control 2), low-, mid- or high-dose ♂, respectively, was 3%:3%, 6.6%, 12% or 12%. The incidence in 0:0 (control 1:control 2), low-, mid- or high-dose ♀, respectively, was 2%:3%, 3%, 5% or 10%. There was an increase in the incidence of hepatocellular adenomas in ♀. The incidence in control 1:control 2, low-, mid- or high-dose ♀, respectively, was 0:0, 0, 2% or 8.3%. There was an increase in the combined incidence of hepatocellular adenomas and carcinomas in ♀. The incidence in control 1:control 2, low-, mid- or high-dose ♀, respectively, was 2%:0%, 0%, 2% or 8.3%. **Evidence of Tumourigenicity**
Reproductive and developmental toxicity studies	
Study/species	**Results/effects**
2-Generation Reproductive Toxicity - Diet (pyrethrum extract) COBS CD Rat PMRA# 1829286, 1829289, 1829291	**Parental Toxicity** **NOAEL = 65 mg/kg bw/day** (♂/♀) **LOAEL = 196 mg/kg bw/day (**♂/♀), based on ↓ bw in F1 during premating, gestation and lactation **Offspring Toxicity** **NOAEL = 6.4 mg/kg bw/day** **LOAEL = 65 mg/kg bw/day** (♂/♀), based on ↓ bw in F1b♀ (6% to 7%) and F2a (5% to 8%) pups at PND 14, 21 **196 mg/kg bw/day** (♂/♀): ↓ bw in F1a (PND 14, 21), F2a (PND 4, 7) and F2b (PND 7, 14, 21) **Reproductive Toxicity** **NOAEL = 65 mg/kg bw/day (♂/♀)** **LOAEL = 196 mg/kg bw/day** (♂/♀), based on ↓ pup birth wt in F1a♂, F1b♂, F2a♀ and F2b ♂/♀ **Marginal evidence of sensitivity of the young**

Toxicokinetic and metabolism studies	
Developmental Toxicity - Gavage (pyrethrum extract) COBS CD Rat PMRA# 1829302	**Maternal Toxicity:** **NOAEL >75 mg/kg bw/day (♀)** **LOAEL not established (♀)**, based on the absence of adverse effects **Developmental Toxicity:** **NOAEL >75 mg/kg bw/day (♂/♀)** **LOAEL not established (♂/♀),** based on the absence of adverse effects **No evidence of developmental toxicity or sensitivity of the young**
Developmental Toxicity - Gavage (pyrethrum extract) COBS CD Rat PMRA# 1829305	**Supplemental (range-finding study)** **Maternal Toxicity:** **≥75 mg/kg bw/day (♀)**: tremors **≥150 mg/kg bw/day (♀):** convulsions, death **Developmental Toxicity:** **NOAEL >600 mg/kg bw/day (♂/♀)** **LOAEL not established (♂/♀),** based on the absence of adverse effects **No evidence of developmental toxicity or sensitivity of the young**
Developmental Toxicity - Gavage (pyrethrum extract) New Zealand White Rabbit PMRA# 1829306	**Maternal Toxicity:** **NOAEL = 25 mg/kg bw/day (♀)** **LOAEL = 100 mg/kg bw/day (♀)**, based on ↓ bwg, excessive salivation, head arching backwards (GD 19) **250 mg/kg bw/day (♀):** labored breathing, hair loss, bw loss **Developmental Toxicity:** **NOAEL >250 mg/kg bw/day (♂/♀)** **LOAEL not established** (♂/♀)**,** based on the absence of adverse effects **No evidence of developmental toxicity or sensitivity of the young**
Developmental Toxicity - Gavage (pyrethrum extract) New Zealand White Rabbit PMRA# 1829307	**Supplemental (range-finding study)** **Maternal Toxicity:** **≥300 mg/kg bw/day (♀)**: ↓ bw, bw loss **600 mg/kg bw/day (♀)**: tremors, convulsions, death **Developmental Toxicity:** **≥300 mg/kg bw/day:** ↑ number of does with resorptions/number of gravid does **600 mg/kg bw/day**: ↑ post-implantation loss, ↓ number of viable fetuses/doe **Evidence of serious effects in the young in the presence of maternal toxicity**

Toxicokinetic and metabolism studies	
In vitro genotoxicity studies	
Study/species	**Results/effects**
Bacterial Reverse Mutation Assay (pyrethrum extract) *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1538 PMRA# 1829308	Negative ± metabolic activation Not tested up to a cytotoxic concentration
Unscheduled DNA Synthesis (pyrethrum extract) Rat Hepatocytes PMRA# 1829311	Negative Tested up to a cytotoxic concentration
In Vitro Forward Mutation Assay in Mammalian Cells (pyrethrum extract) Mouse Lymphoma L5178Y Cells PMRA# 1284074	**Supplemental** No ↑ in mutation frequency in the presence or absence of metabolic activation Tested up to a cytotoxic concentration
In Vitro Forward Mutation Assay in Mammalian Cells (pyrethrum extract) Mouse Lymphoma L5178Y Cells PMRA# 2061279	Negative ± metabolic activation Tested up to a cytotoxic concentration
Sister Chromatid Exchange (pyrethrum extract) Chinese Hamster Ovary Cells PMRA# 1829310	Negative ± metabolic activation Tested up to a cytotoxic concentration

Toxicokinetic and metabolism studies	
Special studies – non-guideline	
Study/species	**Results/effects**
4-Week Oral Toxicity - Diet (pyrethrum extract) Sprague-Dawley Rat Specialized study of liver and thyroid function. PMRA# 1829245	**Supplemental** **≥370 mg/kg bw/day (♀):** bulging eyes, ↓ bwg, ↓ fc, ↑ liver wt, ↑ thyroid wt, ↑ hepatocyte hypertrophy, ↑ follicular cell hypertrophy, ↑ TSH **≥551 mg/kg bw/day (♀):** transient piloerection No effect on T3 and T4 levels. Limitations with PCNA staining were noted.
6-Week Oral Toxicity - Diet (pyrethrum extract) Sprague-Dawley Rat Specialized study of liver and thyroid function. PMRA# 1626597, 1829254, 1829255, 1829256, 1626596, 1829320, 1809019	**≥201 mg/kg bw/day (♀):** ↑ rel thyroid wt, ↑ thyroid follicular cell hypertrophy, ↑ rT3, ↑ TSH, ↑ DNA synthesis in thyroid, ↑ rel liver wt, ↑ hepatocellular hypertrophy, ↑ DNA synthesis in liver, ↑ hepatic microsomal total CYP450, ↑ hepatic microsomal CYP activities at all time points [7-ethoxyresorufin O-deethylase, 7-pentoxyresorufin O-dependentylase, testosterone 16β-hydroxylase, testosterone 6β –hydroxylase], ↑ thyroxine UDPGT, ↑ palmitoyl-CoA oxidation activity **422/509 mg/kg bw/day (♂/♀)**: ↓ bwg, ↑ plasma total bilirubin, ↑ hepatic microsomal total CYP450, ↑ thyroxine UDPGT; ↑ rel thyroid wt, follicular cell hypertrophy, ↓ T3, ↓ T4, ↑ TSH , ↑ DNA synthesis in thyroid, ↑ rel liver wt, ↑ hepatocellular hypertrophy, ↑ DNA synthesis in liver, ↑ microsomal CYP activities [7-ethoxyresorufin O-deethylase, 7-pentoxyresorufin O-dependentylase, testosterone 16β-hydroxylase, testosterone 6β –hydroxylase, ↑ palmitoyl-CoA oxidation activity] (♂); ↓ bw (♀) **42-Day Recovery Period:** Recovery of rel liver and rel thyroid wt changes were noted except for ♀ rel thyroid wt, recovery of thyroid and liver DNA labelling, ↑ thyroxine UDPGT, CYP content and activity, ↑ thyroid pathology, ↓ incidence of hepatocyte hypertrophy
In Vitro CYP450 Enzyme Activity and Expression (pyrethrum extract) Rat or Human Hepatocytes PMRA# 1808178	Rat hepatocytes: **≥0.05 µM**: ↑ 7-ethoxyresorufin O-deethylase activity (CYP 1A marker) **0.2 µM:** ↑ CYP 2B1/2 mRNA **0.5µM:** ↑ CYP 2B1 mRNA **≥2 µM:** ↑ BFC-O-debenzylase activity (CYP1A/2B marker) **≥5 µM:** ↑ testosterone 6β –hydroxylase (CYP 3A marker) Human hepatocytes: **≥2 µM:** ↑ CYP3A4 mRNA **≥5 µM:** ↑ testosterone 6β –hydroxylase (CYP 3A marker), ↑ CYP2B6 mRNA Pyrethrum or PB did not significantly ↑ 7-ethoxyresorufin *O*-deethylase activity (CYP 1A marker) in human hepatocytes.

Toxicokinetic and metabolism studies	
In Vitro PPARα, PPARγ, or RXRα Reporter Gene Assay (Luciferase) in CV-1 Cells In Vivo Induction of CYP4A10 and CYPA14 in Mouse Hepatocytes - Acute I.P. Injection (pyrethrum extract) PMRA# 1626595	In vitro: **≥1.0 × 10^{-5} M:** ↑ PPARα activity Not a PPARγ or RXRα agonist. In vivo: **300 mg/kg bw**: ↑ CYP4A10 and CYP4A14 mRNA
In Vitro Human Estrogen or Androgen Receptor Reporter Gene Assays (Luciferase) (pyrethrum extract) CHO-K1 Cells PMRA# 2061586	Pyrethrum extract was not a human estrogen receptor or human androgen receptor agonist.
In Vitro Gap-Junction Intercellular Communication (GJIC) and In Vitro DNA Synthesis (F344 Rat or Human Hepatocytes) In Vitro Oxidative Stress (F344 Rat Hepatocytes) PMRA# 1809019, 1829322	Rat hepatocytes, assessment of GJIC at 4 or 24 hrs: **≥50 µg/mL** (♀)**:** concentration-dependent ↓ GJIC at 4 hrs (♀) **≥100 µg/mL** (♂/♀): ↑ DNA synthesis at 24 hrs (♂/♀) **≥250 µg/mL** (♂)**:** ↓ GJIC at 4 hrs (♂) Rat hepatocytes, assessment of oxidative stress, GJIC and DNA synthesis at 1-24 hrs: **400/100 µg/mL (**♂/♀): ↓ GJIC at all time points (peak effect at 1-2 hrs), ↑ DNA synthesis at 24 hrs **(**♂/♀). No ↑ oxidative stress. Rat hepatocytes, assessment of the role of CYP450 inhibition in GJIC and DNA synthesis at 2 or 24 hrs: **400/100 µg/mL ± 1-ABT (**♂/♀**)**: 1-ABT prevented the induction of DNA synthesis and the inhibition of GJIC either partially (following 2 hr exposure) or completely (following 24 hr exposure) (♂/♀**)**. Thus, P450-mediated metabolism of pyrethrins is required for the inhibition of GJIC. Human hepatocytes, assessment of GJIC or DNA synthesis at 4 or 24 hrs: No effect on GJIC or DNA synthesis

Table 2 Toxicology reference values for the human health risk assessment of pyrethrum extract and the pyrethrins

Exposure scenario	study	Point of departure (POD) and endpoint	CAF or target MOE[a]
Acute Dietary	acute oral neurotoxicity study - rat	NOAEL = 20 mg/kg bw tremors in ♀ on the day of dosing	300
ARfD = 0.07 mg/kg bw			
Repeated Dietary	2-year dietary toxicity study - rat	NOAEL = 4.4 mg/kg bw/day thyroid follicular cell hyperplasia in ♂ and bile duct	300

Exposure scenario	study	Point of departure (POD) and endpoint	CAF or target MOE[a]
		hyperplasia in ♀	
ADI = 0.01 mg/kg bw/day			
Short-, Intermediate- and Long-Term Dermal	21-day dermal toxicity study - rabbit	NOAEL = 1000 mg/kg bw/day no systemic effects at the limit dose	300
Short-Term Inhalation	13-week inhalation toxicity study - rat	LOAEL = 2.6 mg/kg bw/day (0.01 mg/L) laryngeal histopathology in both sexes at the lowest tested dose level	300
Intermediate-and Long-Term Inhalation	13-week inhalation toxicity study - rat	LOAEL = 2.6 mg/kg bw/day (0.01 mg/L) laryngeal histopathology in both sexes at the lowest tested dose level	1000
Short- and Intermediate-Term Non-Dietary Incidental Oral Ingestion	2-generation reproductive toxicity study - rat	Offspring NOAEL = 6.4 mg/kg bw/day slight decrease in pup body weight	300
Long-Term Non-Dietary Incidental Oral Ingestion	2-year dietary toxicity study - rat	NOAEL = 4.4 mg/kg bw/day thyroid follicular cell hyperplasia in ♂ and bile duct hyperplasia in ♀	300
Aggregate Short- and Intermediate-Term (Oral, Inhalation)	oral: acute oral neurotoxicity study – rat inhalation: 13-week inhalation toxicity study - rat	Common Endpoint: neurotoxicity (tremors) oral NOAEL = 20 mg/kg bw inhalation NOAEL = 8.1 mg/kg bw/day (0.03 mg/L)	 300 300
Aggregate Long-Term Oral (Diet, Drinking Water, Incidental Oral Ingestion)	2-year dietary toxicity study - rat	NOAEL = 4.4 mg/kg bw/day thyroid follicular cell hyperplasia in ♂ and bile duct hyperplasia in ♀	300
Cancer	Evidence of carcinogenicity based on increased incidences of liver and thyroid tumours in rats, and equivocal evidence of lung tumours in mice. Cancer risk (threshold) was addressed through the selected toxicology reference values.		

[a] CAF (Composite assessment factor) refers to the total uncertainty and PCPA factors for dietary and residential risk assessment; MOE refers to the target margin of exposure for occupational and residential assessment.

Appendix III – Dietary exposure and risk estimates for pyrethrins

Table 1 Acute dietary exposure and risk estimates for pyrethrins

Population subgroup	Acute dietary[a] (Food and drinking water) 95th percentile of exposure		Mitigated acute dietary[1] (Food and drinking water) 95th percentile of exposure	
	Dietary exposure (mg/kg bw)	%ARfD	Dietary exposure (mg/kg bw/day)	%ADI
General Population (total)	0.032909	47	0.010559	15
All Infants (< 1 year old)	0.067211	96	0.023402	33
Children 1–2 years old	0.062093	89	0.023074	33
Children 3–5 years old	0.053178	76	0.017474	25
Children 6–12 years old	0.041325	59	0.012189	17
Youth 13–19 years old	0.029573	42	0.008587	12
Adults 20–49 years old	0.023152	33	0.007085	10
Adults 50+ years old	0.016276	23	0.005175	7
Female 13–49 years old	0.021673	31	0.006622	9
[a] Acute Reference Dose (ARfD) of 0.07 mg/kg bw for all population subgroups				

Table 2 Chronic dietary exposure and risk estimates for pyrethrins

Population subgroup	Chronic dietary[a] (food and drinking water)		Mitigated chronic dietary[a] (food and drinking water)	
	Dietary exposure (mg/kg bw)	%ARfD	Dietary exposure (mg/kg bw/day)	%ADI
General Population (total)	0.010293	103	0.002646	26
All Infants (< 1 year old)	0.018177	182	0.006573	66
Children 1–2 years old	0.025222	252	0.007070	70
Children 3–5 years old	0.024145	242	0.005809	58
Children 6–12 years old	0.016990	170	0.003800	38
Youth 13–19 years old	0.010780	108	0.002487	25
Adults 20–49 years old	0.008758	88	0.002315	23
Adults 50+ years old	0.006594	66	0.001776	18
Female 13–49 years old	0.008085	81	0.002075	21
[a]Acceptable Daily Intake (ADI) of 0.01 mg/kg bw/day for all population subgroups Note that the ADI and selected toxicology reference values for residential and occupational risk assessment provide sufficient margins to the dose levels at which tumours were observed.				

Appendix IV Food residue chemistry summary

Pyrethrins are botanical insecticides with mixed active ingredients present in commercially available extracts of the pyrethrum flower, Chrysanthemum cinerariaefolium and are used to target many different types of flying and crawling insects. Such extracts, used for formulating the final product, contain up to 51% total pyrethrins, the main active constituents being pyrethrin I and pyrethrin II plus smaller amounts of the related cinerins (1 and 2) and jasmolins (1 and 2). Pyrethrins are often co-formulated with synergists, such as piperonyl butoxide and MGK-264, which lack pesticidal effects of their own, or other registered active ingredients. Pyrethrins are used on crops, stored grains, the direct treatment of livestock, livestock housing and in food handling establishments. The application rates are 20–62.5 g a.i./ha for agricultural use and 0.02–0.136 g a.i./animal for direct use on animals.

The residue chemistry database for pyrethrins is sufficient to assess the acceptability of the food uses assessed through this re-evaluation. However, there are limitations to the available residue chemistry data which may need to be addressed for future use expansions.

The nature of the residue in livestock and plant commodities is adequately understood for the registered uses of pyrethrins, based on acceptable metabolism studies in ruminants, poultry, lettuce, potatoes and tomatoes. No change is proposed to the residue definition for enforcement or risk assessment. However, the chemical nomenclature of the residue definition listed on the Residue Definitions for Chemicals with Maximum Residue Limits regulated under the *Pest Control Products Act* table will be revised from:

> 4-hydroxy-3-methyl-2-(2,4-pentadienyl)-2-cyclopenten-1-one 2,2-dimethyl-3-(2-methylpropenyl)cyclopropanecarboxylate and 4-hydroxy-3-methyl-2-(2,4-pentadienyl)-2-cyclopenten-1-one 1-methyl 3-carboxy-α,2,2-trimethylcyclopropaneacrylate ester

to:

> The sum of (1S)-2-methyl-4-oxo-3-(2Z)-2,4-pentadien-1-yl-2-cyclopenten-1-yl (1R,3R)-2,2-dimethyl-3-(2-methyl-1-propen-1-yl)cyclopropanecarboxylate and (1S)-2-methyl-4-oxo-3-(2Z)-2,4-pentadien-1-yl-2-cyclopenten-1-yl (1R,3R)-3-[(1E)-3-methoxy-2-methyl-3-oxo-1-propen-1-yl]-2,2-dimethylcyclopropanecarboxylate.

Analytical methods were previously reviewed and found to be acceptable for data collection and enforcement. The reviewed methods use high performance liquid chromatography with ultraviolet detector (HPLC-UV), gas chromatography with electron capture detector (GC-ECD), gas-liquid chromatography with electron capture detector (GLC-ECD) and liquid chromatography with mass spectrometry (LC-MS/MS) with recoveries within the 70–120% range and LOQ of 0.01–0.1 ppm. The methods quantitate pyrethrin I (the sum of pyrethrin I, cinerin I and jasmolin I) which was considered adequate for the determination by extrapolation of the total pyrethrins residues. All methods were validated as data-gathering methods and some were found adequate as enforcement methods. Pyrethrins are adequately analysed by the multiresidue analytical methods (MRM) available.

Field trial data are available from studies conducted in North America for beans (dry and succulent), blackberry, blueberry, broccoli, cabbage, cantaloupe, carrots, celery, cranberry, cucumber, grapes, grapefruit, herbs and spices, lemon, lettuce, mustard greens, orange, peach, peas (dry and succulent), potato, radish, spinach, squash, strawberry, sugar beet and tomatoes.

Freezer storage stability studies were available for some but not all of the assessed food uses. Experimental processing studies were available for potatoes, beans, grapes, oranges, sugar beets and tomatoes

Animal residue data is available for feeding and topical treatment of poultry and ruminants with pyrethrins. Residue data is available in food processed in treated food handling establishments

No confined or field rotational crop studies are available, therefore a plant-back interval (PBI) of 12 months will be established for all crops other than the ones for whom pyrethrins is registered for use.

