Proposed Regulatory Decision Document PRDD2003-03

Lambda-Cyhalothrin
Demand CS Insecticide

The end-use product Demand CS, containing the insecticide active ingredient lambda-cyhalothrin, is proposed for the control of structural pests in and (or) around buildings and transport vehicles under Section 13 of the Pest Control Product Regulations.

This Proposed Regulatory Decision Document provides a summary of data reviewed and the rationale for the proposed Section 13 registration of this product. The Pest Management Regulatory Agency (PMRA) will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to the Publications Coordinator at the address below.

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Foreword

The registration of the end-use product Demand CS, containing the insecticide active ingredient lambda-cyhalothrin, for the control of structural pests (e.g., cockroaches, ants, carpenter ants) as a perimeter treatment around buildings (e.g., residential, farm, office and commercial structures) and as a crack and crevice treatment in non-residential buildings and non-passenger areas of transport vehicles (e.g., aircraft, boats, trailers, train cars, trucks), is proposed by Syngenta. The active ingredient is currently registered in Canada for the control of certain insect pests in agricultural commodities.

Health Canada's Pest Management Regulatory Agency (PMRA) has carried out an assessment of available information in accordance with Section 9 of the Pest Control Product (PCP) Regulations and has found it sufficient pursuant to Section 18*b*), to allow a determination of the safety, merit and value of Demand CS. The PMRA has concluded that the use of Demand CS in accordance with the label has merit and value consistent with Section 18*c*) of the PCP Regulations and does not entail an unacceptable risk of harm pursuant to Section 18*d*). Therefore, the PMRA is proposing the full registration of Demand CS under Section 13 of the PCP Regulations.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document to allow interested parties an opportunity to provide input into the proposed registration decision for this product.

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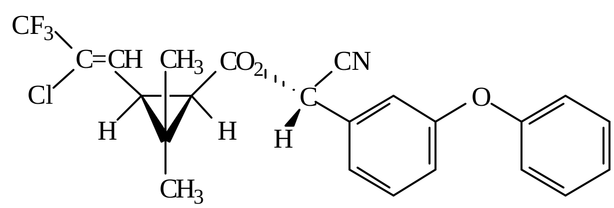
1.0 The active substance, its properties and uses

1.1 Identity of the active substance and impurities

Table 1.1.1 Technical grade active ingredient (TGAI) identification

Active substance	Lambda-cyhalothrin
Function	Insecticide
Chemical name:	
1. International Union of Pure and Applied Chemistry (IUPAC)	A reaction product containing equal quantities of (S)-α-cyano-3-phenoxybenzyl (Z)-(1R,3R)-3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropanecarboxylate and (R)-α-cyano-3-phenoxybenzyl (Z)-(1S,3S)-3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropanecarboxylate
2. Chemical Abstract Services (CAS)	[1α(S*),3α(Z)]-(±)-cyano-(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate
CAS number	91465-08-6
Molecular formula	$C_{23}H_{19}ClF_3NO_3$
Molecular weight	449.9
Structural formula	 (S) (Z)-(1R)-cis
Nominal purity of active	85.5% (limits 82.9–88.1%)
Registration number	24567
Identity of relevant impurities of toxicological, environmental or other significance	The technical grade active ingredient lambda-cyhalothrin does not contain any impurities or microcontaminants known to be Toxic Substances Management Policy (TSMP) Track-1 substances as listed in Appendix II of DIR99-03

1.2 Physical and chemical properties of end-use products

Table 1.2 End-use product: Demand CS

Property	Results
Colour	Off-white
Odour	Typical of aromatic petroleum solvents
Physical state	Liquid
Formulation type	Microencapsulated suspension
Guarantee	100 g/L nominal (limits 95–105 g/L)
Container material and description	Plastic 235 mL and 1 L
Specific gravity	1.026 at 20°C
pH of 1% dispersion in water	5
Oxidizing or reducing action	N/A
Storage stability	The product is stable for 24 months at 25 ±2°C in the commercial packaging.
Explodability	Not explosive
Identity of relevant impurities of toxicological, environmental or other significance	Contains a formulant, Aromatic 100 at 6.79%, which is on the EPA List 2 Potentially Toxic Inerts.

1.3 Details of uses

Demand CS (Sub. No. 1999-2153), a new capsule suspension formulation containing 100 g/L lambda-cyhalothrin, is proposed as a structural insecticide (USC #20) for crack and crevice and barrier treatment. The product is to be applied at 0.03% concentration for indoor use and perimeter barrier treatment of structures and means of transport. Demand CS can be reapplied at 21-day intervals for indoor uses.