Appendix V Residential and occupational exposure and risk assessment tables

Table 1 Short-term residential applicator exposure and risk assessment

Scenario	Formulation	Application equipment	Application type	Application rate [a]	ATPD [b]	Dermal exposure (mg/kg bw/day) [c]	Inhalation exposure (mg/kg bw/day) [d]	Dermal MOE [e]	Inhalation MOE [f]
Lawns and Turf	Liquid	Hose-end Sprayer	Broadcast [g]	0.000014 kg a.i./m^2	2000 m^2	0.0103	1.7×10^{-5}	97 000	150 000
		MPHW		0.00048 kg a.i./L	18.927 L	0.0158	4.5×10^{-6}	63 000	570 000
		Sprinkler Can		0.014 g a.i./m^2	93 m^2	0.0005	8.0×10^{-7}	2 100 000	3 300 000
		Backpack		0.00048 kg a.i./L	18.927 L	0.0325	3.5×10^{-5}	31 000	74 000
	RTU	Aerosol Can		0.003875 kg a.i./can	1 can	0.0395	3.2×10^{-4}	25 000	8100
		Trigger-Spray Bottle		0.008 kg a.i./bottle	1 bottle	0.0188	1.3×10^{-5}	53 000	200 000
		Hose-end Sprayer		0.000014 kg a.i./m^2	2000 m^2	0.0048	2.6×10^{-5}	210 000	99 000
Gardens and Trees	Liquid	MPHW	Broadcast [g]	0.0000056 kg a.i./m^2	111.48 m^2	0.0011	3.1×10^{-7}	920 000	8 300 000
		Hose-end Sprayer, Sprinkler Can				0.0010	2.4×10^{-8}	1 000 000	110 000 000
		Backpack				0.0022	2.4×10^{-6}	450 000	1 100 000
	RTU	Aerosol Can	Surface spray: Broadcast, CC, Spot, Nest Spray	0.003875 kg a.i./can	2 cans	0.0790	6.4×10^{-4}	13 000	4100
		Trigger-Spray Bottle		0.00491 kg a.i./bottle	2 bottles	0.0230	1.6×10^{-5}	43 000	160 000
		Hose-end Sprayer		0.0000055 kg a.i./m^2	111.48 m^2	0.0001	5.7×10^{-7}	9 500 000	4 500 000
	Dust	Bulb Duster, Plunger Duster	Broadcast	0.0000065 kg a.i./can [h]	111.48 m^2	0.0050	3.4×10^{-5}	200 000	77 000
		Shaker Can, Hand Crank Duster, Electric/Power Duster				0.0860	3.6×10^{-4}	12 000	7200

Scenario	Formulation	Application equipment	Application type	Application rate [a]	ATPD [b]	Dermal exposure (mg/kg bw/day) [c]	Inhalation exposure (mg/kg bw/day) [d]	Dermal MOE [e]	Inhalation MOE [f]
Outdoor Fogging/Misting System	RTU	OASS	Space Spray	0.0012 kg a.i./day	1 can	0.0122	9.9×10^{-5}	82 000	26 000
	Solid	CCTM (coil)	Negligible handler exposure						
Indoor Environments	Liquid	MPHW, Backpack	Surface spray: Broadcast, Perimeter, Spot, Bed bug (coarse and pinstream), CC	0.0389 kg a.i./L	1.89 L	0.1398	0.0022	7200	1200
	RTU	Aerosol Can [i]	Space Spray	0.0136 kg a.i./can	0.25 can	0.0347	0.0003	29 000	9300
			Surface spray: Broadcast, Perimeter, Spot, Bed bug (coarse and pinstream), CC		1 can	0.1387	0.0011	7200	2300
			Space spray: Metered Release	Negligible handler exposure					
		Trigger-Spray Bottle	Surface spray: Broadcast, Perimeter, Spot, Bed bug	0.0389 kg a.i./bottle	1 bottle	0.0912	6.3×10^{-5}	11 000	41 000
	Dust	Bulb Duster	Perimeter, Spot, Bed bug, CC	0.01 kg a.i./kg dust	0.113 kg dust	0.0078	5.3×10^{-5}	130 000	49 000
		Plunger Duster	Broadcast, Perimeter, Spot, Bed bug	0.01 kg a.i./kg dust	0.227 kg dust	0.0156	1.1×10^{-4}	64 000	24 000

Scenario	Formulation	Application equipment	Application type	Application rate [a]	ATPD [b]	Dermal exposure (mg/kg bw/day) [c]	Inhalation exposure (mg/kg bw/day) [d]	Dermal MOE [e]	Inhalation MOE [f]
		Hand Crank Duster, Electric/Power Duster	Broadcast, Perimeter, Spot, Bed bug	0.01 kg a.i./kg dust	0.227 kg dust	0.2690	0.0011	3700	2300
		Shaker Can	Broadcast, Perimeter, Spot, Bed bug	0.01 kg a.i./can	1 can	1.185	0.0050	840	520
Treated Pets	RTU	Shampoo [j]	Pets	0.001814 kg a.i./pet	2 pets	0.2000	2.9×10^{-5}	5000	90 000
		Trigger-spray bottle, Aerosol can				0.0820	3.3×10^{-4}	12 000	7900
	Liquid	Sponge [k]	Livestock	0.167 g a.i./animal	24 animals [l]	0.2673	3.9×10^{-4}	3700	6700
	RTU	Trigger-spray bottle, Aerosol can				0.0906	3.6×10^{-4}	11 000	7100

ATPD = area treated per day; MOE = margin of exposure; RTU = ready to use; MPHW = manually pressurized handwand; CC = crack and crevice; OASS = outdoor aerosol space spray; CCTM = candles, coils, torches, mats

[a] Maximum rates assessed. Trigger sprayer, aerosol can and space spray application rates could also be based on net contents, maximum guarantee, and density.

[b] Based on Residential SOP defaults (USEPA, 2012), PYR RED (USEPA, 2006), and Statistics Canada (2016).

[c] Where dermal exposure (mg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg. Dermal absorption is not required as the dermal NOAEL is based on a dermal toxicity study.

[d] Where inhalation exposure (mg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg.

[e] Based on a short-term dermal NOAEL of 1000 mg/kg bw/day and a target MOE of 300 applicable to short-, intermediate-, and long-term scenarios.

[f] Based on a short-term inhalation NOAEL of 2.6 mg/kg bw/day and a target MOE of 300. Residential scenarios are considered to be short-term in duration.

[g] Includes nest spray.

[h] Rate from domestic agriculture scenario.

[i] Includes total release foggers.

[j] Exposure from shampoo will address exposure from ear drops.

[k] Used sponge scenario as a surrogate for the cloth/wipe-on scenario. This scenario will also address exposure from paste application.

[l] 95th percentile of horses and ponies from Statistics Canada (2016).

Table 2 Short- to intermediate-term residential postapplication dermal exposure and risk assessment

Exposure scenario			Lifestage	TR [a] (µg/cm^2)	TC [b] (cm^2/hr)	ET [c] (hr/day)	Dermal dose [d] (mg/kg bw/day)	MOE [e]
Lawns &Turf	Liquid, Aerosol [f]	High Contact Lawn Activities	Adult	0.06	180 000	1.5	0.1908	5200
			Children (1<2)		49 000	1.5	0.3777	2600
		Mowing Turf	Adult		5500	1	0.0039	260 000
			Youth (11<16)		4500	1	0.0045	220 000
Gardens & Trees	Liquid, Aerosol [g]	Gardens	Adult	1.473	8400	2.2	0.3403	2900
			Child (6<11)		4600	1.1	0.2330	4300
		Trees	Adult		1700	1	0.0313	32 000
			Child (6<11)		930	0.5	0.0214	47 000
		Indoor Plants [i]	Adult	1.150	220	1	0.0032	320 000
			Child (6<11)		120	0.5	0.0022	460 000
	Solid (Dust) [h]	Gardens	Adult	0.208	8400	2.2	0.0481	21 000
			Child (6<11)		4600	1.1	0.0329	30 000
		Trees	Adult		1700	1	0.0044	230 000
			Child (6<11)		930	0.5	0.0030	330 000
		Indoor Plants [i]	Adult	0.163	220	1	0.0004	2 200 000
			Child (6<11)		120	0.5	0.0003	33 00 000
Outdoor Fogging/Misting Systems	Outdoor Aerosol Space Spray [j]	Residues on Turf	Adult	0.0415	180 000	1.5	0.1402	7100
			Children (1<2)		49 000	1.5	0.2776	3600
	Mosquito Abatement [k]		Adult	6.7×10^{-3}	180 000	1.5	0.0226	22 000
			Children (1<2)		49 000	1.5	0.0448	11 000
	Animal Barn Misting Systems [l]	Residues on Hard Surfaces	Adult	8.22	6800	4	0.2237	4500
			Children (3<6)		2700	2	0.1870	5300
Indoor Environments [m]	Broadcast	Soft Surface	Adults	1.8	6800	8	1.224	820
			Children (1<2)		1800	4	1.178	850
		Hard Surface	Adults	2.4	6800	2	0.408	2500
			Children (1<2)		1800	2	0.785	1300
	Perimeter/Spot/Bed bug (Coarse and Pin Stream)	Soft Surface	Adults	0.9	6800	8	0.612	1600
			Children		1800	4	0.589	1700

Exposure scenario			Lifestage	TR [a] (µg/cm²)	TC [b] (cm²/hr)	ET [c] (hr/day)	Dermal dose [d] (mg/kg bw/day)	MOE [e]
			(1<2)					
		Hard Surface	Adults	1.2	6800	2	0.204	4900
			Children (1<2)		1800	2	0.393	2500
	Crack and Crevice	Soft Surface	Adults	0.18	6800	8	0.122	8200
			Children (1<2)		1800	4	0.118	8500
		Hard Surface	Adults	0.24	6800	2	0.041	25 000
			Children (1<2)		1800	2	0.079	13 000
	Fogger	Soft Surface	Adults	1.49	6800	8	1.013	990
			Children (1<2)		1800	4	0.975	1000
		Hard Surface	Adults	1.99	6800	2	0.338	3000
			Children (1<2)		1800	2	0.650	1500
	Space Spray (includes metered release)	Soft Surface	Adults	1.55	6800	8	1.051	950
			Children (1<2)		1800	4	1.012	990
		Hard Surface	Adults	2.06	6800	2	0.350	2900
			Children (1<2)		1800	2	0.675	1500
Treated Pets [n]	Dog	All Sizes [o]	Adults	0.003	5200	0.77	0.17	6100
			Children (1<2)		1400	1	0.42	2400
	Cat	All Sizes [p]	Adults	0.001	5200	0.77	0.05	22 000
			Children (1<2)		1400	1	0.12	8700

TR = transferable residue; TC = transfer coefficient; ET = exposure time; MOE = margin of exposure; OASS = outdoor aerosol space sprays

[a] Transferable residue calculated based on the application rate and the exposure scenario using fraction transferred values of 1% for lawns and turf, 25% for gardens & trees, 6% for soft surfaces, 8% for hard surfaces. For some scenarios (OASS), this value is the deposited residue based on calculations using the application rate.

[b] Transfer coefficient default values from USEPA Residential SOPs (2012) were used.

[c] Exposure time default values from USEPA Residential SOPs (2012) were used.

[d] Dermal dose (mg/kg bw/day) = TR × TC × ET/BW (kg). Body weights of 80, 57, 19, and 11 kg were used for adults, youth (11 <16 years), children (3 <6 years), and children (1<2 years) respectively, as stated in the USEPA Residential SOPs (2012). Dermal absorption was not required as the dermal point of departure was based on a dermal toxicity study.

[e] MOE = NOAEL/exposure, based on a short- to long-term dermal NOAEL of 1000 mg/kg bw/day and a target MOE of 300. Long-term dermal exposure estimates were not presented as they are addressed by the short-, intermediate-term calculations.

[f] Based on commercial application rate of 0.046 g a.i./m² (2 applications per year; 14 day interval).

[g] Based on commercial liquid application rate of 0.046 g a.i./m² (3 applications per year; 14 day interval).

[h] Based on domestic agriculture dust rate of 65 g a.i./ha (3 applications per year, 14 day interval).

[i] Based on only 1 application (as per RES SOP) (USEPA, 2012).

[j] Based on a maximum domestic product can size of 600 g (0.2% guarantee) (3 applications per year; 14 day interval).
[k] Based on a maximum commercial product rate of 35 g a.i./ha (26 applications per year; 7 day interval)
[l] Based on a maximum commercial product guarantee of 1.8% and USEPA Residential SOP (2012) defaults.
[m] Based on maximum domestic product rate of 0.3 g a.i./m^2. Long-term dermal exposure estimates are not presented as they are addressed by the short- to intermediate-term calculations.
[n] Based on a maximum domestic product rate of 0.016 g a.i./kg body weight.
[o] Based on a 250 lb dog which has the highest exposure and addresses exposure to smaller animals.
[p] Based on a 25 lb cat which has the highest exposure and addresses exposure to smaller animals.

Table 3 Short- to intermediate-term residential postapplication dermal exposure and risk assessment from mattresses

Exposure scenario			Lifestage	DR (µg/cm^2)	Surface area/body weight ratio (cm^2/kg)	Dermal dose (mg/kg bw/day) [b]	Dermal MOE [c]
Indoor Environments [d]	Bed Bug Treatment [a]	Application to Mattresses	Adults	6	280	0.0252	40 000
			Children (1<2)		640	0.0576	17 000

DR = deposited residue; MOE = margin of exposure
[a] Based on the maximum domestic dust rate of 0.06 g a.i./m^2.
[b] Dermal Dose (mg/kg bw/day) = DR (µg/cm^2) × Surface Area/Body Weight Ratio (cm^2/kg) × Fraction of body that contacts residue (0.5) × Fraction of a.i. available for transfer from treated mattress (6%) × protection factor (0.5)
[c] Based on a short- to long-term NOAEL of 1000 mg/kg bw/day with a target MOE of 300.
[d] Long-term dermal exposure estimates are not presented as they are addressed by the short- to intermediate-term calculations.

Table 4 Short-term residential postapplication inhalation exposure and risk assessment

Exposure scenario		Lifestage	C_0 or mass a.i.[a]	Exposure time (hr/day) [b]	Inhalation dose (mg/kg bw/day) [c]	MOE [d]
Outdoor Fogging/Misting Systems	Outdoor Aerosol Space Spray [e]	Adult	1200 mg a.i./day	NA	0.0018	1500
		Children (1<2)			0.0067	390
	Coils [f]	Adult	77.14 mg a.i./product	2.3	7.1×10^{-5}	36 000
		Children (1<2)			2.7×10^{-4}	9700
	Mosquito Abatement	Adult	7 mg/m^3	1.5	8.40×10^{-4}	3100
		Children (1<2)			3.15×10^{-3}	830
Indoor Environments	Space Spray [g] (Commercial – max rate [h], 2 hr re-entry interval)	Adult	1.98 mg a.i./m^3	2	0.0209	120
		Children (1<2)			0.0783	33
	Space Spray [g] (Commercial – 2.1×10^{-6} kg a.i./m^3)	Adult	2.14 mg a.i./m^3	2	0.0226	120
		Children (1<2)			0.0847	31
	Space Spray [g] (Commercial – 2.1×10^{-6} kg a.i./m^3, 2 hr re-entry interval)	Adult	0.17 mg a.i./m^3	2	0.0018	1400
		Children (1<2)			0.0068	380
	Space Spray [g]	Adult	5.3 mg a.i./m^3	2	0.0559	46

Exposure scenario		Lifestage	C_o or mass a.i.[a]	Exposure time (hr/day) [b]	Inhalation dose (mg/kg bw/day) [c]	MOE [d]
	(domestic – max rate [i])	Children (1<2)			0.2097	12
	Space Spray [g] (domestic – min rate 0.00143 g a.i./m^3)	Adult	1.43 mg a.i./m^3	2	0.0151	170
		Children (1<2)			0.0566	46

NA = not applicable; MOE = margin of exposure; hr = hours; C_o = initial concentration; max = maximum; min= minimum
Shaded cells indicate target MOE not met.
[a] Outdoor Fogging/Misting Systems application rate determined from maximum container/product size and highest % guarantee. Mosquito abatement and indoor space spray based on the maximum application rates.
[b] Exposure time based on default values from the USEPA Residential SOP (USEPA, 2012).
[c] Inhalation dose calculated based on calculations from the USEPA Residential SOPS (USEPA, 2012).
[d] MOE = LOAEL/exposure, based on an inhalation LOAEL of 2.6 mg/kg bw/day and a target MOE of 300.
[e] Rate calculated using maximum domestic can size (600 g) with highest guarantee (0.2%).
[f] Rate based on largest product size (12.86 g) and highest guarantee (0.6%).
[g] Addresses exposure from total release foggers.
[h] Rate based on maximum commercial space spray rate of 0.0246 g a.i./m^3.
[i] Rate based on maximum domestic space spray rate of 0.053 g a.i./m^3.

Table 5 Intermediate-term residential postapplication inhalation exposure and risk assessment

Exposure scenario		Lifestage	Air concentration (µg/m^3) [a]	Exposure time (hr/day) [b]	Inhalation dose (mg/kg bw/day) [c]	MOE [d]
Indoor Environments	Metered Release – Indoor Environments	Adult	5.76 µg/m^3	16	1.0×10^{-4}	25 000
		Children (1<2)		18	3.8×10^{-4}	6800
	Metered Release – Agricultural Premises (ABMS)	Adult	5.76 µg/m^3	4	1.8×10^{-4}	14 000
		Children (3<6)		2	2.6×10^{-4}	10 000

MOE = margin of exposure; ABMS = animal barn misting systems
[a] Average air concentration (peak to end of study) after metered release spray at 1.8 m away from the device (Selim, 2008).
[b] Exposure Time (hr/day) default values obtained from the USEPA Residential SOPs (2012) for vapours for indoor residential environments and barn misting systems for agricultural premises.
[c] Inhalation dose was calculated = AC × IR × ET/BW. Where AC = Air Concentration, IR = Inhalation Rate (m^3/hour) 0.64, 0.42 and 0.33 m^3/hr for adult, children (3<6 years old) and children (1<2 years old) respectively, ET = Exposure Time, BW = Body Weight (80 kg for adults, 19 kg for children (3<6 years old) and 11 kg for children (1<2 years old). Default values were obtained from the USEPA Residential SOPs (2012).
[d] MOE = LOAEL/Exposure, based on a LOAEL of 2.6 mg/kg bw/day and a target MOE of 1000.

Table 6 Short- to intermediate-term residential postapplication hand-to-mouth exposure and risk assessment for children (1<2 years)[a]

Exposure scenario			Hand residue (mg/cm^2) [b]	ET (hr/day) [c]	Oral dose (mg/kg bw/day) [d]	MOE [e]
Lawns & Turf	Liquid [f]		0.0831	1.5	0.0013	4800
Outdoor Fogging/Misting Systems	OASS	Residue Deposited on Lawns/Turf [g]	0.0611	1.5	0.0010	6600
	Mosquito Abatement	Residues Deposited on Lawns/Turf	0.0099	1.5	0.0002	41000
	Animal Barn Misting Systems (Children (3<6 years))	Broadcast, Hard Surface [j]	0.1332	2	0.0016	3900
Indoor Environments [h]	HtM Broadcast	Soft Surface	0.2430	4	0.0111	580
		Hard Surface	0.3240	2	0.0074	870
	HtM Perimeter/Spot/Bed bug (Coarse and Pin Stream)	Soft Surface	0.1215	4	0.0055	1200
		Hard Surface	0.1620	2	0.0037	1700
	HtM Crack and Crevice	Soft Surface	0.0243	4	0.0011	5800
		Hard Surface	0.0324	2	0.0007	8700
	HtM Fogger	Soft Surface	0.2011	4	0.0091	700
		Hard Surface	0.2681	2	0.0061	1000
	HtM Space Spray	Soft Surface	0.2087	4	0.0094	670
		Hard Surface	0.2783	2	0.0063	1000
Treated Pets [i]	HtM Dog	All sizes [k]	0.0924 mg/hr	1	0.0011	6100
	HtM Cat	All sizes [l]	0.0254 mg/hr	1	0.0003	22 000

HtM = hand-to-mouth; OASS = outdoor aerosol space spray; MOE = margin of exposure; ET = exposure time

[a] Risk assessment for children (1<2 years) except for animal barn misting system scenario where the index lifestage for this scenario is children (3<6 years).

[b] For lawns & turf and outdoor fogging/misting systems scenarios: Hand residue loading is based on the dermal postapplication exposure from indoor applications without the body weight × fraction of a.i. on hands compared to body (0.15). For Indoor Environments, based on the dermal postapplication exposure from indoor applications without the body weight/(dermal exposure time (hour) × replenishment intervals (intervals/hr)) × fraction of a.i.on hands compared to body (0.15). For Treated Pets scenario: Based the postapplication dermal exposure from spot-on applications without the body weight/(dermal exposure time (hour) × replenishment intervals (intervals/hr)) × fraction of a.i. on hands compared to body (0.04).

[c] Exposure time based on default values from the USEPA Residential SOPs (2012).

[d] Where Oral Dose (mg/kg bw/day) = [Hand Residue (mg/cm^2) × Fraction of hand mouthed/event (0.12) × Surface Area of one hand (150 cm^2)) × Exposure Time (hr) × Replenishment Intervals (4/hr) × (1 – (1 – Saliva Extraction Factor (0.48)) $^{\text{Number events per hour (14)/Replenishment Intervals (4/hr)}}$)]/ Body Weight (kg). Exposure times for soft surfaces and hard surfaces were 4, and 2 hrs, respectively, as stated in the USEPA Residential SOPs (2012).

[e] Oral MOE = NOAEL/Oral exposure, based on an NOAEL 6.4 mg/kg bw/day from an oral toxicity study and a target MOE of 300.

[f] Based on commercial product rate of 0.046 g a.i./m^2 (2 applications per year; 7 day interval).

[g] Based on max container size (600 g), max guarantee (0.2%) of domestic-class products.

[h] Based on the overall maximum application rates (0.3 g a.i./m^2 for surface sprays, and max container size (350 g and 775 g) and guarantee (0.96% and 1.8%) for fogger and space sprays, respectively).

[i] Based on maximum application rate (0.016 g a.i./kg bw).

[j] Based on maximum guarantee (1.8%) from commercial end-use products as it is higher than the domestic end-use product guarantee.

[k] Based on a 250 lb dog which has the highest exposure and addresses exposure to smaller animals.

[l] Based on a 25 lb cat which has the highest exposure and addresses exposure to smaller animals.

Table 7 Short- to intermediate-term residential postapplication object-to-mouth exposure and risk assessment for children (1<2 years)

Exposure scenario			Object residue (mg/cm^2) [a]	ET (hr/day) [b]	Oral dose (mg/kg bw/day) [c]	MOE [d]
Lawns & Turf	Liquid		0.0565	1.5	0.0002	27 000
Indoor Environments	OtM Broadcast	Soft Surface	1.800	4	0.0235	270
		Hard Surface	2.400	2	0.0157	410
	OtM Perimeter/Spot/Bed bug (Coarse and Pin Stream)	Soft Surface	0.900	4	0.0118	540
		Hard Surface	1.200	2	0.0078	820
	OtM Crack and Crevice	Soft Surface	0.180	4	0.0024	2700
		Hard Surface	0.240	2	0.0016	4100
	OtM Fogger	Soft Surface	1.490	4	0.0195	330
		Hard Surface	1.986	2	0.0130	490
	OtM Space Spray	Soft Surface	1.546	4	0.0202	320
		Hard Surface	2.062	2	0.0135	480

OtM = object-to-mouth; ET = exposure time; MOE = margin of exposure

[a] For lawns and turf scenario: Object residue = turf transferable residue (µg/cm^2), deposited residue based on overall maximum application rate (0.046 g a.i./m^2; 2 applications, 7 days apart). For Indoor Environment scenario: Deposited Residue (ug/cm^2) × Fraction of residue transferred (6% for soft surfaces and 8% for hard surfaces). Deposited residue based on overall maximum application rates (0.3 g a.i./m^2 for surface sprays and maximum container size (350 g, 775 g) and guarantee (0.96% and 1.8%) for foggers and space sprays, respectively).

[b] Exposure time based on default values from the USEPA Residential SOPs (2012).

[c] Where Oral Dose (mg/kg bw/day) = [Object Residue (ug/cm^2) × 0.001 mg/ug × Surface Area of object mouthed (10 cm^2/event) × (Exposure Time (hr) × Replenishment Intervals (4/hr)) × (1 – (1 – Saliva Extraction Factor (0.48)) $^{\text{Number events per hour (14)/Replenishment Intervals (4/hr)}}$)]/ Body Weight (11 kg).

[d] Oral MOE = NOAEL/Oral exposure, based on an NOAEL 6.4 mg/kg bw/day from an oral toxicity study and a target MOE of 300.

Table 8 Short- to intermediate-term postapplication incidental soil ingestion exposure and risk assessment for children (1<2 years)

Exposure scenario	Application rate	Ingestion rate (mg/day) [a]	Soil volume to weight conversion factor [a]	Oral dose (mg/kg bw/day) [c]	MOE [c]
Lawns and Turf	0.046 g a.i./m^2	50	0.67 cm^3/g soil	1.40×10^{-5}	460 000

[a] Default from the USEPA Residential SOPs (USEPA, 2012).

[b] Where Oral Dose (mg/kg bw/day) = Application rate × fraction available in the top cm of soil (1) × soil volume to weight conversion factor (0.67) × soil ingestion rate/BW (11 kg)

[c] MOE = margin of exposure; oral MOE = NOAEL/Oral exposure, based on an oral NOAEL of 6.4 mg/kg bw/day from an oral toxicity study and a target MOE of 300.

Table 9 Long-term residential postapplication hand-to-mouth exposure and risk assessment for children (1<2 years) [a]

Exposure scenario			Hand residue (mg/cm^2) [b]	ET (hr/day) [c]	Oral dose (mg/kg bw/day) [d]	MOE [e]
Indoor Environments [f]	HtM Perimeter/Spot/Bed bug (Coarse and Pin Stream)	Soft Surface	0.0293	4	0.0011	3800
		Hard Surface	0.0439	2	0.0009	5100
	HtM Crack and Crevice	Soft Surface	0.0059	4	0.0002	19 000
		Hard Surface	0.0088	2	0.0002	26 000

HtM = hand-to-mouth; MOE = margin of exposure; ET = exposure time

[a] Dermal exposure based on refined long-term exposure values using 50th percentile values for fraction transferred and TCs.

[b] Deposited residue based on the dermal postapplication long-term exposure from indoor applications without the body weight/(dermal exposure time (hour) × replenishment intervals (intervals/hr)) × fraction of a.i. on hands compared to body (0.15).

[c] Exposure time based on default values from the USEPA Residential SOPs (USEPA, 2012).

[d] Where Oral Dose (mg/kg bw/day) = [Hand Residue (mg/cm^2) × Fraction of hand mouthed/event (0.12) × Surface Area of one hand (150 cm^2)) × Exposure Time (hr) × Replenishment Intervals (4/hr) × (1 – (1 – Saliva Extraction Factor (0.48)) $^{\text{Number events per hour (14)/Replenishment Intervals (4/hr)}}$)]/ Body Weight (kg).

[e] Oral MOE = NOAEL/Oral exposure, based on an NOAEL 4.4 mg/kg bw/day from an oral toxicity study and a target MOE of 300.

[f] Based on the overall maximum application rates for bed bug applications (0.3 g a.i./m^2).

Table 10 Long-term residential postapplication object-to-mouth exposure and risk assessment for children (1<2 years)

Exposure scenario			Object residue (mg/cm^2) [a]	ET (hr/day) [b]	Oral dose (mg/kg bw/day) [c]	MOE [d]
Indoor Environments	OtM Perimeter/Spot/Bed bug (Coarse and Pin Stream)	Soft Surface	0.300	4	0.004	1200
		Hard Surface	0.450	2	0.003	1600
	OtM Crack and Crevice	Soft Surface	0.060	4	0.001	5900
		Hard Surface	0.090	2	0.001	7800

OtM = object-to-mouth; ET = exposure time; MOE = margin of exposure

[a] Deposited Residue (ug/cm^2) × 50th percentile values for Fraction of residue transferred (2% for soft surfaces and 3% for hard surfaces). Deposited residue based on overall maximum application rate for bed bug applications (0.3 g a.i./m^2).

[b] Exposure time based on default values from the USEPA Residential SOPs (USEPA, 2012).

[c] Where Oral Dose (mg/kg bw/day) = [Object Residue (ug/cm^2) × 0.001 mg/ug × Surface Area of object mouthed (10 cm^2/event) × (Exposure Time (hr) × Replenishment Intervals (4/hr)) × (1 – (1 – Saliva Extraction Factor (0.48)) $^{\text{Number events per hour (14)/Replenishment Intervals (4/hr)}}$)]/ Body Weight (11 kg).

[d] Oral MOE = NOAEL/Oral exposure, based on an NOAEL 4.4 mg/kg bw/day from an oral toxicity study and a target MOE of 300.

Table 11 Short- to long-term exposure estimates and MOEs for occupational handlers for agricultural uses

Crop	Application equipment	Formulation	Maximum application rate	ATPD/AHPD	Dermal exposure (µg/kg bw/day) [a]	Inhalation exposure (µg/kg bw/day) [b]	Dermal MOE [c]	Inhalation MOE [d]
PPE: Baseline – long pants, long-sleeved shirt, CR gloves								
Blueberry, Raspberry, Herbs and Spices, Bean (pinto, snap, wax), Field Tomato, Outdoor Ornamentals, Ornamental Shrubs	Groundboom (custom)	Liquid	0.075 kg/ha	360 ha	28.32	0.78	35 000	3300
Blueberry, Grape, Raspberry, Pear orchard, Outdoor Ornamentals, Ornamental Trees and Shrubs	Airblast	Liquid	0.075 kg/ha	20 ha	71.77	0.18	14 000	14 000
Greenhouse peppers, Blueberry, Grape, Raspberry, Herbs and Spices, Beans (pinto, snap, wax), Tomato (field), Outdoor Ornamentals, Ornamental Trees and Shrubs	MPHW	Liquid	0.75 g/L [e]	150 L	1.33	0.06	750 000	41 000
	Backpack	Liquid	0.75 g/L [e]	150 L	7.66	0.09	130 000	30 000
	MPHG	Liquid	0.75 g/L [e]	3800 L	198.98	5.38	5000	480
Pasture – Mosquito abatement	Truck Mounted Sprayer (fogger) [f]	Liquid	0.003 kg/ha	1200 ha	172.25	0.44	5800	6000
Livestock [g]	MPHW	Liquid	0.13 g/animal	6440 animals	9.87	0.47	100 000	5500
	Backpack				56.99	0.65	18 000	4000
	MPHG				58.45	1.58	17 000	1600
Poultry	MPHW	Liquid	0.02 g/animal	70 000 animals	16.51	0.79	61 000	3300
	Backpack				95.30	1.09	10 000	2400
	MPHG				97.75	2.64	10 000	980
Livestock [g]	Aerosol Can	Pressurized Product	0.136 g/animal	120 animals	29.90	0.34	33 000	7700
	Cloth [j]				40.60	0.49	25 000	5300
Poultry Buildings	Aerosol Can		0.0033 g/m^3 [h]	2540 m^3	15.36	0.17	65 000	15000
Horses	Cloth [k]	Liquid	0.13 g/animal	120 animals	10.23	0.15	98 000	18000
PPE: CR coveralls with a CR hood over long-sleeved shirt, long pants, CR gloves, socks, CR footwear and a respirator [i]								
Greenhouse peppers, Pear orchard, Blueberry, Grape,	HH AB/MB	Liquid	0.00075 kg/L	150 L	45.87	5.54	22 000	470

Crop	Application equipment	Formulation	Maximum application rate	ATPD/AHPD	Dermal exposure (µg/kg bw/day) [a]	Inhalation exposure (µg/kg bw/day) [b]	Dermal MOE [c]	Inhalation MOE [d]
Raspberry, Outdoor Ornamentals, Ornamental Trees and Shrubs								
Livestock [g]			0.13 g/animal	6440 animals	341.63	41.24	2900	63
Poultry			0.02 g/animal	70 000 animals	571.29	68.96	1750	38

MLA = mixer, loader, applicator; MOE = margin of exposure; MPHW = manually pressurized handwand; MPHG = mechanically pressurized handgun; CR = chemical resistant; HH AB/MB = handheld airblast/mistblower; ATPD = area treated per day; AHPD = amount handled per day; PPE = personal protective equipment
Shaded cells indicate that the target MOE was not met and further mitigation is required.
[a] Where dermal exposure (µg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg.
[b] Where inhalation exposure (µg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg.
[c] Based on a short-, intermediate-term dermal NOAEL of 1000 mg/kg bw/day and a target MOE of 300.
[d] Based on an intermediate-term inhalation NOAEL of 2.6 mg/kg bw/day and a target MOE of 1000. For pastures, based on a short-term inhalation NOAEL of 2.6 mg/kg bw/day and a target MOE of 300.
[e] Maximum application rate was calculated based on a spray volume of 100 L/ha and the highest application rate for roses and ornamental tress/shrubs.
[f] Airblast application equipment exposure was used as surrogate for truck-mounted ultra low volume (ULV) sprayer.
[g] Includes horses, beef and diary cattle, hogs, mules, sheep, goats, swine, and ponies.
[h] Rate is expressed in m^3 and not per animal since the product is applied as mist over the birds.
[i] NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
[j] Assessed using unit exposures for aerosol (M/L) + paintbrush (A)
[k] Assessed using unit exposures for liquid (M/L) + paintbrush (A)

Table 12 Intermediate-term exposure estimates and MOEs for occupational handlers for agricultural uses requiring mitigation

Crop	Application equipment	Formulation	Maximum application rate	ATPD/ AHPD	Dermal exposure (µg/kg bw/day) [a]	Inhalation exposure (µg/kg bw/day) [b]	Dermal MOE [c]	Inhalation MOE [d]
PPE: Baseline – long pants, long-sleeved shirt, CR gloves + Respirator [f]								
Greenhouse peppers, Blueberry, Grape, Raspberry, Herbs and Spices, Beans (pinto, snap, wax), Tomato (field), Outdoor Ornamentals, Ornamental Trees and Shrubs	MPHG	Liquid	0.75 g/L [e]	3800 L	198.98	0.54	5000	4800

Crop	Application equipment	Formulation	Maximum application rate	ATPD/ AHPD	Dermal exposure (µg/kg bw/day) [a]	Inhalation exposure (µg/kg bw/day) [b]	Dermal MOE [c]	Inhalation MOE [d]
PPE: CR coveralls with a CR hood over long-sleeved shirt, long pants, CR gloves, socks, CR footwear and a respirator [f] + Limit amount handled per day to 0.05 kg a.i./day								
Greenhouse peppers, Pear orchard, Blueberry, Grape, Raspberry, Outdoor Ornamentals, Ornamental Trees and Shrubs	HH AB/MB	Liquid	0.05 kg a.i./day		21.41	2.59	47 000	1000
Livestock [g]					21.73	2.63	46 000	1000
Poultry					21.20	2.56	47 000	1000

MLA = mixer, loader, applicator; MOE = margin of exposure; MPHG = mechanically pressurized handgun; CR = chemical resistant; ATPD = area treated per day; AHPD = amount handled per day; PPE = personal protective equipment; HH AB/MB = handheld airblast/mistblower

[a] Where dermal exposure (µg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg.

[b] Where inhalation exposure (µg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg.

[c] Based on an intermediate-term dermal NOAEL of 1000 mg/kg bw/day and a target MOE of 300.

[d] Based on an intermediate-term inhalation NOAEL of 2.6 mg/kg bw/day and a target MOE of 1000.

[e] Maximum application rate was calculated based on a spray volume of 100 L/ha and the highest application rate for outdoor ornamentals (0.0075 g a.i./m^2).

[f] NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.

[g] Includes horses, beef and diary cattle, hogs, mules, sheep, goats, swine, and ponies.

Table 13 Short-, intermediate-, and long-term commercial application to non-agricultural/structural areas (commercial and residential sites)

Formulation	Application method	Application equipment	PPE	Max application rate	ATPD	Dermal exposure (mg/kg/day) [a]	Inhalation exposure (mg/kg/day) [b]	Dermal MOE [c]	Inhalation MOE [d]
PP	Space; Surface spray: Spot, CC, Broadcast (Indoor and Outdoor); Total Release Fogger	Aerosol (RTU)	Baseline	0.01 kg a.i./can	14 cans [e]	0.2565	0.0029	3900	900
	Metered Release (Indoor) [f]	Automatic Dispenser	-	-	-	-	-	-	-
	Mosquito Abatement (broadcast	Aerosol (RTU)	Baseline	0.0055 kg a.i./can	14 cans [e]	0.1411	0.0016	7100	1600

Formulation	Application method	Application equipment	PPE	Max application rate	ATPD	Dermal exposure (mg/kg/day) [a]	Inhalation exposure (mg/kg/day) [b]	Dermal MOE [c]	Inhalation MOE [d]
	spray) (Outdoor)								
	Mosquito Abatement (fogging spray) (Outdoor)	Machine that produces mist/fog [g]	CR coveralls, CR hood, CR gloves, CR footwear and socks, respirator	0.035 kg a.i./ha	0.81 ha [h]	0.0115	0.0014	87 000	1900
SN, EC	Space Spray (Indoor)	MPHS [g]	CR coveralls, CR hood, CR gloves, CR footwear and socks, respirator	0.0000497 kg a.i./m^3	28317 m^3 [i]	0.5738	0.0693	1700	38
		Stationary Fogger	Baseline			0.0010	0.00001	970 000	230 000
	Surface spray: Broadcast, Spot, CC (Indoor)	PCO MPHW [j]	Baseline	0.00028 kg a.i./m^2	1040 m^2 [k]	0.3125	0.0012	3200	2200
		Trigger-pump Sprayer				0.3835	0.0003	2600	9100
	Surface Spray (Stored Grains)	MPHS [g]	CR coveralls, CR hood, CR gloves, CR footwear and socks, respirator	0.000165 kg a.i./m^2	465 m^2 [l]	0.0313	0.0038	32 000	690
	Surface spray: Broadcast, Perimeter, CC (Outdoor)	MPHW	Baseline	0.000046 kg a.i./m^2	8100 m^2 [m]	0.0044	0.0002	230 000	12 000
		Backpack				0.0254	0.0003	39 000	9000
		MPHG			40 500 m^2 [m]	0.1301	0.0035	7700	740
		Hose-end Sprayer			20 000 m^2 [m]	0.3681	0.00006	2700	44000
		Turf-gun Sprayer				0.0090	0.00005	110 000	57 000
	Mosquito Abatement Fogging spray (Outdoor)	MPHS [g]	CR coveralls, CR hood, CR gloves, CR footwear and socks, respirator	0.00295 kg a.i./ha	0.81 ha [h n]	0.0010	0.0001	1000 000	22 000
SN	Mosquito Abatement – Truck mounted	Truck mounted Sprayer	Baseline	0.00295 kg a.i./ha	1200 ha [n]	0.1694	0.0004	5900	6100
DU	Dust-on: CC, Spot, Perimeter	Bulbous/Plunger Duster	Baseline	0.00006 kg a.i./m^2	111 m^2 [o]	0.0130	0.0002	77 000	12 000

Formulation	Application method	Application equipment	PPE	Max application rate	ATPD	Dermal exposure (mg/kg/day) [a]	Inhalation exposure (mg/kg/day) [b]	Dermal MOE [c]	Inhalation MOE [d]
	(Indoor)	Shaker Can, Hand-Crank Duster, Electric/Power Duster				0.0202	0.0032	50 000	810

PPE = personal protection equipment; MOE = margin of exposure; RTU = ready-to-use; PP = pressurized product; CC = crack and crevice; CR = chemical resistant; PCO = pest control operator; MPHW = manually pressurized handwand; MPHG = mechanically pressurized handgun; MPHS = mechanically pressurized handheld sprayer for mists, aerosols, and fogs; Max = maximum; SN = solution; EC = emulsifiable concentrate; DU = dust
Baseline PPE = long pants, long sleeved shirt, CR gloves
Shaded cells indicate that target MOE was not met and mitigation measures are required.
[a] Where dermal exposure (µg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg.
[b] Where inhalation exposure (µg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg.
[c] Based on an intermediate-term dermal NOAEL of 1000 mg/kg bw/day and a target MOE of 300.
[d] Based on an intermediate-term inhalation NOAEL of 2.6 mg/kg bw/day and a target MOE of 1000.
[e] Based on USEPA Revised RED for PYR (USEPA, 2006a) - 7 sites treated per day. USEPA Revised RED for PBU (USEPA, 2006b) - 2 cans used per site.
[f] Minimal applicator exposure expected.
[g] Unit exposures based on Thouvenin (2015) and Testman (2015).
[h] Value from USEPA Revised RED for PYR (USEPA, 2006a) for MPHW (2 acres).
[i] Value from USEPA review of PYR (USEPA, 2017a) for size of livestock housing/barns, warehouses, and food handling establishments (1 000 000 ft^3).
[j] Unit exposures based on Krolski (2014).
[k] Value from USEPA Revised RED for PYR (USEPA, 2006a) for surface and crack and crevice application to indoor sites; 7 sites per day, each site is 1600 ft^2.
[l] Value rom USEPA Revised RED for PYR (USEPA, 2006a); 5 grain storage bins treated per day, 1000ft^2 per bin.
[m] Based on PMRA default assumptions.
[n] Value from USEPA Revised RED for PYR (USEPA, 2006a, 2017a).
[o] Value based on USEPA PBU RED (USEPA, 2017b) for MPHW/Backpack for wettable powder formulations.