Demand CS (EPA Reg. No. 10182-361) is registered in the United States (U.S.) for the control of structural pests (e.g., cockroaches, ants, flour beetles, weevils, carpenter bees), biting/stinging insects (e.g., mosquitoes, ticks, fleas, wasps, bees) and other arthropods (e.g., millipedes, sowbugs, pillbugs, crickets).

2.0 Methods of analysis

2.1 Method for formulation analysis

Product	Method	Linearity range (mg)	Recovery range (%)	Standard deviation (n)	Method
Demand EC	GC/FID	11–33	Waived	0.78% (12)	Acceptable

3.0 Impact on human and animal health

3.1 Integrated toxicological summary

Lambda-cyhalothrin is a synthetic pyrethroid consisting of two of the four enantiomeric forms of cyhalothrin. The submission for lambda-cyhalothrin technical included toxicity studies with lambda-cyhalothrin and cyhalothrin. Core studies (chronic/oncogenicity studies, multi-generation reproduction study in rats, teratology studies in rats and rabbits) were conducted only with cyhalothrin rather than lambda-cyhalothrin. The acute, short-term and genotoxicity studies were carried out using both cyhalothrin and lambda-cyhalothrin.

At the time of the original review it was determined that there are sufficient data to demonstrate that the pharmacokinetics, metabolism, and toxicity of cyhalothrin and lambda-cyhalothrin are similar. Removal of the other two isomers (present in cyhalothrin) did not appear to greatly affect the overall mammalian toxicity. In short-term (90-day) studies in rats with both compounds there was no difference in target organs or effect levels. In dogs, although clinical signs of toxicity were observed at lower dose levels in dogs that received lambda-cyhalothrin for 52 weeks, compared with dogs that received cyhalothrin for 26 weeks, the pattern of toxicity was similar for both compounds. Therefore, it was determined that the results obtained in the chronic toxicity/oncogenicity, teratology, and reproductive studies in the rat with cyhalothrin may be used to assess the toxicity of lambda-cyhalothrin. A previous Health Canada position document (identified as Pesticide Rulings Proposal) was prepared on April 25, 1996. This most recent document has been re-examined with a view toward the use currently under consideration.

A study conducted to compare the absorption, metabolism and excretion of lambda-cyhalothrin and cyhalothrin in the rat demonstrated that approximately 25 and 65% of a single oral dose of both chemicals were excreted in the urine and feces, respectively, within 72 hours. Levels of radioactivity in the tissues were similar, fat being the tissue with the highest concentration. Major metabolites were similar with both lambda-cyhalothrin and cyhalothrin, and included cyclopropylcarboxylic acid and its glucuronide conjugate, 3-phenoxybenzoic acid, 3,4′-hydroxyphenoxybenzoic acid and its sulphate conjugate.

Lambda-cyhalothrin is highly acutely toxic via the oral route of exposure in rats and mice. It is moderately acutely toxic to rats via both the dermal and inhalation routes of exposure. Lambda-cyhalothrin is mildly irritating to the eyes, not irritating to the skin of rabbits and a potential skin sensitizer.

In all the acute oral, dermal and inhalation studies, the overt signs of toxicity were characteristic of neurotoxic effects associated with the synthetic pyrethroids. However there were no gross pathological lesions of the nervous tissues observed.

Acute toxicity data for the end-use product, Demand CS, as a 100 g/L CS formulation and a microencapsulated formulation were submitted. Demand CS exhibited low acute toxicity via the oral and dermal routes of exposure, in rats and rabbits, respectively. It was mildly irritating to the eyes of rabbits and slightly irritating to the skin of rabbits and is a potential skin sensitizer. The acute inhalation toxicity study was conducted on the microencapsulated formulation only and was found to be of low toxicity to rats.

The end-use formulation, Demand CS, contains an aromatic hydrocarbon which appears on the U.S. EPA List 2 (inerts of toxicological concern with a high priority for testing). A preliminary examination of some data submitted in support of the formulant has not identified issues of toxicological concern, however the applicant should be made aware that U.S. List 2 formulants may be subject to a data call-in and to disclosure labelling in the near future.