Table 14 Short-, intermediate-, and long-term commercial application to non-agricultural/structural areas (commercial and residential) requiring mitigation

Formulation	Application method	Application equipment	PPE	Max application rate (amount handled per day)	Dermal exposure (mg/kg/day) [a]	Inhalation exposure (mg/kg/day) [b]	Dermal MOE [c]	Inhalation MOE [d]
SN, EC	Space Spray (Indoor), Surface Spray (Stored Grains)	MPHS [e]	CR coveralls, CR hood, CR gloves, CR footwear and socks, respirator	(0.05 kg a.i./day) [f]	0.0215	0.0026	46 000	1000
	Surface spray:	MPHG	Baseline +	0.000046 kg	0.1301	0.0004	7700	7400

Formulation	Application method	Application equipment	PPE	Max application rate (amount handled per day)	Dermal exposure (mg/kg/day) [a]	Inhalation exposure (mg/kg/day) [b]	Dermal MOE [c]	Inhalation MOE [d]
	Broadcast, Perimeter, CC (Outdoor)		Respirator	a.i./m^2				
DU	Dust-on: CC, Spot, Perimeter (Indoor)	Shaker Can, Hand-Crank Duster, Electric/Power Duster	Baseline + Dust Mask	0.00006 kg a.i./m^2	0.0202	0.0006	50 000	4000

PPE = personal protection equipment; MOE = margin of exposure; CR = chemical resistant; MPHG = mechanically pressurized handgun; Max = maximum; SN = solution; EC = emulsifiable concentrate; CC = crack and crevice; MPHS = mechanically pressurized handheld sprayer for mists, aerosols, and fogs
Baseline PPE = long pants, long sleeved shirt, CR gloves; Respirator = NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides.
[a] Where dermal exposure (µg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg.
[b] Where inhalation exposure (µg/kg bw/day) = (unit exposure × area treated per day × application rate)/80 kg.
[c] Based on an intermediate-term dermal NOAEL of 1000 mg/kg bw/day and a target MOE of 300.
[d] Based on an intermediate-term inhalation NOAEL of 2.6 mg/kg bw/day and a target MOE of 1000.
[e] Unit exposures based on Thouvenin (2015) and Testman (2015).
[f] Limit amount handled per day to 0.05 kg a.i./day.

Table 15 Postapplication exposure and risk assessment for agricultural crops

Crop	Activity	TC (cm^2/hr)	Rate	Maximum number of applications per year	Minimum interval between applications (days)	MOE (Day 0) [a]	REI (Days) [b]
Blueberry, Raspberry, Herbs and Spices, Beans, Tomato	All	1750	0.06 kg/ha	8	7	20 000	0.5
Ornamental Trees and Shrubs	All	1750	0.059 kg/ha	10	7	20 000	0.5
Outdoor Ornamentals	All	4000	0.075 kg/ha	8	7	7000	0.5
Grape	All	19 300	0.06 kg/ha	8	7	1800	0.5
Pear Orchards	All	3000	0.059 kg/ha	10	7	12 000	0.5
Greenhouse Peppers	All	1400	0.059 kg/ha	10	7	4800	0.5

Crop	Activity	TC (cm^2/hr)	Rate	Maximum number of applications per year	Minimum interval between applications (days)	MOE (Day 0) [a]	REI (Days) [b]
Pasture	All	1750	0.003 kg/ha	25	1	82 000	0.5
Golf Course [c]	Scouting	1000	0.00295 kg/ha	180	1	510 000	Until sprays have dried

MOE = margin of exposure; TC = transfer co-efficient; REI = restricted-entry interval

Since no DFR/TTR studies were submitted, a peak default DFR value of 25% was used for all crops and a peak TTR value of 1% was used for turf. A10% dissipation rate per day was used for outdoor crops, a 10% dissipation rate was used for turf, and a 0% dissipation rate per day was used for greenhouse vegetable crops.

[a] Based on a dermal NOAEL of 1000 mg/kg bw/day and a target MOE of 300.

[b] If the target MOE is met on day 0, the REI is set at 12 hours (0.5 days).

[c] Golf course information indicates that application is to areas where mosquitos are present (in other words, marshlands); therefore, only a scouting postapplication assessment was performed as other golf course maintenance activities are not expected in the application region.

Appendix VI Aggregate exposure and risk assessment tables

Table 1 Summary of co-occurring exposures

Scenario	Lifestage	Co-occurring exposures[a]
Lawns and Turf [b]	Adult	Applicator Inhalation Exposure Dietary Exposure
	Children (1<2)	Hand-to-mouth Exposure Dietary Exposure
Gardens and Trees [b, c]	Adult	Applicator Inhalation Exposure Dietary Exposure
Outdoor Fogging/Misting Systems	Adult	Applicator Inhalation Exposure Postapplication Inhalation Exposure (ABMS, OASS, Coils) Dietary Exposure
	Children (3<6)	Postapplication Inhalation Exposure (ABMS) Hand-to-Mouth Exposure Dietary Exposure
	Children (1<2)	Postapplication Inhalation Exposure (OASS, Coils) Hand-to-Mouth Exposure Dietary Exposure
Indoor Environments	Adult	Applicator Inhalation Exposure Postapplication Inhalation Exposure (space sprays) Dietary Exposure
	Children (1<2)	Postapplication Inhalation Exposure (space sprays) Object-to-Mouth Exposure Dietary Exposure
Mosquito Abatement	Adult	Postapplication Inhalation Exposure Dietary Exposure
	Children (1<2)	Postapplication Inhalation Exposure Hand-to-Mouth Exposure Dietary Exposure
Treated Pets [c]	Adult	Applicator Inhalation Exposure Dietary Exposure
	Children (1<2)	Hand-to-Mouth Exposure Dietary Exposure

ABMS = animal barn misting system; OASS = outdoor aerosol space sprays

[a] Only exposure that had toxicological significance to the aggregate assessment are listed. For short-, intermediate-term exposure, there is no dermal aggregate endpoint. All scenarios were considered to be short-, intermediate-term exposure except for indoor environments, which also considered long-term exposure for bed bug applications. The highest exposure from each scenario was used to determine aggregate exposure.

[b] No postapplication inhalation exposure is expected.

[c] Only children aged 6<11 years are expected to conduct activities in gardens and trees; therefore, no incidental oral exposure is expected.

Table 2 Short- to intermediate-term aggregate exposure and risk assessment

Scenario	Lifestage	Inhalation exposure (mg/kg bw/day) [a]	Inhalation MOE [b]	Incidental oral exposure (mg/kg bw/day) [c]	Chronic dietary exposure (mg/kg bw/day) [d]	Total oral exposure (mg/kg bw/day) [e]	Oral MOE [b]	Aggregate MOE [f]
Lawns and Turf	Adult	3.2×10^{-4}	25 000	-	0.00203	0.0020	9900	7100
	Children (1<2)	-	-	0.0013	0.009296	0.0106	1900	1900
Gardens and Trees	Adult	6.4×10^{-4}	13 000	-	0.00203	0.0020	9900	5500
Outdoor Fogging/Misting Systems	Adult - OASS	1.9×10^{-3}	4300	-	0.00203	0.0020	9900	3000
	Adult – Coils	7.1×10^{-5}	110 000					9100
	Adult - ABMS	1.8×10^{-4}	44 000					8000
	Adult – Mosquito Abatement	8.4×10^{-4}	9600					4900
	Children (3<6) - ABMS	2.6×10^{-4}	32 000	0.0016	0.006942	0.0086	2300	2200
	Children (1<2) - OASS	0.0067	1200	0.00097	0.009296	0.0103	1900	750
	Children (1<2) - Coil	2.7×10^{-4}	30 000	-		0.0093	2200	2000
	Children (1<2) – Mosquito Abatement	3.2×10^{-3}	2600	0.0002		0.0094	2100	1200
Indoor Environments	Adult	0.0068	1200	-	0.00203	0.0020	9900	1100
	Children (1<2)	0.0068	1200	0.0235	0.009296	0.0328	610	400
Treated Pets	Adult	3.9×10^{-4}	20 000	-	0.00203	0.0020	9900	6600
	Children (1<2)	-	-	0.0011	0.009296	0.0103	1900	1900

OASS = outdoor aerosol space sprays; ABMS = animal barn misting systems; MOE = margin of exposure

[a] Inhalation exposure = Handler inhalation exposure (for adults) + Postapplication inhalation exposure. Highest inhalation exposure scenario was used for the aggregate risk assessment.

[b] MOE = NOAEL (mg/kg bw/day)/Exposure (mg/kg bw/day). Short- and intermediate-term aggregate endpoints for oral and inhalation exposure are 20 mg/kg bw/day and 8.1 mg/kg bw/day, respectively. Target MOE is 300.

[c] Incidental oral exposure used for aggregate risk assessment is highest of hand-to-mouth or object-to mouth.

[d] Chronic dietary exposure is based on information provided in the dietary risk assessment.

[e] Total Oral Exposure (mg/kg bw/day) = HtM exposure (for children) + Chronic dietary exposure.

[f] Aggregate MOE = $1/((1/MOE_{inhalation}) + (1/MOE_{oral}))$

Table 3 Long-term aggregate exposure and risk assessment

Scenario	Lifestage	Incidental oral exposure (mg/kg bw/day) [a]	Chronic dietary exposure (mg/kg bw/day) [b]	Total oral exposure (mg/kg bw/day) [c]	Aggregate MOE [d]
Indoor Environments	Children (1<2)	0.0038	0.009296	0.01305	340

MOE = margin of exposure

[a] Incidental oral exposure used for aggregate risk assessment was object-to mouth since it was a higher value than hand-to-mouth.

[b] Chronic dietary exposure is based on information provided in the dietary risk assessment.

[c] Total Oral Exposure (mg/kg bw/day) = Incidental Oral exposure + Chronic dietary exposure.

[d] MOE = NOAEL (mg/kg bw/day)/Exposure (mg/kg bw/day). Long-term aggregate endpoint for incidental oral of 4.4 mg/kg bw/day was used to calculate the long-term aggregate risk. Target MOE is 300.

Appendix VII Environmental assessment

Table 1 Fate and behaviour of pyrethrins in the environment

Type of study (PMRA#)	Endpoint	Value	Comments
Hydrolysis (2134295)	Half-life	pH 5: stable pH 7: stable pH 9: 14-17 d	Important route of transformation at pH 9. Major transformation product: Chrysanthemic acid 65% AR at day 30. (MRID 43188201; 43567502)
Phototransformation in water (2630000)	Half-life	1 h 11.8 h	Pyrethrin 1 underwent photo-initiated isomerization to form primarily the e-isomer Overall calculated half-life of pyrethrin I and E-isomer was 11.8 hrs Important route of transformation. Major transformation product E-isomer 55.7% AR at hour 2. (MRID 43096601; 43567601)
Phototransformation on soil (2630000)	Half-life	12.9 h	Important route of transformation. No major transformation products. USEPA classified as supplemental study. (MRID 43096602)
Phototransformation in air	Half-life	0.036 days (26 min)	AopWin v1.92 estimate based on overall hydroxyl radical rate constant of 300.95 E-012 cm^3/molecule-sec
Aerobic biotransformation in water/sediment (2630000)	DT_{50}	10.5 d 6.44 d 5.37 d	Important route of transformation. Non-persistent Major transformation product chrysanthemic acid 14% AR in water (30 d) and 8.1% AR in sediment. Pyrethrin I has a strong affinity for sediment based on Kx_{oc} values (90^{th} centile of mean = 7.84 d, based on values corrected to 25°C)
Anaerobic biotransformation in water/sediment (2630000)	DT_{50}	Biphasic: Initial half-life = 27.8 d in sediment And second half-life = 86 d in sediment	Slightly – moderately persistent. Pyerethrin 1 was not detected in the water phase. Major transformation product in water chrysanthemic acid 10% (90 d) and chrysanthemum dicarboxylic acid at 14.2% AR (day 254). In sediment jasmolin I measured at 10% AR (day 364). CO_2 = 13.5% AR (day 364).

Type of study (PMRA#)	Endpoint	Value	Comments
Aerobic biotransformation in soil (2958240)	DT_{50}	DT_{50} = 1.88 days (SFO) at 25°C; DT_{50} = 2.66 days adjusted to 20°C	Important route of transformation. Non-persistent Unidentified major transformation products (total) reached maximum of 40.3% AR at day 3 and declined to 12.2%AR at test termination (Day 59) (MRID 43499803)
Aerobic biotransformation in soil (2958241)	DT_{50}	silt loam (EFS-483) = 0.74 days (SFO) loam (EFS-462) = 3.51 days (SFO) Silty Clay Loam (EFS-460 = 5.53 days (SFO)	Important route of transformation. Non-persistent – slightly persistent Unidentified major transformation products 8.79% AR maximum at day 2 in silt loam soil. (MRID 49687101) 90th centile of mean for all aerobic soil endpoints = 4.74 d, based on half-lives adjusted to 20°C)
Adsorption/Desorption (2630000)	K_{oc}	12 472–37 847	Immobile
Volatilization (2630000)	Rate	≤0.02 µg/cm^{2}h	Limited volatility. Maximum volatilized residues at 30 d were 16% of which 9% was CO_2, 0.3% was pyrethrin, 10% was chrysanthemic acid and ≤2.4% was attributed to 2 unidentified transformation products. (MRID 43096604)
Terrestrial Field Dissipation Soil (2630000)	Half-life	<1 d	Bare ground in California, Georgia and Michigan. No Canadian data available
Bioaccumulation	log K_{ow}	5.9 pyrethrin I 4.3 pyrethrin II	Potential for bioaccumulation
Bioconcentration factors		873-fold nonedible tissue 471-fold whole fish 127 edible tissue	Depuration rapid - after 1 d 66% AR in nonedible, 77% AR in edible tissues, 68% AR in whole fish. After 14 d pyrethrin I below detection limit. Pyrethrin I, 56.1% AR and chrysanthemic acid 29.5% AR in edible tissues,. In nonedible tissues pyrethrin I, 19.6% AR and chrysanthemic acid 21.8% AR.

Table 2 Summary of ecotoxicity endpoints for organisms exposed to pyrethrins and pyrethrins formulated with piperynol butoxide

PMRA#	Species	Type of test	Toxicity endpoint	Comments
Terrestrial Organisms				
2134300	Honey bee (*Apis mellifera*)	48-h Acute contact	LD_{50} = 0.022 µg a.i./bee	Highly toxic
2630000	Honey bee (*Apis mellifera*)	48-h Acute Oral	LD_{50} = 0.15 ug a.i./bee	Highly toxic
2837888	Aphid parasitoid (*Aphidius rhopalosiphi)* CPY8EC414 (2% pyrethrins)	Contact (barley seedlings)	LR_{50} = 35.6 g a.i./ha LR_{50} = 35 600 mg a.i./ha Based on reduction in reproductive capacity.	
2134301	Bobwhite quail (*Colinus virginianus*)	Acute oral	LD_{50} = 250 mg a.i./kg bw/day NOEL = 31.3 mg a.i./kg bw/day, based on signs of toxicity.	Moderately toxic
2134299	Bobwhite quail (*Colinus virginianus*)	8-d Acute Dietary	LC50 >5620 ppm a.i. Converted to daily dose >1124 mg a.i./kg bw/day) NOEC = 1780 ppm a.i. (366 mg a.i./kg bw/day).	Practically non-toxic
2837888	Mallard duck	Dietary	LC_{50} >1521 mg a.i./kg bw/day LC_{50} >875.7 mg a.i./kg bw/day	Slightly toxic
2958242	Mallard duck	Reproductive	NOEC = 2000 ppm a.i. (266 mg a.i./kg bw/day)	No adverse effects noted at any test levels
2563931	Rat - Sprague-Dawley (57.57% pyrethrins)	Acute oral	LD_{50} (females) = 700 mg a.i./kg bw LD_{50} (males) = 2140 mg a.i./kg bw	Slightly toxic
2563931	Rat - Sprague-Dawley (57.57% pyrethrins)	Reproductive	NOAEL = 100 ppm (6.4 mg a.i./kg bw/day) LOAEL = 1000 ppm (65 mg/kg/day)	2-generational reproductive endpoint is based on decreases in F1b pup body weight during lactation

PMRA#	Species	Type of test	Toxicity endpoint	Comments
Aquatic Organisms – Freshwater				
2134308	*Daphnia magna*	96-h Acute	EC_{50} = 11.6 ug a.i./L (95% C.I. = 9.6 – 14.2) EC_{50} = 0.0116 mg a.i./L	Very highly toxic
2134309	*Daphnia magna*	48-h acute toxicity (test substance was Pyrenone Crop spray formulated with 6.02% total pyrethrins and 60.25% piperonyl butoxide	EC_{50} = 6.7 (95% C.I. 5.7 – 7.9) ug a.i./L EC_{50} = 0.0067 mg a.i./L	Very highly toxic
2134303	*Daphnia magna*	Chronic (Life-cycle toxicity)	NOEC = 0.86 ug a.i./L (0.00086 mg a.i./L) based on cumulative no. of off-spring	
2837888	Midge (*Chironomus riparius)*	28-d (static)	NOEC = 0.0097 mg .a.i./L	
2929913	Midge, *Chironomus dilutes* Technical grade active ingredient (52.2%)	Chronic, 63-d	Pore water NOEC = 0.04 ug a.i./L NOEC = 0.00004 mg a.i./L Sediment (dry weight) NOEC = 41 ug a.i./kg dw NOEC = 0.041mg a.i./kg dw Sediment, OC NOEC = 1600 ug a.i./kg $_{OC}$ NOEC = 1.60 mg a.i./kg $_{OC}$	
2929913	Amphipod*, Hyalella azteca* Technical grade active ingredient (52.2%)	Chronic, 42-d	Pore water NOEC = 3.5 ug a.i./L NOEC = 0.0035 mg a.i./L Sediment (dry weight) NOEC = 6,200 ug a.i./kg dw NOEC = 6.20 mg a.i./kg dw Sediment, OC NOEC = 124 ug a.i./kg $_{OC}$ NOEC = 0.124 mg a.i./kg $_{OC}$	
2134306	Rainbow trout *(Oncorhynchus mykiss)*	96-h Acute	96-h EC_{50} = 5.1 ug a.i./L 96-h LC_{50} = 0.0051 mg a.i./L	Very highly toxic

PMRA#	Species	Type of test	Toxicity endpoint	Comments
2134307	Rainbow trout *(Oncorhynchus mykiss)*	96-hAcute (conducted with synergist PBU included)	96-h EC_{50} = 3.4 ug a.i./L 96-h LC_{50} = 0.0034 mg a.i./L	Very highly toxic
2134304	Bluegill Sunfish (*Lepomis macorochirus*)	96-h Acute	96-h EC_{50} = 10.6 ug a.i./L 96-h LC_{50} = 0.0106 mg a.i./L	Very highly toxic
2134305	Bluegill Sunfish (*Lepomis macorochirus*)	96-hAcute (conducted with synergist PBU included)	96-h EC_{50} = 3.4 ug a.i./L 96-h LC_{50} = 0.0034 mg a.i./L	Very highly toxic
2134302	Fathead Minnow (*Pimphales promelas*)	Early life-stage	NOEC = 1.9 µg a.i./L based on hatchling success, growth and mean wet weight.	
2929913	Duckweed (*Lemna gibba*) (TEP; 5.9% Pyr + 56.6% PBO)	7-d	EC_{50} = 1,230 ug a.i./L (95% CI = 928-1620 ug a.i./L) based on Reduced frond number, biomass EC_{50} = 1.23 mg a.i./L NOEC = 0.480 mg a.i/L	
2929913	Freshwater Green Alga, (*Pseudokirch-neriella subcapitata*) (TEP; 5.9% Pyr + 56.6% PBO)	96-hr	EC_{50}= 105 ug a.i./L (95%CI = 94-116 ug a.i./L), based on significant reduction in area under the curve EC_{50} = 0.105 mg a.i./L NOEC = 0.0.029 mg a.i/L	
2929913	Freshwater Cyanobacteria (*Anabaena flos-aquae)* (TEP; 5.9% Pyr + 56.6% PBO)	96-hr	EC_{50} = > 460 ug a.i./L no treatment related effects EC_{50} = 0.460 mg a.i./L NOEC = 0.460 mg a.i./L	
2929913	Freshwater Diatom (*Navicula pelliculosa*) (TEP; 5.9% Pyr + 56.6% PBO)		EC_{50} = 210 ug a.i./L (95%CI = 161 - 275 ug a.i./L), based on significant reduction in area under the curve EC_{50} = 0.210 mg a.i./L NOEC = 0.016 mg a.i./L	
Aquatic Organisms – Marine				
2134310	Sheepshead Minnow (*Cyprinodon variegatus*)	96-h Acute toxicity	LC_{50} = 16.0 µg a.i./L (95% C.I. = 14.5 – 17.7 µg a.i./L) LC_{50} = 0.016 mg a.i./L	Very highly toxic
2134311	Sheepshead Minnow (*Cyprinodon variegatus*)	96-h Acute toxicity Conducted with Pyrenone Crop Spray formulated	LC_{50} = 3.8 µg a.i./L (95% C.I. = 3.4 – 4.5 µg a.i./L) LC_{50} = 0.0038 mg a.i./L	Very highly toxic

PMRA#	Species	Type of test	Toxicity endpoint	Comments
		with PYR + PBU		
2134312	Eastern Oyster (*Crassostrea virginica*)	96 h – Shell deposition	96-h LC_{50} = 86 ug ai./L (95% C.I. = 72 - 100 ug a.i./L) 96-h LC_{50} =0.0 86 mg ai./L 96-h NOEC) = <14 ug a.i./L based on reduction in shell deposition	Very highly toxic
2134313	Eastern Oyster (*Crassostrea virginica*)	96 h – Shell deposition Conducted with Pyrenone Crop Spray formulated with PYR + PBU	96-h LC_{50} = 26 ug ai./L (95% C.I. = 21 - 32 ug a.i./L) 96-h LC_{50} =0.0 26 mg ai./L 96-h NOEC) = <3.1 ug a.i./L based on reduction in shell deposition	Very highly toxic
2134314	Mysid shrimp (*Mysidopsis bahia*)	96-h Acute toxicity	96-h LC_{50} = 1.4 ug ai./L (95% C.I. = 1.1 – 1.8 ug a.i./L) 96-h LC_{50} =0.0014 mg ai./L 96-h NOEC) = <0.29 ug a.i./L based on no mortality or abnormal behaviour	Very highly toxic
2134315	Mysid shrimp (*Mysidopsis bahia*)	96-h Acute toxicity Conducted with Pyrenone Crop Spray formulated with PYR + PBU	96-h LC_{50} = 0.14 ug ai./L (95% C.I. = 0.084 – 0.25 ug a.i./L) 96-h LC_{50} = 0.00014 mg ai./L 96-h NOEC) = 0.084 ug a.i./L	Very highly toxic
2929913	Saltwater Diatom (*Skeletonema costatum*) (TEP; 5.9% Pyr + 56.6% PBO)	96-h Acute toxicity	96-h EC_{50} = 128 ug ai./L (95% C.I. = 86-191 ug a.i./L) based on significant reduction in area under the curve 96-h LC_{50} = 0.128 mg ai./L NOEC = 0.036 mg a.i/L	
2991298	American lobster (*Homarus americanus*) Vet Kem Flea and Tick Pump Spray (0.06% pyrethrins + 0.6% piperonyl butoxide)	48-h acute toxicity	EC_{50}s for each Larval stage I = 0.0044 mg a.i/L II = 0.0027 mg a.i/L III = 0.0014 mg a.i/L IV = 0.0010 mg a.i/L	Very highly toxic

Table 3 Screening level risk assessment for non-target organisms

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
Terrestrial Organisms							
EFSA	*Eisenia foetida*	A14-d acute	LC_{50}= 47.45 mg a.i./kg soil	10	4.75 mg a.i./kg soil	93.6 mg a.i./kg soil	**19.7**
EFSA	*Eisenia foetida*	8-week chronic	NOEC= 0.5 mg a.i./kg soil	1	0.5 mg a.i./kg soil	93.6 mg a.i./kg soil	**187.2**
2837888	Aphid parasitoid (*Aphidius rhopalosiphi)* CPY8EC414 (2% pyrethrins)	Contact (barley seedlings)	LR_{50} = 35.6 g a.i./ha LR_{50} = 35 600 mg a.i./ha Based on reduction in reproductive capacity	1	35 600 mg a.i./ha	152 000 mg a.i./ha* (152 g a.i./ha)	**4.3**
2134301	Bobwhite quail (*Colinus virginianus*)	Acute oral	LD_{50} = 250 mg a.i./kg bw/day NOEL = 31.3 mg a.i./kg bw/day, based on signs of toxicity.	10	25.0 mg a.i./kg bw/day	EDE (mg a.i./kg bw) Small bird: 12.44 Medium bird: 9.71 Large bird: 6.27	Small = 0.50 Medium = 0.39 Large = 0.25
2134299	Bobwhite quail (*Colinus virginianus*)	8-d Acute Dietary	LC_{50} >5620 ppm a.i. Converted to daily dose >1124 mg a.i./kg bw/day) NOEC = 1780 ppm a.i. (366 mg a.i./kg bw/day)	10	112.4 mg a.i./kg bw/day	EDE (mg a.i./kg bw) Small bird: 12.44 Medium bird: 9.71 Large bird: 6.27	Small =0.11 Medium = 0.09 Large = 0.06
2837888	Mallard duck	Dietary	LC_{50} >1521 mg a.i./kg bw/day LC_{50} >875.7 mg a.i./kg bw/day	10	87.6 mg a.i./kg bw/day	EDE (mg a.i./kg bw) Small bird: 12.44 Medium bird: 9.71 Large bird: 6.27	Small = 0.14 Medium = 0.04 Large = 0.07

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
2958242	Mallard duck	Reproductive	NOEC = 2000 ppm a.i. (266 mg a.i./kg bw/day)	n/a	266 mg a.i./kg bw/day	EDE (mg a.i./kg bw) Small bird: 12.44 Medium bird: 9.71 Large bird: 6.27	Small = 0.05 Medium = 0.04 Large = 0.02
2563931	Rat (57.57% pyrethrins)	Acute oral	LD_{50} (females) = 700 mg a.i./kg bw LD_{50} (males) = 2140 mg a.i./kg bw	10	70 mg a.i./kg bw	Mammals EDE (mean nomogram) (mg a.i./kg bw) Small: 4.94 Medium:4.93 Large: 2.63	Small = 0.07 Medium = 0.07 Large = 0.04
2563931	Rat (57.57% pyrethrins)	Reproductive	NOAEL = 6.4 mg a.i./kg bw/day LOAEL = 65 mg a.i./kg bw/day	n/a	6.4 mg a.i./kg bw/day	Mammals EDE (mean nomogram) (mg a.i./kg bw) Small: 4.94 Medium:4.93 Large: 2.63	Small = 0.8 Medium = 0.8 Large = 0.4
Aquatic Organisms – Freshwater							
2134308	*Daphnia magna*	96-h Acute	EC_{50} = 11.6 ug a.i./L (95% C.I. = 9.6 – 14.2) EC_{50} = 0.0116 mg a.i./L	2	0.0058 mg a.i./L	0.02 mg a.i./L	**3.45**
2134309	*Daphnia magna*	48-h acute toxicity (test substance: Pyrenone Crop spray formulated with 6.02% pyrethrins and 60.25% piperonyl butoxide	EC_{50} = 6.7 (95% C.I. 5.7 – 7.9) ug a.i./L EC_{50} = 0.0067 mg a.i./L	2	0.0067 mg a.i./L	0.02 mg a.i./L	**2.99**

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
2134303	*Daphnia magna*	Chronic (Life-cycle toxicity)	NOEC = 0.86 ug a.i./L based on cumulative no. of off-spring	n/a	0.0086 mg a.i./L	0.02 mg a.i./L	**2.33**
2837888	Midge (*Chironomus riparius)*	28-d (static)	NOEC = 0.0097 mg .a.i./L	n/a	0.0097 mg .a.i./L	0.02 mg a.i./L	**2.06**
2929913	Midge, *Chironomus dilutes* Technical grade active ingredient (52.2%)	Chronic, 63-d	Pore water NOEC = 0.04 ug a.i./L NOEC = 0.00004 mg a.i./L Sediment (dry weight) NOEC = 41 ug a.i./kg dw NOEC = 0.041mg a.i./kg dw Sediment, OC NOEC = 1600 ug a.i./kg-$_{OC}$ NOEC = 1.60 mg a.i./kg-$_{OC}$	n/a	0.00004 mg a.i./L (pore water)	0.02 mg a.i./L	**500**
2929913	Amphipod, *Hyalella azteca* Technical grade active ingredient (52.2%)	Chronic, 42-d	Pore water NOEC = 3.5 ug a.i./L NOEC = 0.0035 mg a.i./L Sediment (dry weight) NOEC = 6200 ug a.i./kg dw NOEC = 6.20 mg a.i./kg dw Sediment, OC NOEC = 124 ug a.i./kg-$_{OC}$ NOEC = 0.124 mg a.i./kg-$_{OC}$	n/a	0.0035 mg a.i./L (pore water)	0.02 mg a.i./L	5.71
2134306	Rainbow trout *(Oncorhynchus mykiss)*	96-h Acute	96-h EC_{50} = 5.1 ug a.i./L 96-h LC_{50} = 0.0051 mg a.i./L	10	0.00051 mg a.i./L	0.02 mg a.i./L	**39.22**
2134307	Rainbow trout *(Oncorhynchus mykiss)*	96-h Acute (conducted with synergist PBU included)	96-h EC_{50} = 3.4 ug a.i./L 96-h LC_{50} = 0.0034 mg a.i./L	10	0.00034 mg a.i./L	0.02 mg a.i./L	**58.82**
2134304	Bluegill Sunfish (*Lepomis macorochirus*)	96-h Acute	96-h EC_{50} = 10.6 ug a.i./L 96-h LC_{50} = 0.0106 mg a.i./L	10	0.00106 mg a.i./L	0.02 mg a.i./L	**18.87**
2134305	Bluegill Sunfish (*Lepomis macorochirus*)	96-hr Acute (conducted with synergist PBU included)	96-h EC_{50} = 3.4 ug a.i./L 96-h LC_{50} = 0.0034 mg a.i./L	10	0.00034 mg a.i./L	0.02 mg a.i./L	**58.82**
	Amphibians	No data available, using	96-h EC_{50} = 3.4 ug a.i./L 96-h LC_{50} = 0.0034 mg	10	0.00034 mg a.i./L	0.09 mg a.i./L	**176.47**

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
		most sensitive endpoint from fish studies	a.i./L				
2134302	Fathead Minnow (*Pimphales promelas*)	Early life-stage	NOEC = 1.9 µg a.i./L based on hatchling success, growth and mean wet weight.	n/a	0.0019 mg a.i./L	0.02 mg a.i./L	**10.53**
2929913	Duckweed (*Lemna gibba*) (TEP; 5.9% Pyr + 56.6% PBO)	7-d	EC_{50} = 1230ug a.i./L (95%CI = 928-1620 ug a.i./L) based on Reduced frond number, biomass EC_{50} = 1.23 mg a.i./L NOEC = 0.480 mg a.i/L	2	0.615 mg a.i./L	0.02 mg a.i./L	0.03
2929913	Freshwater Green Alga, (*Pseudokirchneriella subcapitata*) (TEP; 5.9% Pyr + 56.6% PBO)	96-h	EC_{50} = 105 ug a.i./L (95%CI = 94-116 ug a.i./L), based on significant reduction in area under the curve EC_{50} = 0.105 mg a.i./L NOEC = 0.0.029 mg a.i/L	2	0.05 mg a.i./L	0.02 mg a.i./L	0.40
2929913	Freshwater Cyanobacteria (*Anabaena flos-aquae)* (TEP; 5.9% Pyr + 56.6% PBO)	96-h	EC_{50} = >460ug a.i./L no treatment related effects EC_{50} = 0.460 mg a.i./L NOEC = 0.460 mg a.i./L	2	0.023 mg a.i./L	0.02 mg a.i./L	0.87
2929913	Freshwater Diatom (*Navicula pelliculosa*) (TEP; 5.9% Pyr + 56.6% PBO)		EC_{50} = 210 ug a.i./L (95% CI = 161 - 275 ug a.i./L), based on significant reduction in area under the curve EC_{50} = 0.210 mg a.i./L NOEC = 0.016 mg 0.016 mg a.i./Ln/aa.i./L	2	0.105 mg a.i./L	0.02 mg a.i./L	0.19
Aquatic Organisms – Marine							
2134310	Sheepshead Minnow (*Cyprinodon variegatus*)	96-h Acute toxicity	LC_{50} = 16.0 µg a.i./L (95% C.I. = 14.5 – 17.7 µg a.i./L) LC_{50} = 0.016mg a.i./L	10	0.0016 mg a.i./L	0.02 mg a.i./L	**12.50**

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
2134311	Sheepshead Minnow (*Cyprinodon variegatus*)	96-h Acute toxicity Conducted with Pyrenone Crop Spray formulated with PYR + PBU	LC_{50} = 3.8 µg a.i./L (95% C.I. = 3.4 – 4.5 µg a.i./L) LC_{50} = 0.0038 mg a.i./L	10	0.00038 mg a.i./L	0.02 mg a.i./L	**56.63**
2134312	Eastern Oyster (*Crassostrea virginica*)	96-h – Shell deposition	96-h LC_{50} = 86 ug ai./L (95% C.I. = 72 - 100 ug a.i./L) 96-h LC_{50} =0.0 86 mg ai./L 96-h NOEC) = <14 ug a.i./L based on reduction in shell deposition	10	0.0086 mg a.i./L	0.02 mg a.i./L	**2.33**
2134313	Eastern Oyster (*Crassostrea virginica*)	96-h - Shell deposition Conducted with Pyrenone Crop Spray formulated with PYR + PBU	96-h LC_{50} = 26 ug ai./L (95% C.I. = 21 - 32 ug a.i./L) 96-h LC_{50} =0.0 26 mg ai./L 96-h NOEC) = <3.1 ug a.i./L based on reduction in shell deposition	10	0.0026 mg a.i./L	0.02 mg a.i./L	**7.69**
2134314	Mysid shrimp (*Mysidopsis bahia*)	96-h Acute toxicity	96-h LC_{50} = 1.4 ug ai./L (95% C.I. = 1.1 – 1.8 ug a.i./L) 96-h LC_{50} =0.0014 mg ai./L 96-h NOEC) = <0.29 ug a.i./L based on no mortality or abnormal behaviour	10	0.00014 mg a.i./L	0.02 mg a.i./L	**142.86**
2134315	Mysid shrimp (*Mysidopsis bahia*)	96-h Acute toxicity Conducted with Pyrenone Crop Spray formulated with PYR + PBU	96-h LC_{50} = 0.14 ug ai./L (95% C.I. = 0.084 – 0.25 ug a.i./L) 96-h LC_{50} = 0.00014 mg ai./L 96-h NOEC) = 0.084 ug a.i./L	10	0.000014 mg a.i./L	0.02 mg a.i./L	**1428.57**
2929913	Saltwater Diatom (*Skeletonema costatum*) (TEP; 5.9% Pyr + 56.6%	96-h Acute toxicity	96-h EC_{50} = 128 ug ai./L (95% C.I. = 86-191 ug a.i./L) based on significant reduction in area	2	0.064 mg a.i./L	0.02 mg a.i./L	0.31

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
	PBO)		under the curve 96-h LC_{50} = 0.128 mg ai./L NOEC = 0.036 mg a.i/L				
2991298	American lobster (*Homarus americanus*) Vet Kem Flea and Tick Pump Spray (0.06% pyrethrins + 0.6% piperonyl butoxide)	48-h acute toxicity	Larval stage I = 0.0044 mg a.i/L II = 0.0027 mg a.i/L III = 0.0014 mg a.i/L IV = 0.0010 mg a.i/L	10	Larval stage I = 0.00044 mg a.i/L II = 0.00027 mg a.i/L III = 0.00014 mg a.i/L IV = 0.00010 mg a.i/L	0.02 mg a.i./L	Larval stage **I = 45.55** **II = 74.07** **III = 142.86** **IV = 200**

***** Highest cumulative application rate to beans, grape and tomato, all treated using groundboom and airblast spray equipment at 60 g a.i./ha with 8 applications per season and a minimum 7-day application interval.

Table 4 Refined risk assessment for drift

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
Terrestrial Organisms							
2837888	Aphid parasitoid (*Aphidius rhopalosiphi)* CPY8EC414 (2% pyrethrins)	Contact (barley seedlings)	LR_{50} = 35.6 g a.i./ha LR_{50} = 35 600 mg a.i./ha Based on reduction in reproductive capacity	1	35 600 mg a.i./ha	Groundboom** On-field 38 225 mg a.i./ha Off-field 917 mg a.i./ha	**On-field 1.07** Off-field 0.05
Aquatic Organisms – Freshwater							
2134308	*Daphnia magna*	96 h Acute	EC_{50} = 11.6 ug a.i./L (95% C.I. = 9.6 – 14.2) EC_{50} = 0.0116 mg a.i./L	2	0.0058 mg a.i./L	0.00036 mg a.i./L	0.05
2134309	*Daphnia magna*	48-h acute toxicity (test substance: Pyrenone Crop spray formulated	EC_{50} = 6.7 (95% C.I. 5.7 – 7.9) ug a.i./L EC_{50}= 0.0067 mg a.i./L	2	0.0067 mg a.i./L	0.00064 mg a.i./L	0.10

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
		with 6.02% pyrethrins and 60.25% piperonyl butoxide					
2134303	*Daphnia magna*	Chronic (Life-cycle toxicity)	NOEC = 0.86 ug a.i./L based on cumulative no. of off-spring	n/a	0.0086 mg a.i./L	0.00014 mg a.i./L	0.02
2837888	Midge (*Chironomus riparius)*	28-d (static)	NOEC = 0.0097 mg .a.i./L	n/a	0.0097 mg .a.i./L	0.00014 mg a.i./L	0.01
2929913	Midge, *Chironomus dilutes* Technical grade active ingredient (52.2%)	Chronic, 63-d	Pore water NOEC = 0.04 ug a.i./L NOEC = 0.00004 mg a.i./L Sediment (dry weight) NOEC = 41 ug a.i./kg dw NOEC = 0.041mg a.i./kg dw Sediment, OC NOEC = 1600 ug a.i./kg-$_{OC}$ NOEC = 1.60 mg a.i./kg-$_{OC}$	n/a	0.00004 mg a.i./L (pore water)	0.00014 mg a.i./L (water column) 0.000090 mg a.i./L (pore water)	**3.5** **2.25**
2929913	Amphipod, *Hyalella azteca* Technical grade active ingredient (52.2%)	Chronic, 42-d	Pore water NOEC = 3.5 ug a.i./L NOEC = 0.0035 mg a.i./L Sediment (dry weight) NOEC = 6200 ug a.i./kg dw NOEC = 6.20 mg a.i./kg dw Sediment, OC NOEC = 124 ug a.i./kg-$_{OC}$ NOEC = 0.124 mg a.i./kg-$_{OC}$	n/a	0.0035 mg a.i./L (pore water)	0.00014 mg a.i./L	0.04
2134306	Rainbow trout *(Oncorhynchus mykiss)*	96-h Acute	96-h EC_{50} = 5.1 ug a.i./L 96-h LC_{50} = 0.0051 mg a.i./L	10	0.00051 mg a.i./L	0.00036 mg a.i./L	0.71
2134307	Rainbow trout *(Oncorhynchus mykiss)*	96-h Acute (conducted with synergist PBU included)	96-h EC_{50} = 3.4 ug a.i./L 96-h LC_{50} = 0.0034 mg a.i./L	10	0.00034 mg a.i./L	0.00036 mg a.i./L	**1.06**
2134304	Bluegill Sunfish (*Lepomis macorochirus*)	96-h Acute	96-h EC_{50} = 10.6 ug a.i./L 96-h LC_{50} = 0.0106 mg a.i./L	10	0.00106 mg a.i./L	0.00036 mg a.i./L	0.34
2134305	Bluegill Sunfish	96-h Acute	96-h EC_{50} = 3.4 ug a.i./L	10	0.00034 mg a.i./L	0.00036 mg	**1.06**