In a subchronic (90-day) feeding study in rats with lambda-cyhalothrin, adaptive liver changes were observed at a dose of 12.5 mg/kg bw/day (no observed adverse effect level (NOAEL) of 2.5 mg/kg bw/day), whereas, in a one-year study in dogs, clinical signs which may indicate neurotoxicity (subdued behaviour, salivation, muscle tremors, severe ataxia and convulsions) were observed at the highest dose of 3.5 mg/kg bw/day (NOAEL = 0.5 mg/kg bw/day), without any corresponding neuropathology. This indicates that the dog is a more sensitive species than the rat to the toxic effects of lambda-cyhalothrin. In a 21-day dermal study in rabbits with cyhalothrin, skin irritation was the only effect observed at a limit dose of 1000 mg/kg.

In long-term rodent studies, cyhalothrin technical was not oncogenic up to the highest dose tested in the rat or the mouse. The NOAEL in mice was 2 mg/kg bw/day based on clinical signs in males (piloerection and aggressive behaviour), and increases in AST (both sexes) and ALT (females) at the next highest dose. The NOAEL in rats was 2.5 mg/kg bw/day based on a slight increase in mortality (males), decreases in body weight gain (both sexes), alterations in clinical chemistry parameters, increased relative liver weight (both sexes), and increased absolute and relative adrenal weight (females). Lambda-cyhalothrin and cyhalothrin were both negative in a battery of genotoxicity studies (in vitro and in vivo).

In a three-generation reproduction study with cyhalothrin in rats, the NOAEL for both maternal and offspring toxicity was 0.6 mg/kg bw/day, based on decreased body weights in the dams and pups (during lactation) observed at the next highest dose (1.7 mg/kg bw/day). There was no indication of increased sensitivity of the young to exposure to lambda-cyhalothrin.

In teratology studies with cyhalothrin in rats and rabbits, no developmental effects were observed in either species. The maternal NOAEL in rats was 10 mg/kg bw/day, based on decreased body weight gain and clinical signs of neurotoxicity observed in dams (lowest observed adverse effect level (LOAEL) = 15 mg/kg bw/day). The signs of neurotoxicity were observed in two animals, between days 8–10 and days 12–18. The NOAEL for developmental effects was 15 mg/kg/day, the highest dose tested. No significant effects were observed in the rabbits, with a NOAEL for maternal and developmental effects of 30 mg/kg bw/day. There was no indication of any increased sensitivity of the young to exposure to cyhalothrin.

In an acute neurotoxicity study conducted with lambda-cyhalothrin in rats, the NOAEL was 2.5 mg/kg bw, based on increased breathing rate observed in 5 males on day 2, and 5 females on day 1 at the next highest dose (10 mg/kg). Clinical signs indicative of neurotoxicity (decreased activity, ataxia, reduced stability, salivation, piloerection, tiptoe gait, upward curvature of the spine, urinary incontinence, and (or) tremors) were observed in animals from both sexes at the highest dose (35 mg/kg) approximately 7 hours post-administration. Clinical signs including decreased activity, ataxia, increased breathing rate, reduced stability and shaking were also observed in some animals from either sex on days 2 and 3. All clinical signs were reversible by day 5 of the study. In addition, landing food splay measurements were statistically significantly reduced on day 1 for males dosed with 35 mg/kg bw lambda-cyhalothrin. There were no corresponding alterations in brain weight, or gross and histologic neuropathology noted in any of the animals.

In a subchronic neurotoxicity study in rats, the NOAEL was 4.6/5.2 mg/kg bw/day (males/females, respectively) based on a decrease in body weight throughout the study period observed in males exposed to the next highest dose level (11.4/12.5 mg/kg bw/day for males/females, respectively). A decrease in food consumption was also observed at this dose level in both sexes for the first half of the study period. There were no treatment-related neuropathological effects observed at any dose level, in either sex.

No evidence for delayed neurotoxicity of cyhalothrin was observed in hens.

There is no evidence in the database to suggest lambda-cyhalothrin has any adverse effects on the endocrine or immune systems.

Therefore, in both acute (rats and mice) and subchronic (dogs) toxicity studies, the primary endpoint of concern for lambda-cyhalothrin is clinical signs of neurotoxicity, characteristic of the neurotoxic effects associated with the synthetic pyrethroids. In addition, a teratology study in rats resulted in clinical signs of neurotoxicity (uncontrolled limb movements) observed in two dams. No corresponding neuropathology was observed, however, in the database.