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
	(*Lepomis macorochirus*)	(conducted with synergist PBU included)	96-h LC_{50} = 0.0034 mg a.i./L			a.i./L	
	Amphibians	No data available, using most sensitive endpoint from fish studies	96-h EC_{50} = 3.4 ug a.i./L 96-h LC_{50} = 0.0034 mg a.i./L	10	0.00034 mg a.i./L	0.00044 mg a.i./L	**1.29**
2134302	Fathead Minnow (*Pimphales promelas*)	Early life-stage (35-d)	NOEC = 1.9 µg a.i./L based on hatchling success, growth and mean wet weight.	n/a	0.0019 mg a.i./L	0.00014 mg a.i./L	0.07
Aquatic Organisms – Marine							
2134310	Sheepshead Minnow (*Cyprinodon variegatus*)	96-h Acute toxicity	LC_{50} = 16.0 µg a.i./L (95% C.I. = 14.5 – 17.7 µg a.i./L) LC_{50} = 0.016mg a.i./L	10	0.0016 mg a.i./L	0.00036 mg a.i./L	0.23
2134311	Sheepshead Minnow (*Cyprinodon variegatus*)	96-h Acute toxicity Conducted with Pyrenone Crop Spray formulated with PYR + PBU	LC_{50} = 3.8 µg a.i./L (95% C.I. = 3.4 – 4.5 µg a.i./L) LC_{50} = 0.0038 mg a.i./L	10	0.00038 mg a.i./L	0.00036 mg a.i./L	0.95
2134312	Eastern Oyster (*Crassostrea virginica*)	96 h – Shell deposition	96-h LC_{50} = 86 ug ai./L (95% C.I. = 72 - 100 ug a.i./L) 96-h LC_{50} =0.0 86 mg ai./L 96-h NOEC) = <14 ug a.i./L based on reduction in shell deposition	10	0.0086 mg a.i./L	0.00036 mg a.i./L	0.04
2134313	Eastern Oyster (*Crassostrea virginica*)	96 h – Shell deposition Conducted with Pyrenone Crop Spray formulated with PYR + PBU	96-h LC_{50} = 26 ug ai./L (95% C.I. = 21 - 32 ug a.i./L) 96-h LC_{50} =0.0 26 mg ai./L 96-h NOEC) = <3.1 ug a.i./L based on reduction in shell deposition	10	0.0026 mg a.i./L	0.00036 mg a.i./L	0.14

PMRA#	Species	Type of test	Toxicity endpoint	Uncertainty factor	Toxicity endpoint adjusted for uncertainty	EECs*	Risk Quotient
2134314	Mysid shrimp (*Mysidopsis bahia*)	96-h Acute toxicity	96-h LC_{50} = 1.4 ug ai./L (95% C.I. = 1.1 – 1.8 ug a.i./L) 96-h LC_{50} =0.0014 mg ai./L 96-h NOEC) = <0.29 ug a.i./L based on no mortality or abnormal behaviour	10	0.00014 mg a.i./L	0.00036 mg a.i./L	**2.57**
2134315	Mysid shrimp (*Mysidopsis bahia*)	96-h Acute toxicity Conducted with Pyrenone Crop Spray formulated with PYR + PBU	96-h LC_{50} = 0.14 ug ai./L (95% C.I. = 0.084 – 0.25 ug a.i./L) 96-h LC_{50} = 0.00014 mg ai./L 96-h NOEC) = 0.084 ug a.i./L	10	0.000014 mg a.i./L	0.00036 mg a.i./L	**25.71**
2991298	American lobster (*Homarus americanus*) Vet Kem Flea and Tick Pump Spray (0.06% pyrethrins + 0.6% piperonyl butoxide)	48-h acute toxicity	Larval stage I = 0.0044 mg a.i/L II = 0.0027 mg a.i/L III = 0.0014 mg a.i/L IV = 0.0010 mg a.i/L	10	Larval stage I = 0.00044 mg a.i/L II = 0.00027 mg a.i/L III = 0.00014 mg a.i/L IV = 0.00010 mg a.i/L	0.00036 mg a.i./L	Larval stage I = 0.82 **II = 13.33** **III = 25.71** **IV = 36.0**

*Maximum application rate of 60 g a.i./ha with 8 applications per season and a minimum 7-day application interval based on modelled run-off EECs for aquatic organisms and foliar interception factor/vegetative distribution factors and 11% off-field spray drift for terrestrial arthropods.
** Highest single application rate was used to refine exposure assessment to beneficial insects.

Table 5 Fate inputs for the ecological modelling

Fate Parameter	Value
Residues modelled	Pyrethrins
K_{oc}	240 L/kg
Water half-life	7.84 days at 25 °C
Sediment half-life	86 days at 25 °C
Photolysis half-life	0.49 days at 34 °N latitude
Hydrolysis	Stable
Soil half-life	4.74 days at 20 °C

Table 6 Level 1 aquatic ecoscenario modelling EECs (µg a.i./L) for pyrethrins, overlying water layer, excluding spray drift

Use pattern	Water Depth	Water column					Pore water	
		Peak	24 hour	96 hour	21 day	Yearly	Peak	21 day
Blueberries, 8 × 60 g a.i./ha	80cm	0.00083 (0.83)	0.00064 (0.64)	0.00036 (0.36)	0.00014 (0.14)	0.000043 (0.043)	0.000091 (0.091)	0.000090 (0.090)
	15cm	0.0041 (4.1)	0.0014 (1.4)	0.00044 (0.44)	0.00015 (0.15)	0.00005 (0.050)	0.00097 (0.097)	0.000094 (0.094)
Beans, 8 × 60 g a.i./ha	80cm	0.00083 (0.83)	0.00064 (0.64)	0.00036 (0.36)	0.00014 (0.14)	0.000043 (0.043)	0.000091 (0.091)	0.000089 (0.089)
	15cm	0.0041 (4.1)	0.0014 (1.4)	0.00044 (0.44)	0.00015 (0.15)	0.00005 (0.050)	0.000097 (0.097)	0.000094 (0.094)
Pear, 10 × 59 g a.i./ha	80cm	0.00022 (0.22)	0.00015 (0.15)	0.000089 (0.089)	0.000026 (0.026)	0.000005 (0.005)	0.000013 (0.013)	0.000012 (0.012)
	15cm	0.0011 (1.1)	0.00033 (0.33)	0.00013 (0.13)	0.000032 (0.032)	0.000006 (0.006)	0.000014 (0.014)	0.000013 (0.013)
Mustard Seed, 8 × 59.625 g a.i./ha	80cm	0.00079 (0.79)	0.00059 (0.59)	0.00033 (0.33)	0.00012 (0.12)	0.000027 (0.027)	0.000074 (0.074)	0.000071 (0.071)
	15cm	0.0042 (4.2)	0.0013 (1.3)	0.00039 (0.39)	0.00013 (0.13)	0.00003 (0.030)	0.000079 (0.079)	0.000077 (0.077)
Tomato, 8 × 60 g a.i./ha	80cm	0.00043 (0.43)	0.00034 (0.34)	0.00019 (0.19)	0.000067 (0.067)	0.000017 (0.017)	0.000038 (0.038)	0.000037 (0.037)
	15cm	0.0022 (2.2)	0.00076 (0.76)	0.00022 (0.22)	0.000071 (0.071)	0.00002 (0.020)	0.000014 (0.041)	0.000039 (0.039)

Table 7 Refined risk assessment for run-off *

Organism	Exposure	Species	Endpoint for RA (mg a.i./L)	Use scenario	Application method	Cumulative application rate (g a.i./ha)	EEC (µg a.i./L)	RQ	LOC exceeded
Freshwater (80-cm depth)									
Fish	Acute	Rainbow trout *(Oncorhynchus mykiss)*	1/10 EC_{50} = 0.00034	Blueberry, Grape, Raspberry	GB – fine spray	129.1	0.0018	**5.2**	**Yes**
				Blueberry, Grape, Raspberry	Airblast – early season	129.1	0.012	**35.1**	**Yes**
				Blueberry, Grape, Raspberry	Airblast – late season	129.1	0.010	**28.0**	**Yes**
				Herbs and Spices (CG 19)	GB – fine spray	129.1	0.0018	**5.2**	**Yes**
				Beans	GB – fine spray	129.1	0.0018	**5.2**	**Yes**
				Tomato	GB – fine spray	129.1	0.0018	**5.2**	**Yes**
				Pear	Airblast – early season	127.6	0.0118	**34.7**	**Yes**
				Pear	Airblast – late season	127.6	0.0094	**27.7**	**Yes**
Marine and estuarine (2-m depth)									
Invertebrate	Acute	Mysid shrimp	1/10 EC_{50} = 0.000014	Blueberry, Grape, Raspberry	GB – fine spray	129.1	0.0007	**50.7**	**Yes**
				Blueberry, Grape, Raspberry	Airblast – early season	129.1	0.0048	**341.3**	**Yes**
				Blueberry, Grape, Raspberry	Airblast – late season	129.1	0.0038	**272.1**	**Yes**
				Herbs and Spices (CG 19)	GB – fine spray	129.1	0.0007	**50.7**	**Yes**
				Beans	GB – fine spray	129.1	0.0007	**50.7**	**Yes**
				Tomato	GB – fine spray	129.1	0.0007	**50.7**	**Yes**
				Pear	Airblast – early season	127.6	0.0047	**337.3**	**Yes**
				Pear	Airblast – late season	127.6	0.0038	**268.9**	**Yes**

*Most sensitive freshwater (Rainbow trout) and marine organism (mysid shrimp) endpoints used to assess risk from spray drift for aquatic organisms

Table 8 Toxic substances management policy considerations-comparison to TSMP track 1 criteria[a]

TSMP Track 1 criteria	TSMP Track 1 criterion value		Active ingredient endpoints	Transformation products endpoints
CEPA toxic or CEPA toxic equivalent	Yes		Pyrethrins can be considered toxic to terrestrial invertebrates and aquatic organisms.	No toxicity information is available for major transformation products chrysanthemic acid and dicarboxylic-chrysanthemic acid.
Predominantly anthropogenic	Yes		-	-
Persistence	Soil	Half-life ≥ 182 days	Half-life = 0.74–5.35 days Pyrethrins do not meet the soil persistence criterion.	No soil degradation information is available for major transformation products chrysanthemic acid and dicarboxylic-chrysanthemic acid.
	Water	Half-life ≥ 182 days	Half-life = 5.37–10.5 days Pyrethrins do not meet the aquatic persistence criterion.	No aquatic degradation information is available for major transformation products chrysanthemic acid and dicarboxylic-chrysanthemic acid.
	Sediment	Half-life ≥ 365 days	Biphasic: Initial half-life = 27.8 d in sediment And second half-life = 86 d in sediment Pyrethrins do not meet the sediment persistence criterion.	No sediment degradation information is available for major transformation products chrysanthemic acid and dicarboxylic-chrysanthemic acid.
	Air	Half-life ≥ 2 days or evidence of long range transport	0.036 days (26 min) Not expected to persist in air thus not expected to undergo long-range atmospheric transport.	Estimated half-life in air for Chrysanthemic acid = 0.12 days (1.5 hrs) Estimated half-life in air for dicarboxylic-chrysanthemic acid = 0.33 days (4.0 hrs) Chrysanthemic acid and dicarboxylic-chrysanthemic acid are not expected to persist in air and thus not expected to undergo long range atmospheric transport.
Bioaccumulation	Log K_{ow} ≥ 5		5.9 pyrethrin I 4.3 pyrethrin II Pyrethrin I may be expected to bioaccumulate	Log K_{ow} estimate for major transformation products chrysanthemic acid and dicarboxylic-chrysanthemic acid are 3.49 and 1.66, respectively. Chrysanthemic acid and dicarboxylic-chrysanthemic acid are not expected to bioaccumulate.
	BCF ≥ 5000		873X non-edible tissue 471X whole fish 127X edible tissue Not expected to bioaccumulate	Not available
	BAF ≥ 5000		No data available	Not available
Is the chemical a TSMP Track 1 substance (all four			No	No

TSMP Track 1 criteria	TSMP Track 1 criterion value	Active ingredient endpoints	Transformation products endpoints
criteria must be met)?			

[a] All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (in other words, all other TSMP criteria are met). The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases. If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met. Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, log K_{ow}).

Appendix VIII Water monitoring data

Water Monitoring Data

In general, water sampling occurred in use areas and during the summer months when pyrethrin-I would be applied. Based on available monitoring data, pyrethrin-I was not detected in any Canadian water sources and was only detected in the single sample from the United States.

Potential drinking water sources for humans

Based on available monitoring data, pyrethrin-I is seldom detected in samples from Canada and the United States. Out of a total of 249 potential drinking water samples analysed, only one sample (0.4%) showed detectable residues though the limit of detection was not reported for the available data. The maximum concentration of pyrethrin-I detected in potential drinking water sources was 0.003 µg/L, which was from the only surface water sample collected in the United States. There were no detections in Canadian potential drinking water sources. The small number of samples and lack of detections in Canada preclude the use of an EEC based on Canadian monitoring data for acute and chronic drinking water exposure assessment.

Water monitoring data, particularly for surface water, may miss peak concentrations, as sampling is typically sporadic and peak concentrations can be flushed through a system in a short amount of time after a run-off event. Therefore, particularly for surface water, EECs generated through modelling are typically better suited for use in an acute dietary risk assessment as opposed to surface water monitoring values. Additionally, due to the small number of samples with extremely low detection frequencies, a reliable chronic exposure estimate cannot be obtained using the Canadian monitoring data.

The use of the daily and yearly modelling EECs are recommended as conservative estimates for the acute and chronic dietary risk assessments of pyrethrin-I in drinking water, respectively.

Surface water relevant for aquatic risk assessments

For aquatic risk assessment purposes, the highest concentration of pyrethrin-I detected in water (0.003 µg/L) was the only sample collected in the United States. When considering Canadian data, there were no detections in any of the 47 surface water samples taken in Ontario and British Columbia creeks. Due to the limited amount of data available, water modelling values should be used as conservative estimates for the aquatic risk assessments.

The modelling estimates should be considered as conservative estimates in the risk assessment for aquatic organisms (both 15-cm and 80-cm depths).

Appendix IX Label amendments for products containing pyrethrins

Information on labels of currently registered products should not be removed unless it contradicts the following label statements.

1. GENERAL LABEL IMPROVEMENTS (ALL LABELS)

Most pyrethrins-containing products were registered prior to the development of modern standardized label language and the labels do not contain comprehensive use directions. After making a final re-evaluation decision for pyrethrins, which will be communicated in the re-evaluation decision document (RVD), registrants will be required to update registered labels to current standards by including use directions that reflect the final risk assessment and required mitigation. The following aspects will require updating:

- Identification of specific pests that are controlled. For example, simply stating "crawling insects" is not sufficient.
- More detailed application instructions, including but not limited to the following:
    - Specific information about how much product is to be applied, which can be related to the application rates used for the health risk assessment and which would be easily understood by users, including consumers
    - Frequency of application
    - Type of application (for example, broadcast, perimeter/spot, crack and crevice)
    - Use directions or restrictions (for example, inside cupboards only, areas inaccessible to children, etc.)
    - Clear identification of application sites such as specific areas of the home (for example, kitchen, living areas), items on which application occurs (for example, carpets, mattresses), specific outdoor sites (for example, playing fields, parks, industrial areas)
- Consideration of whether some application sites listed on domestic-class labels should be removed from domestic-class products, as these are not intended for commercial uses (for example, greenhouses, livestock housing).

2. TECHNICAL GRADE ACTIVE INGREDIENTS

The following statements are proposed to be added to the **Environmental Hazards/Precautions** section:

"TOXIC to aquatic organisms."

"**DO NOT** discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters."

The following statements are proposed to be added to the **Disposal** section:

"Canadian manufacturers should dispose of unwanted active ingredients and containers in accordance with municipal or provincial regulations. For additional details and clean up of spills, contact the manufacturer or the provincial regulatory agency."

3. COMMERCIAL-CLASS PRODUCTS

Pyrethrins are co-formulated with other active ingredients. When updating the label statements, follow the more stringent label directions of all the actives for which a given product is co-formulated.

3.1 Agricultural food/feed crop use products:

The following changes are proposed for all commercial agricultural product labels:

- Any references to "trees" should be changed to "Ornamental Trees"
- Any references to "shrubs" should be changed to "Ornamental Shrubs"
- Any references to "greenhouse and interior plantings" should be removed
- Any references to vague crops (in other words, fruits", "vegetables", "fruit trees", etc.) should be removed

Use Precautions:

In order to promote best practices, and to minimize human exposure from spray drift or from spray residues resulting from drift due to the agricultural use of pyrethrins, the following label statement is proposed:

> "Apply only to agricultural crops when the potential for drift to areas of human habitation and human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings."

When applying using a handheld airblast/mistblower, the following statement is proposed:

> "**DO NOT** handle more than 0.05 kg a.i. per person, per day when using a handheld airblast/mistblower (droplet sizes 0.1–100 μm). These restrictions are in place to minimize exposure to individual applicators. Application may need to be performed over multiple days or using multiple applicators."

The following statement is proposed for all commercial agricultural products labels:

> "**DO NOT** apply in greenhouses, except on greenhouse peppers."

Personal Protection Equipment:

For application to agricultural crops and livestock using handheld airblast/mistblower, the following statement is proposed:

> "Wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, socks, chemical-resistant footwear, and a respirator with a NIOSH-approved

> organic-vapour removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides when applying using a handheld airblast/mistblower."

For mixing, loading, and application to agricultural crops using a mechanically-pressurized handgun, the following label statement is proposed:

> "Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides during mixing, loading, application, clean-up and repair with a mechanically-pressurized handgun."

For mixing, loading, and application using all other application equipment (including mechanically pressurized handgun used on livestock), the following statement is proposed for all commercial agriculture-class product labels unless similar or more protective statements are already present or unless indicated otherwise:

> "Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during mixing, loading, application, clean-up and repair."

The following label statement is proposed for all products labels with automatic fogger and handheld airblast/mistblower applications:

> **"**If entering treated indoor areas prior to venting, wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, chemical-resistant footwear, socks, chemical-resistant gloves, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides."

Restricted-Entry Interval:

The following statement is proposed for all commercial agricultural product labels, except when more restrictive statements are already in place:

> "**DO NOT** enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours."

Plant-Back Interval:

The following statement is proposed for all commercial agricultural product labels with crop uses, except when more restrictive statements are already in place:

Plant-Back Interval: A plant back-interval (PBI) of 12 months is required for all crops other than the ones for whom pyrethrins is registered for use

Add to ENVIRONMENTAL PRECAUTIONS:

"TOXIC to aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE."

Add to DIRECTIONS FOR USE:

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) fine classification. Boom height must be 60 cm or less above the crop or ground.

DO NOT apply by air.

Buffer zones:

Spot treatments using hand-held equipment **DO NOT** require a buffer zone.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of application	Crop		Buffer zones (metres) required for the protection of:			
			Freshwater habitat of depths:		Estuarine/marine habitats of depths:	
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
Groundboom sprayer	Blueberry, grape, raspberry, Herbs and Spices (Crop Group 19), Pinto bean, snap bean, wax bean, and tomato		25	4	45	25
Airblast sprayer	Pear, blueberry, grape, raspberry	Early airblast	45	15	50	40
		Late airblast	35	10	40	30

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

The buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator on the Pest Management Regulatory Agency web site.

3.2 Commercial non-agricultural/structural products:

Use Precautions:

Any reference to the use to control lice on mattresses, bedding, furniture, and garments are to be removed from commercial-class product labels.

The following statement is proposed for all commercial-class product labels, with application using mechanically-pressurized handheld sprayer for mists, aerosols, and fogs:

"**DO NOT** handle more than 0.05 kg a.i. per person per day when using mechanically-pressurized handheld sprayer for mists, aerosols, and fogs (droplet size 0.1–100µm). These restrictions are in place to minimize exposure to individual applicators. Application may need to be performed over multiple days or using multiple applicators."

The following statements are proposed for all commercial-class product labels, where applicable:

"Apply only when the potential for drift to non-target areas of human habitation or other areas of human activity such as parks, school grounds, and playing fields is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings."

"Outdoor broadcast application is to large outdoor structural surfaces (in other words, roofs, walls, doors, windows, porches, patios and foundations). Outdoor perimeter application is 1 m or less out from the building's foundation and to a maximum height of 1 m starting where the foundation meets the ground."

"Indoor broadcast application is to broad expanses of indoor structural surfaces such as walls, floors, ceilings and indoor foundation walls/crawlspaces. Indoor perimeter application is less than 0.3 m wide along the edges of a room to baseboards, wall-floor and ceiling-wall joints, and around doorways or windows. Spot application is localized to a surface area not more than 0.2 m^2. Spots are not to be adjoining. The combined area of spots is not to exceed 10% of the total surface area of a room. Crack and crevice is an application directly into narrow openings on the surface of the structure. It does not include the treatment of exposed surfaces. Narrow openings typically occur at expansion joints, utility entry points and along baseboards and mouldings. Void application applies to inaccessible, enclosed empty spaces of a structure. For example, hollow walls and suspended ceilings."

"Residential areas are defined as any use site where the general public, including children, could be exposed during or after application. For structural uses, in residential sites, this includes homes, schools, restaurants, public buildings or any other areas where the general public including children may potentially be exposed. Non-residential areas include, but are not limited to: industrial/commercial indoor sites (for example, laboratories, warehouses, food granaries); modes of transport in areas where passengers are not present (for example, buses, railcars, trailers); and animal housing (for example, livestock and poultry housing, and pet kennels)."

To all labels with furniture applications, the following definitions are proposed to be added: "Broadcast – Broadcast furniture application covers large areas or the entire surface of listed items. Spot – Spot furniture application is up to 10% of the surface of the treated item. Crack and crevice – Crack and crevice furniture treatments are applications to junction points on items. Tufts and/or seams (mattresses and upholstered furniture only) – Tufts and/or seam furniture treatment is to the junction of two or more pieces of fabric and any decorative trim (for example, buttons). Void – Void furniture treatment targets inaccessible empty spaces of items. For example, inside the dust cover on the underside of furniture or hollow table legs."

The following is proposed for all labels with use in golf courses:

"**DO NOT** apply to golf course greens, fairways, or tees."

"**DO NOT** enter or allow entry into treated areas until sprays have dried."

For all commercial end-use product labels with surface application, the following statement(s) are proposed:

"**DO NOT** apply to overhead areas or in confined spaces without appropriate respiratory and eye protection."

"Ventilate treated areas after application either by opening windows and doors or using fans, where required, to aid in the circulation of air. Air exchange/ventilation systems confirmed to be operational may also be used."

For broadcast, perimeter and spot spray (liquid formulation) applications, add "Use a coarse droplet size and low pressure spray not exceeding 345 kPa (50 psi) to avoid splashing onto non-target surfaces."

"**DO NOT** apply when a food/feed processing facility is in operation."

"**DO NOT** apply when people, pets, or livestock are present, unless otherwise specified."

For Liquid/Aerosol products, add: "**DO NOT** allow people, pets, or livestock to enter treated areas until sprays have dried, unless otherwise specified."

For Liquid/Aerosol products, add: "**DO NOT** allow spray to drip or allow drift onto non-target surfaces."

For Dust products, add: "**DO NOT** allow people or pets to enter treated areas until dusts have settled."

For Dust products, add: "**DO NOT** allow dust to deposit onto non-target surfaces."

For all products not registered for use on stored food/feed, add: "**DO NOT** apply to surfaces that may come into contact with food/feed."

For all products not registered for use on stored food/feed, add: "Cover or remove all food/feed. Cover all food/feed processing surfaces, equipment, and utensils or thoroughly wash following treatment."

If only surface application types are supported on the product labels, add: "**DO NOT** apply as a space spray treatment."

For product labels approved for use on mattresses and furniture, the following statements are proposed:

> For products with furniture treatment, including but not limited to upholstered furniture, hard surface furniture, mattresses, box spring, pet bedding, bed frames, dressers, curtains, picture frames, wall coverings, hollow furniture legs, etc., equipment treatment including those used in food and feed establishments, garbage can/bins, etc., add: "Broadcast – Broadcast furniture application covers large areas or the entire surface of listed items. Spot – Spot furniture application is up to 10% of the surface of the treated item. Crack and crevice – Crack and crevice furniture treatments are applications to junction points on items. Tufts and/or seams (mattresses and upholstered furniture only) – Tufts and/or seam furniture treatment is to the junction of two or more pieces of fabric and any decorative trim (for example, buttons). Void –Void furniture treatment targets inaccessible empty spaces of items. For example, inside the dust cover on the underside of furniture or hollow table legs."
>
> "**DO NOT** use on items which can be laundered (for example, pillows, bedding, toys, etc)."
>
> "Remove bedding before treating mattresses. Treated mattress must be dry before replacing laundered bedding."
>
> "Remove all objects before treatment of furniture, luggage, closets or other areas where clothing, toys, towels, and other items are stored. Treated furniture must be dry before replacing stored items."
>
> When approved for tuft and/or seam application only, add: "**DO NOT** apply to the entire mattress or piece of furniture. Apply to tufts [and/or] seams only."

For product labels with void application, the following statements are proposed:

> "Care should be taken to avoid the pesticide exiting the void. Any residue deposits on non-target surfaces must be removed by the applicator."

For product labels approved for use on clothing, the following statements are proposed:

> "Remove all objects before treatment of furniture, luggage, closets or other areas where clothing, toys, towels, and other items are stored. Treated furniture and treated surfaces must be dry before replacing stored items."
>
> "Only apply to clothing which can be laundered. Treated clothing must be laundered prior to wearing."

For all commercial product labels with space spray application, the following statements are proposed:

> "Space spray application is a suspension of fine droplets (0.1 to 100 μm) in the air within an indoor space."

"**DO NOT** allow people, pets, or livestock to enter treated areas until sprays have settled."

"When applying to overhead areas or in confined spaces, wear appropriate respiratory and eye protection."

"Ventilate treated areas after application either by opening windows and doors or using fans, where required, to aid in the circulation of air. Air exchange/ventilation systems confirmed to be operational may also be used."

"**DO NOT** apply when a food/feed processing facility is in operation."

"**DO NOT** apply when people or pets [or livestock] are present."

"**DO NOT** remain in treated area after application."

"Cover or remove all food/feed. Cover all food/feed processing surfaces, equipment and utensils or thoroughly wash following treatment."

For all indoor aerosol space spray applications in residential areas, the following statement is proposed:

"**DO NOT** apply as an indoor space spray using rates higher than 0.00214 g a.i./m^3. **DO NOT** allow people or pets to enter treated areas until 2 hours after application."

For all commercial product labels with fogging applications, the following statement is proposed:

"Ventilate treated areas after application either by opening windows and doors or using fans, where required, to aid in the circulation of air. Air exchange/ventilation systems confirmed to be operational may also be used."

For all commercial non-agricultural/structural EP labels which mention applications in greenhouses, the following statement is proposed:

"**DO NOT** apply in greenhouses."

Personal Protection Equipment:

For application using mechanically-pressurized handheld sprayer for mists, aerosols, and fogs, the following statement is proposed:

"Wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, socks, chemical-resistant footwear, and a respirator with a NIOSH-approved organic-vapour removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides when applying using a handheld airblast/mistblower."

For mixing, loading, and application using a mechanically-pressurized handgun, the following label statement is proposed:

> "Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides, or a NIOSH-approved canister approved for pesticides during mixing, loading, application, clean-up and repair with a mechanically-pressurized handgun."

For mixing, loading, and application using all equipment for dust formulations, the following label statement is proposed:

> "Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, shoes, and a NIOSH approved N95 (minimum) filtering facepiece respirator (dust mask) during mixing, loading, application, clean-up and repair."

For mixing, loading, and application using all other application equipment, the following statement is proposed for all commercial-class product labels unless similar or more protective statements are already present or unless indicated otherwise:

> "Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during mixing, loading, application, clean-up and repair."

The following label statement is proposed for all labels with indoor automatic fogger applications, mechanically-pressurized handheld equipment for mists, aerosols, and fogs, and total release foggers:

> **"**If entering treated indoor areas prior to venting, workers must wear chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant hood, chemical-resistant footwear, socks, chemical-resistant gloves, and a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides."

4. DOMESTIC-CLASS PRODUCTS

The following is proposed for all liquid and aerosol domestic-class product labels which indicate application using a mechanically-pressurized handheld equipment for mists, aerosol, and fogs (handheld mister/fogger):

> "**DO NOT** apply using mechanically-pressurized handheld equipment for mists, aerosols, and fogs."

The following is proposed for all aerosol domestic-class product labels:

> "**DO NOT** apply as an indoor space spray."

For all domestic-class product labels with surface application, the following statements are proposed:

> "**DO NOT** apply when people, pets, or livestock are present."
>
> "**DO NOT** apply to overhead areas or in confined spaces (for example, attics, crawlspaces, small storage rooms, closets)."
>
> "Ventilate treated areas after application by opening windows and doors or using fans, where required, to aid in the circulation of air."
>
> **"DO NOT** apply to surfaces that may come into contact with food/feed."
>
> "Cover or remove all food/feed. Cover all food/feed processing surfaces, equipment and utensils or thoroughly wash them following treatment."
>
> For liquid/aerosol products, add: "**DO NOT** allow people or pets [or livestock] to enter treated areas until sprays have dried."

For liquid/aerosol products, add: "**DO NOT** allow spray to drip or allow drift onto non-target surfaces."

> For dust products, add: "**DO NOT** allow people or pets [or livestock] to enter treated areas until dusts have settled."
>
> For dust products, add: "**DO NOT** allow dust to deposit onto non-target surfaces."

For domestic-class product labels approved for use on mattresses and furniture, the following statements are proposed:

> "**DO NOT** use on items which can be laundered (for example, pillows, bedding, toys, clothing, etc)."
>
> "Remove bedding before treating mattresses. Treated mattress must be dry before replacing laundered bedding."
>
> "Remove all objects before treatment of furniture, luggage, closets or other areas where clothing, toys, towels, and other items are stored. Treated furniture and treated surfaces must be dry before replacing stored items."

For domestic-class product labels with void application, the following statement is proposed:

> "Care should be taken to avoid the pesticide exiting the void. Any residue deposits on non-target surfaces must be removed by the applicator."

For product labels approved for use for treating clothing, the following statements are proposed:

> "Remove all objects before treatment of furniture, luggage, closets or other areas where clothing, toys, towels, and other items are stored. Treated furniture and treated surfaces must be dry before replacing stored items."
>
> "Only apply to clothing which can be laundered. Treated clothing must be laundered prior to wearing."

For all domestic-class product labels with outdoor space spray application, the following statements are proposed:

> "**DO NOT** apply when people, or pets, or livestock are present."
>
> "**DO NOT** remain in treated areas after application."

For all domestic-class product coil labels, the following statement is proposed:

> "**DO NOT** use indoors or in enclosed spaces."

For domestic-class products with greenhouse uses, the following statement is proposed:

> "**DO NOT** use in commercial greenhouses."

Remove the following crops/uses that appear on domestic product labels:

- Apple tree, "fruit" tree (except pear)
- Outdoor and greenhouse applications to asparagus, beets, broccoli, Brussels sprout, cabbage, carrots, cauliflower, celery, cole crops, collards, cranberries, cucumbers, eggplant, kale, lettuce, mustard green, onion, pea, potato, radish, spinach, squash, turnip, "vegetables" (except for those listed in the table above), and vine products
- Outdoor application to peppers
- Greenhouse application to beans, herbs, tomatoes, "Greenhouse plantings" (except peppers)

5. ALL END-USE PRODUCTS (DOMESTIC AND COMMMERCIAL)

Add to **Environmental Precautions** section of all end-use product labels:

"TOXIC to aquatic organisms and small, wild mammals."

"To reduce run-off from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay."

"Avoid application of this product when heavy rain is forecast."

"TOXIC to bees. Bees may be exposed through direct spray, spray drift, and residues on leaves, pollen and nectar in flowering crops and weeds. Minimize spray drift to reduce harmful effects on bees in habitats close to the application site. Avoid applications when bees are foraging in the treatment area in ground cover containing blooming weeds.

To further minimize exposure to pollinators, refer to the complete guidance "Protecting Pollinators during Pesticide Spraying – Best Management Practices" on the Health Canada website (www.healthcanada.gc.ca/pollinators). Follow crop specific directions for application timing."

For crops that are highly attractive to pollinators (tomatoes, roses, beans, blueberry, grape, raspberry, pears) or when using managed bees for pollination services:

"**DO NOT** apply during the crop blooming period."

For all other crops:

"Avoid application during the crop blooming period. If applications must be made during the crop blooming period, restrict applications to evening when most bees are not foraging."

"Toxic to certain beneficial insects. Minimize spray drift to reduce harmful effects on beneficial insects in habitats next to the application site such as hedgerows and woodland. Pyrethrins may impact predatory and parasitic arthropod species used in IPM programs within the treatment area. Unsprayed refugia for beneficial species of at least 1 metre from treatment area will help maintain beneficial arthropod populations."

The following statement is proposed to be added for all greenhouse uses:

"Greenhouse use: Toxic to bees and other beneficial insects. May harm bees and other beneficial insects, including those used in greenhouse production. **DO NOT** apply when bees or other beneficial insects are foraging in the treatment area."

"**DO NOT** allow effluent or run-off from greenhouses containing this product to enter lakes, streams, ponds or other waters."

The following statements are proposed to be added to the Directions for Use section on all product labels:

"To protect pollinators, follow the instructions regarding bees in the Environmental Precautions section."

For tomatoes, roses, beans, blueberry, grape, raspberry, pears include:

"Toxic to bees. **DO NOT** apply during the crop blooming period."

For all other crops on label:

"Toxic to bees. Avoid application during the crop blooming period. If applications must be made during the crop blooming period, restrict applications to evening when most bees are not foraging. When using managed bees for pollination services, **DO NOT** apply during the crop blooming period."

"As this product is not registered for the control of pests in aquatic systems, **DO NOT** use to control aquatic pests."

"**DO NOT** contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes."

"**DO NOT** wet plants to the point of run-off or drip."

"Before making widespread applications of this product, treat a limited number of plants and observe for plant damage over a 10-day period."

References

Studies Considered in the Chemistry Assessment

A. Studies/Information Submitted by the Registrants

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Toxicology

A. Studies/Information Provided by the Registrants

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1287383 USEPA. 2005. Pyrethrins: Revised Human Health Risk Assessment for the Reregistration Eligibility Decision. Office of Prevention, Pesticides and Toxic Substances. Dated September 14, 2005. DACO 12.5.4

1287395 USEPA. 2006. Human Health Risk Assessment for the Reregistration Eligibility Decision (RED) for Pyrethrins. Dated June 7, 2006. DACO 12.5.4

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2166060 USEPA. 2011. Pyrethrins: Summary Document in Support of Registration Review. Initial Docket, December 2011. Dated December 13, 2011. DACO 12.5.4

Information Considered in the Dietary Assessment

A. Studies/Information Provided by the Registrants

PMRA Document Number	Reference
815758	Summaries and Overall Assessments; NEU1161 Residual Pest Spray

PMRA Document Number	Reference
1183929	Summaries: Metabolism/Toxicokinetics Studies. [NEU1161I;Subn#97-0540;Regn#26243;Binder#5;Metabolism/Toxicokinetics Volume 1 of 1;Date Submitted: February 25,1998]
1183930	Livestock-Waiver Request + Pyrethrum: the Natural Insecticide. Edited by: J.Casida. Academic Press, Inc. New York and London. 1973. (Pp#108-117). [NEU1161I;Subn#97-0540;Regn#26243;Binder#5;Metabolism/Toxicokinetics Volume 1 of 1;Date Submitted: February 25,1998]
1183931	Plants-Waiver Request. [NEU1161I;Subn#97-0540;Regn#26243;Binder#5;Metabolism/Toxicokinetics Volume 1 of 1;Date Submitted: February 25,1998]
1183933	Summaries: Food, Feed and Tobacco Residue Studies Eup. [NEU1161I;Subn#97-0540;Regn#26243;Binder#6;Food, Feed and Tobacco Residue Studies Volume 1 of 1;Date Submitted: February 25,1998]
1183937	Supervised Residue Trial Analytical Methodology-Waiver Request + Rapid Method for the Determination of Multiple Pyrethroid Residues in Fruits and Vegetables By Capillary Column Gas Chromatography. G.Pang et.al. Journal of Chromatography A, 667 (1994). (Pp#348-353). [NEU1161I;Subn#97-0540;Regn#26243;Binder#6;Food, Feed and Tobacco Residue Studies Volume 1 of 1;Date Submitted: February 25,1998]
1183938	Supervised Residue Trial Study-Waiver Request + Pyrethrum: the Natural Insecticide. Edited by J.Casida. Academic Press New York and London 1973. (Pp#78-87). [NEU1161I;Subn#97-0540;Regn#26243;Binder#6;Food, Feed And Tobacco Residue Studies Volume 1 of 1;Date Submitted: February 25,1998]
1183968	Metabolism/Toxicokinetics Studies: Summaries. [Waiver Request]. [NEU1161I RTU;Subn#97-0541;Regn#26244;Binder#5;Metabolism/Toxicokinetics Studies Volume 1 Of 1;Date Submitted: February 25,1998]
1183969	Livestock-Waiver Request + Pyrethrum The Natural Insecticide. Edited by J.Casida. Academic Press New York and London 1973. (Pp#108-117]. [NEU1161I RTU;Subn#97-0541;Regn#26244;Binder#5;Metabolism/Toxicokinetics Studies Volume 1 of 1;Date Submitted: February 25,1998]
1183970	Plants-Waiver Request. [NEU1161I RTU;Subn#97-0541;Regn#26244;Binder#5;Metabolism/Toxicokinetics Studies Volume 1 of 1;Date Submitted: February 25,1998]
1183971	Summaries-Waiver Request. [NEU1161I RTU;Subn#97-0541;Regn#26244;Binder#6;Food, Feed and Tobacco Residue Studies Volume 1 of 1;Date Submitted: February 25,1998]

PMRA Document Number	Reference
1183972	Supervised Residue Trial Analytical Methodology-[Waiver Request] + Rapid Method for the Determination of Multiple Pyrethroid Residues In Fruits and Vegetables by Capillary Column Gas Chromatography. G.Pang Et.Al. Journal of Chromatography A, 667 (1994). (Pp#348-353). [NEU1161I RTU;Subn#97-0541;Regn#26244;Binder#6;Food, Feed And Tobacco Residue Studies Volume 1 of 1;Date Submitted: February 25,1998]
1183973	Supervised Residue Trial Study-Waiver Request + Pyrethrum the Natural Insecticide. Edited By J.Casida. Academic Press New York And London 1973. (Pp#78-87). [NEU1161I RTU;Subn#97-0541;Regn#26244;Binder#6;Food, Feed and Tobacco Residue Studies Volume 1 of 1;Date Submitted: February 25,1998]
1190631	Summary Compilation, Acute Studies - Eup, Exposure, Metabolism/Toxicokinetics, Food, Feed and Tobacco Residue, Environmental Chemistry and Fate, Environmental Toxicology and Value [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted March 18, 1997;Volume 1 of 1 Cover Letter, Part 0 Index and Part 1 Label, MSDS, Summaries]
1190636	Summary Compilation, Acute Studies - Eup, Exposure, Metabolism/Toxicokinetics, Food, Feed and Tobacco Residue, Environmental Chemistry and Fate, Environmental Toxicology and Value [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted June 5, 1997;Volume 1 of 1 Cover Letter, Part 0 Index, Part 1 Label, MSDS, Summaries]
1190642	Summary Compilation, Acute Studies - Eup, Exposure, Metabolism/Toxicokinetics, Food, Feed and Tobacco Residue, Environmental Chemistry and Fate, Environmental Toxicology and Value [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted February 25, 1998;Volume 1 of 1 Cover Letter, Part 0 Index, Part 1 Label, MSDS, Summaries]
1190643	Metabolism/Toxicokinetics Summaries, Request for Waiver, Binder #5 [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted February 25, 1998;Volume 1 of 1 Part 6, Metabolism]
1190644	Livestock Request for Waiver and Publication Pyrethrum, the Natural Insecticide, Academic Press, J.E. Casida, 1973 [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted February 25, 1998;Volume 1 of 1 Part 6, Metabolism]
1190645	Plants Request for Waiver [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted February 25, 1998;Volume 1 of 1 Part 6, Metabolism]
1190646	Food, Feed And Tobacco Residue Studies Eup, Summaries - Request for Waiver, Binder #6 [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted February 25, 1998;Volume 1 of 1 Part 7, Residues]