Pyrethroid-induced paraesthesia (including symptoms of tingling, itching, numbness or a sensation of burning) is frequently seen after dermal exposure to pyrethroids in occupational settings. While large differences exist in individual susceptibility to paraesthesia, it can occur at doses lower than those causing central or system toxicity, and occurs as a result of a direct effect on intracutaneous nerve endings (Wilks)[1]. In a dermal absorption study, lambda-cyhalothrin dermally applied to the backs of human volunteers resulted in symptoms of paraesthesia.

Table 3.1 Summary of the toxicity studies with lambda-cyhalothrin (with bridging of longer-term studies with cyhalothrin)

Metabolism			
Rate and extent of absorption and excretion: In rats, approximately 25 and 65% of a single oral dose of both cyhalothrin and lambda-cyhalothrin were excreted in the urine and feces, respectively, within 72 hours. **Distribution/target organ(s)**: Distribution was comparable for both cyhalothrin and lambda-cyhalothrin with fat > kidney > liver > blood. **Toxicologically significant compound(s)**: Major metabolites were similar for cyhalothrin and lambda-cyhalothrin. After administration of cyhalothrin, analysis indicated there was no unchanged cyhalothrin in urine or bile, and the feces contained largely unchanged cyhalothrin. Urine and bile metabolites were formed by hydrolysis of the ester bond and included: cyclopropylcarboxylic acid and its glucuronide conjugate, 3-phenoxybenzoic acid, 3,4′-hydroxyphenoxybenzoic acid and its sulphate conjugate.			
Study	**Species/Strain and Doses**	**NOAEL and LOAEL mg/kg bw/day**	**Target Organ/Significant Effects/Comments**
Acute Studies: Lambda-cyhalothrin			
Oral (92.6% purity)	Rats, Alderley Park 5/sex/dose 29.7, 50.8, 62.5, 75.3, 94.1 mg/kg	LD_{50} = 54 (♂,♀)	**Highly toxic—**most deaths in first 24 h. Clinical signs included decreased activity, splayed gait, upward curvature of the spine, urinary incontinence, piloerection, salivation.
Oral (96% purity)	Rats, Alderley Park 5/sex/dose 11.3, 23, 24, 47, 102, 136, 137, 216 mg/kg	LD_{50} = 100 (♂) LD_{50} = 59 (♀) combined = 75 mg/kg	**Highly toxic—**deaths occurred between days 1 and 3. Clinical signs at doses above 11.3 mg/kg included ataxia, dehydration, piloerection, signs of urinary incontinence, ungroomed appearance, upward curvature of the spine.

1 Wilks, Martin F., (2000); "Pyrethroid-Induced Paresthesia—A Central or Local Toxic Effect?" Clinical Toxicology, 38(2).

Study	Species/Strain and Doses	NOAEL and LOAEL mg/kg bw/day	Target Organ/Significant Effects/Comments
Oral (96.5% purity)	Mice, Alderley Park 5/sex/dose 1, 5, 25, 100 mg/kg	LD_{50} = 19.9	**Highly toxic**—Deaths occurred between days 1 and 5. Clinical signs at 25 mg/kg included piloerection, upward curvature of spine, ataxia and salivation. No signs at 100 mg/kg since deaths occurred on day 1.
Dermal (92.6% purity)	Rats, Alderley Park 5/sex/dose 300, 600, 750, 900, 1200 mg/kg	LD_{50} = 632 (♂) LD_{50} = 696 (♀)	**Moderately toxic**—Deaths occurred within 2–3 days. Clinical signs included decreased activity, tiptoe gait, splayed gait, loss of stability, dehydration, signs of urinary incontinence, piloerection, and upward curvature of spine.
Inhalation	Rats, Wistar-derived 5/sex/dose 0.015, 0.041, 0.071 mg/L	LC_{50} = 0.0648 mg/L (♂,♀)	**Moderately toxic**—Time of deaths not stated. Clinical signs included red nasal discharge, chromodacryorrhea, subdued or agitated behaviour, hunched posture, piloerection, abnormal respiratory noise, tiptoe gait, reduced righting reflex.
Eye irritation	Rabbits, NZW (6 ♂) 100 mg test material	MAS = 3.8 MIS = 11.3	**Mildly irritating**—All scores were not zero by day 3
Primary skin irritation	Rabbits, NZW (6 ♀) 500 mg test material	MAS = 0 MIS = 1 (1hr)	**Non-irritating**
Skin sensitization (Maximization test)	Guinea pigs, Hartley albino (♂; 20 test animals, 10 controls)	Potential skin sensitizer	**Potential skin sensitizer**
Acute Studies: Demand CS			
Oral	Rat, Wistar-derived 5/sex/dose single dose— 5000 mg/kg CS formulation and microencapsulated formulation tested	LD_{50} > 5000 mg/kg (♂,♀)	**Low toxicity** No mortality Clinical signs—salivation, reduced stability, piloerection
Dermal	Wistar-derived rats 5/sex/dose single dose— 2000 mg/kg CS formulation and microencapsulated formulation tested	LD_{50} > 2000 mg/kg (♂,♀)	**Low toxicity** No mortality Clinical signs—slight-moderate irritation including desquamation, scabbing