PMRA Document Number	Reference
1190647	Supervised Residue Trial Analytical Methodology and Publication, Short Communication, Rapid Method For The Determination Of Multiple Pyrethroid Residues in Fruits and Vegetables by Capillary Column Gas Chromatography, Journal Of Chromatography, P. Guo-Fang et al, 1994 (348-353;0021-9673/94) [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted February 25, 1998;Volume 1 of 1 Part 7, Residues]
1190648	Supervised Residue Trial Study, Request for Waiver and Publication, Pyrethrum, the Natural Insecticide, Academic Press, J.E. Casida, 1973 [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted February 25, 1998;Volume 1 of 1 Part 7, Residues]
1190655	Summary Compilation, Acute Studies - Eup, Exposure, Metabolism/Toxicokinetics, Food, Feed And Tobacco Residue, Environmental Chemistry And Fate, Environmental Toxicology and Value, Requests For Waivers [NEU1161I RTU Insecticide/Miticide;Subn.#97-0541;Regn.#26244;Submitted March 18, 1997;Volume 1 of 1 Cover Letter, Part 0 Index and Part 1 Label, MSDS, Summaries]
1190660	Summary Compilation, Acute Studies - Eup, Exposure, Metabolism/Toxicokinetics, Food, Feed and Tobacco Residue, Environmental Chemistry and Fate, Environmental Toxicology and Value [NEU1161I RTU Insecticide/Miticide;Subn.#97-0541;Regn.#26244;Submitted March 18, 1997;Volume 1 of 1 Cover Letter, Part 0 Index and Part 1 Label, MSDS, Summaries]
1190666	Summary Compilation, Acute Studies - Eup, Exposure, Metabolism/Toxicokinetics, Food, Feed and Tobacco Residue, Environmental Chemistry and Fate, Environmental Toxicology and Value [NEU1161I RTU Insecticide/Miticide;Subn.#97-0541;Regn.#26244;Submitted February 25, 1998;Volume 1 of 1 Cover Letter, Part 0 Index, Part 1 Label, MSDS, Summaries]
1190667	Metabolism/Toxicokinetics Summaries, Request For Waiver, Binder #5 [NEU1161I RTU Insecticide/Miticide;Subn.#97-0541;Regn.#26244;Submitted February 25, 1998;Volume 1 of 1 Part 6, Metabolism]
1190668	Livestock Request for Waiver And Publication Pyrethrum, the Natural Insecticide, Academic Press, J.E. Casida, 1973 [NEU1161I RTU Insecticide/Miticide;Subn.#97-0541;Regn.#26244;Submitted February 25, 1998;Volume 1 of 1 Part 6, Metabolism]
1190669	Plants Request for Waiver [NEU1161I RTU Insecticide/Miticide;Subn.#97-0541;Regn.#26244;Submitted February 25, 1998;Volume 1 of 1 Part 6, Metabolism]

PMRA Document Number	Reference
1190670	Food, Feed and Tobacco Residue Studies Eup, Summaries - Request For Waiver, Binder #6 [NEU1161I RTU Insecticide/Miticide;Subn.#97-0541;Regn.#26244;Submitted February 25, 1998;Volume 1 of 1 Part 7, Residues]
1190671	Supervised Residue Trial Analytical Methodology and Publication, Short Communication, Rapid Method for the Determination of Multiple Pyrethroid Residues in Fruits and Vegetables by Capillary Column Gas Chromatography, Journal of Chromatography, P. Guo-Fang Et Al, 1994 (348-353;0021-9673/94) [NEU1161I RTU Insecticide/Miticide;Subn.#97-0541;Regn.#26244;Submitted February 25, 1998;Volume 1 of 1 Part 7, Residues]
1190673	Supervised Residue Trial Study, Request for Waiver And Publication, Pyrethrum, The Natural Insecticide, Academic Press, J.E. Casida, 1973 [Neu 1161i RTU Insecticide/Miticide;Subn.#97-0541;Regn.#26244;Submitted February 25, 1998;Volume 1 of 1 Part 7, Residues]
1238181	Pyrethrum - Metabolism and Pharmacodynamics - Literature Review
1238182	Metabolism
1238189	Analytical Methodology- Pyrethrum Residues -
1238216	Summary - Metabolism of the Pyrethrins
1238217	Analytical Methodology - Pyrethrins & Synergists
1240370	Metabolism Studies – Summary
1240371	Metabolism Studies – Plants
1240372	Pharmacokinetics - Neurotoxicity Summary
1240373	Metabolism Studies - Pharmacokinetics - Interactions in Toxicity of Pyrethrum, Synergists & Others – Mammals
1240374	Metabolism Studies - Other – Index
1240376	Food, Feed & Tobacco Residue Studies – Summary
1240378	Analytical Methodology (Food Crops & Tobacco) – Index
1240379	Crop Residue Data - Food Additive Tolerances
1240380	Livestock, Poultry, Egg & Milk Residue Data (Dermal Application)
1240381	Livestock, Poultry, Egg & Milk Residue Data (Feeding of Treated Crops)
1240383	Residue Data for Crops Used as Livestock Feed
1240384	Tobacco Residue Data
1240385	Freezer Stability Tests
1245045	Bendiocarb Food Residue Summary
1256378	Comprehensive Summaries, Chemistry, Toxicology, Exposure, Metabolism, Residues, Environmental Chemistry and Fate, Environmental Toxicology and Value, March 1997 [NEU1161I Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted February 25, 1998;Volume 1 of 1 Comprehensive Summaries]

PMRA Document Number	Reference
1256379	Comprehensive Summaries, Chemistry, Toxicology, Exposure, Metabolism, Residues, Environmental Chemistry and Fate, Environmental Toxicology and Value, March 1997 [NEU1161I RTU Insecticide/Miticide;Subn.#97-0540;Regn.#26243;Submitted February 25, 1998;Volume 1 Of 1 Comprehensive Summaries]
1257168	Summary Compilation. NEU1161I. [NEU1161I;Subn#97-0540;Regn#26243;Three Duplicate Copies Were Submitted On The Following Dates: March 18,1997 & June 5,1997 & February 25,1998]
1257169	Comprehensive Summaries: NEU1161I. [Chemistry + Toxicology + Exposure (Occupational And/Or Bystander) + Metabolism/Toxicokinetics + Food, Feed and Tobacco Residue Studies Eup + Environmental Chemistry And Fate + Environmental Toxicology + Value) [NEU1161I;Subn#97-0540;Regn#26243;Comprehensive Summaries Volume 1 of 1;Date Submitted: February 25,1998]
1257174	Summary Compilation: NEU1161I RTU. [NEU1161I RTU;Subn#97-0541;Regn#26244;Binder#1;Summary Volume 1 of 1;Date Submitted: June 5,1997]
1257175	Comprehensive Summaries: NEU1161I RTU. [Chemistry + Toxicology + Exposure (Occupational And/Or Bystander) + Metabolism/Toxicokinetics + Food, Feed And Tobacco Residue Studies Eup + Environmental Chemistry And Fate + Environmental Toxicology + Value). [NEU1161I RTU;Subn#97-0541;Regn#26244;Comprehensive Summary Binder Volume 1 of 1;Date Submitted: February 25,1998]
1413534	Residue and Tolerance Considerations with Pyrethrum, Piperonyl Butoxide, and MGK 264. Pyrethrum: The Natural Insecticide (J.E. Casida, Ed) - Chapter 16. Academic Press, New York. pgs 293-306 (1973)
1413535	Advantages and Disadvantages of Pyrethrum. Pyrethrum: The Natural Insecticide (J.E. Casida, Ed) - Chapter 17. Academic Press, New York, pgs. 307-311 (1973)
1413536	Recommended Methods for the Determination of Residues of Pyrethrins and Piperonyl Butoxide. Pyrethrum Post 17(4): 133-139 (1979)
1413537	Determination of pyrethrum and piperonyl butoxide in milk by high performance liqiud chromatography. Pyrethrum Post 16(1): 14-17 (1982)
1413539	Data sheets on pesticides, No. 11, Pyrethrins. World Health Organization (1975)
1632990	Metabolic Fate of Pyrethrin I, Pyrethrin II, and Allethrin Administered Orally to Rats
1729749	Metabolism Study of Pyrethrin I in Lactating Goat Following Oral and Dermal Administration

PMRA Document Number	Reference
1729750	Nature of 14C-Pyrethrin I (PYI) residues in leaf lettuce
1729751	Pyrethrin Analytical Phase on the Raw Agricultureal Commodity Residue Evaluation of Pyrethrin + Piperonyl Butoxide Applied as Pyrenone Crop Sprray to Leafy Vegetables
1729753	Residue Study of Pyrethrins, Piperonyl Butoxide, and MGK 264 in Certain Food Commodities Resulting From Use as a Space Spray in a Simulated Feed and Food Processing Situation
1729754	Multiresidue Analytical Procedure for Insecticides Used by Organic Farmers
1729755	Determination of Pyrethrins I Concentration in Sprayate Samples from the Leafy Vegetables Crop Group
1729756	Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrum + Piperonyl Butoxide Applied as Pyrenone Crop Spray to Leafy Vegetables
1729758	Amendment Pyrethrin Analytical Phase on the Raw Agriculture Commodity Evalution of Pyrethrin + PBO Applied as Pyperone Crop Spray to Cucubits
1729760	Raw Agricultural Commodity (RAC) Residue Decline of Pyrethrin/PBO Applied to Blueberry
1729761	Residue Study of Pyrethrins, PBO and MGK 264 in Certain Food Commodities Resulting from Use as a Spacy Spray in a Simmulated Feed and Food Processing Situations
1729762	Residue Study of Pyrethrins, PBO and MGK 254 in Certain Food Commodities Resulting from use as a spacy spray in a Simmulated Feed and Food Processing Situation.
1729764	Metabolism Study of Pyrethrin I in Laying Hens Following Oral and dermal Administration
1729765	Nature of 14C-Pyrethrin I (PYI) residues in potatoes.
1729768	Nature of 14C-Pyrethrin I (PYI) residues in tomato.
1729770	Amended Pyrethrin Analytical Phase on Raw Agricultural Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Legumes
1729771	Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrin + PBO Applied as Pyrenone Crop Spray to Brassica.
1729772	Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrum Applied as Pyrenone Crop Spray in Root and Tuber crops
1729775	Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethum + PBO Applied as Pyrenone Crop Spray in Fruting Vegetables
1729776	Amended Pyrethrn Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrin + PBO Applied as Pyrenone Crop Spray to Leafy Vegetables

PMRA Document Number	Reference
1729777	Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Small Fruits.
1729778	Raw Agricultural Commodity (RAC) Residue Decline of Pyrethrin/ PBO Applied to Lettuce
1729779	Raw Agricultural Commodity (RAC) Residue Decline of Pyrethrin/PBO Applied to Peaches
1729781	Raw Agricultural Commodity (RAC) Residue Decline of Pyrethrin/PBO Applied to Tomatoes
1749952	Piperonyl Butoxide Analytical Phase on the Processed Commodity Residue Evaluation of Piperonyl Butoxide Applied as Pyrenone Crop Spray to Grape
1749953	Amended Piperonyl Butoxide Analytical Phase on the Processed Commodity Residue Evaluation of Pyrethrin + Piperonyl Butpxide Applied as Pyrenone Crop Spary to Tomato
1749954	Piperonyl Butoxide Analytical Phase on the Processed Commodity Residue Evaluation of Piperonyl Butoxide Applied as Pyrenone Crop Spray to Tomatoes
1749955	Pyrethrin Analytical Phase of the Processed Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Tomato
1749956	Pyrethrin Analytical Phase on the Processed Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Grape
1758855	Appendix A: Uses of Pyrethrins Eligible for Reregistration
1918995	DACO 7.4.1_Crop Field Trial
1921107	Metabolism Study of Pyrethrin 1 in Lactating Goat Following Oral or Dermal Administration
1921108	Metabolism Study of Pyrethrin 1 in Laying Hens Following Oral or Dermal Administration
1921112	Identification of ((carbon 14)-Acid) Pyrethrin I Metabolite in Goat Fat and Hen Liver and Egg Yolk
1921113	Response to Chemistry and Exposure Branch Review Dated May 20, 1999 Regarding the Nature of Pyrethrin (PY) Residues in Plants and Animals
1921114	Nature of the (carbon 14)-Pyrethrin 1 (PY 1) Residues in Potato
1921115	Nature of the (carbon 14)-Pyrethrin 1 (PY 1) Residues in Tomato
1921121	Nature of the (carbon 14)-Pyrethrin 1 (PY 1) Residues in Leaf Lettuce
1921128	Residue Study of Pyrethrins Piperonyl Butoxide and MGK-264 in Certain Food Commmodities REsulting from use as a space spray in a Warehouse Situation.
1921130	Residue Study of Pyeethrin, Piperonyl Butoxide, and MGK-264 in certain Food commodities and surfaces resulting fromuse as an Intermittent Aerosol Spray in a Simulated Restaurant Situation

PMRA Document Number	Reference
1921135	Residue Study of Pyrethrins, Piperonyl Butoxide and MGK-264 in Certain Food Commodities REsulting from use as a Contact Spray in a Simulated warehouse situation.
1921136	Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Legumes: Final Report: (Includes "Field Phase for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Raw Agricultural Commodity Trial on Legumes FL, WI, ND, CO, CA, MN, TX, and WA")
1921147	Field Phase for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Raw Agricultural Commodity Trials on Cucurbits in Michigan, North Carolina, Arizona, California, Florida, Texas, New Jersey and Georgia: Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrin + Piperonyl Butoxide Applied as Pyrenone Crop Spray to Cucurbits: Final Report
1921151	Field Phase for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Raw Agricultural Commodity Trials on Fruiting Vegetable in Florida, Michigan, New Jersey, North Carolina, California, and Texas: Final Report: including Analytical Phase
1921152	Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrin & Piperonyl Butoxide Applied as Pyrenone Crop Spray to Leafy Vegetables (Also Field Phase for Raw Agricultural Commodity Trials on Leafy Vegetables)
1921154	Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Citrus Crops: (Including Field and Processing Phases for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Raw Agricultural Commodity Trials on Citrus in FL, CA, TX, and AZ)
1921155	Volume I: Field Phase for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Raw Agricultural Commodity Trials on Small Fruits in New York, Oregon, Michigan, North Carolina, Florida, and Massachusetts; Volume II: Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Small Fruits: Final Report
1921156	Pyrethrin Analytical Phase on the Raw Agricultural Commodity residue evaluation of Pyrethrin + Piperonyl Butoxide Applied as Pyrenone Crop Spray to Brassica, including Field Phase for LX1180-20: Final Report
1921159	Raw Agricultural Commodity (RAC) Residue Decline of Pyrethrins/Piperonyl Butoxide Applied to Tomatoes
1921165	Raw Agricultural Commodity (RAC) Residue Decline of Pyrethrins/Piperonyl Butoxide Applied to Lettuce
1921168	Raw Agricultural Commodity (RAC) Residue Decline of Pyrethrins/Piperonyl Butoxide Applied to Peaches
1921173	Raw Agricultural Commodity (RAC) Residue Decline of Pyrethrins/Piperonyl Butoxide Applied to Blueberry

PMRA Document Number	Reference
1921174	Response to Chemistry and Exposure Branch Review Dated March 19, 1999 Regarding Magnitude of Pyrethrin (PY) Residues in Plants
1921175	Residue Study of Pyrethrins, Piperonyl Butoxide, and MGK 264 in Certain Food Commodities Resulting from Use as a Space in a Simulated Feed and Food Processing Situation
1921176	Residue Study of Pyrethrins, Piperonyl Butoxide, and MGK 264 in Certain Food Commodities Resulting from Use as a Contact Spray in a Simulated Feed and Food Processing Situation
1921179	Pyrethrin Analytical Phase on the Processed Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Grape: (including Field and Processing Phases for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Processed Commodity Trial on Grape in California)
1921181	Pyrethrin Analytical Phase on the Processed Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Tomato: Final Report: (Includes "Field and Processing Phases for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Processed Commodity Trial on Tomato in CA")
1921190	Pyrethrin Analytical Phase on the Processed Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Succulent Beans: Final Report: (Includes "Field and Processing Phases for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Processed Commodity Trial on Succulent Beans in NY")
1921194	Pyrethrin Analytical Phase on the Processed Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Root and Tuber Crops: Final Report: (Includes "Field and Processing Phases for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Processed Commodity Trial on Potatoes and Sugarbeets in WA and CA")
1921197	Pyrethrin Analytical Phase on the Processed Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Oranges: Final Report: (Includes "Field and Processing Phases for LX1180-02 (Pyrethrin + Piperonyl Butoxide) Processed Commodity Trial on Oranges in FL")
1921199	Magnitude of Residues in Meat and Milk from Lactating Dairy Cows Exposed to Pyrethrum Extract: Addendum No. 1 to Amended Final Report
1921202	Magnitude of Residues in Meat and Eggs from Laying Hens Exposed to Pyrethrum Extract: Amended Final Report
2134324	Metabolism Study of Pyrethrin 1 In Lactating Goat Following Oral Or Dermal Administration - Mrid #43628301 (Amended Report)
2134326	Metabolism Study of Pyrethrin 1 In Laying Hens Following Oral Or Dermal Administration - Mrid #43628302 (Amended Report)
2134328	Review Of The Mammalian Metabolism Of The Natural Pyrethrins

PMRA Document Number	Reference
2134329	Piperonyl Butoxide Analytical Phase on The Raw Agricultural Commodity Residue Evaluation of Piperonyl Butoxide Applied as Pyrenone Crop Spray to Small Fruits
2134330	Pyrethrin Analytical Phase on the Raw Agricultural Commodity Residue Evaluation of Pyrethrin Applied as Pyrenone Crop Spray to Citrus Crops
2134331	Independent Laboratory Validation of Golden Pacific Laboratories #GPL-MTH-074 "Determination of Pyrethrins and Piperonyl Butoxide (PBO) in Crops"
2230333	Metabolism/Toxicokinetics Studies
2567916	Determination of Pyrethrins and Piperonyl Butoxide in Crops
2567917	Pyrethrins + PBO: Magnitude of the Residue on Cucumber
2612526	Analytical Method - Pyganic Crop Protection EC 1.4 (pyrethrins) on low growing berry subgroup (13-07G)
2612527	Residue Report - Pyrethrins + PBO: Magnitude of the Residue on Strawberry
2711706	Residue Report - Pyrethrins + PBO: Magnitude of the Residue on Crop Group 19 (Herbs and Spices)
2751113	Residue report - Pyrethrins + PBO: Magnitude of the Residue on Carrot
2751122	Residue report - Pyrethrins + PBO: Magnitude of the Residue on Onion, Dry Bulb
2833483	Residue report - Pyrethrins: Magnitide of the Residue on Hops
2834946	Residue report - Pyrethrins: Magnitude of the Residue on Broccoli

B. Additionla Information Considered

Foreign Review

PMRA Document Number	Reference
3027683	JMPR Review of Pyrethrins

Information Considered in the Occupational and Residential Assessment

A. Studies/Information Provided by Task Force

PMRA Document Number	Reference
2572745	AHETF, 2015. Agricultural Handler Exposure Scenario Monograph: Open Pour Mixing and Loading of Liquid Formulations. Report Number AHE1003-1. March 31, 2015.

PMRA Document Number	Reference
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