Study	Species/Strain and Doses	NOAEL and LOAEL mg/kg bw/day	Target Organ/Significant Effects/Comments
Inhalation	Wistar-derived rats 5/sex/dose single dose—5 mg/L microencapsulated formulation only	LC_{50} > 4.62 mg/L	**Low toxicity** 2 deaths (killed in extremis) Clinical signs related to mild respiratory irritation and pyrethroid induced toxicity Survivors showed delayed recovery
Eye irritation	Rabbit, NZW (6 ♀) 100 mg test material CS formulation and microencapsulated formulation tested	CS formulation MAS = 6.7 MIS = 2.8 microencapsulated MAS = 3.7 MIS = 0.4	**Mildly irritating** No mortality Clinical signs—slight-moderate redness, slight chemosis, slight-moderate discharge
Primary skin irritation	Rabbit, NZW (6 ♀) 500 mg test material CS formulation only	MAS = 1.1 MIS = 1.3	**Slightly irritating** No mortality Clinical signs—very slight erythema, very slight edema
Skin sensitization	Guinea Pig, Dunkin-Hartley albino (♀) CS formulation— 10 test/10 control microencapsulated — 20 test/10 control	Potential skin sensitizer	**Potential skin sensitizer**
Short Term Toxicity: **Lambda-cyhalothrin**			
90-day dietary	Rats, Alpk/AP Wistar 20/sex/dose 0, 10, 50, 250 ppm (0, 0.5, 2.5, 12.5 mg/kg bw/day)	NOAEL = 2.5 mg/kg bw/day LOAEL = 12.5 mg/kg bw/day	**2.5 mg/kg and above:** ↑hepatic aminopyrine-N-demethylase activity and ↑relative liver weights (considered adaptive responses). **12.5 mg/kg:** ↓bw gain and food consumption.
52-week oral (in corn oil via gelatin capsules)	Dogs, Beagle 6/sex/dose 0, 0.1, 0.5, 3.5 mg/kg bw/day	NOAEL = 0.5 mg/kg bw/day LOAEL = 3.5 mg/kg bw/day	**0.5 mg/kg:** slight increases in incidence of subdued behaviour and fluid feces **3.5 mg/kg:** severe ataxia, convulsions, salivation, muscle tremors, auditory hyperaesthesia, subdued behaviour, vomiting, diarrhoea; ↓ food consumption; ↓testes wt and slightly ↑ liver wts.
Short-term Toxicity: Cyhalothrin			
90-day dietary	Rats, Alpk/AP Wistar derived 20/sex/dose 0, 10, 50, 250 ppm (0, 0.5, 2.5, 12.5 mg/kg bw/day)	NOAEL = 2.5 mg/kg bw/day LOAEL = 12.5 mg/kg bw/day	**2.5 mg/kg:** ↓ in plasma triglycerides, ↑ hepatic aminopyrine-N-demethylase, mild proliferation of SER (considered non-adverse responses) **12.5 mg/kg:** ↓ bw gain in males

Study	Species/Strain and Doses	NOAEL and LOAEL mg/kg bw/day	Target Organ/Significant Effects/Comments
21-day dermal	Rabbits, NZW 5/sex/dose 10, 100, 1000 mg/kg bw/day	NOAEL (systemic effects) = 1000 mg/kg bw/day	**1000 mg/kg:** increased incidence of erythema and edema compared to controls; no systemic toxicity
26-week oral (in corn oil via gelatin capsule)	Dogs, Beagle 6/sex/dose 0, 1, 2.5, 10 mg/kg bw/day	NOAEL not determined	**1 mg/kg and above:** ↑ incidence of diarrhoea (dose-dependent) **2.5 mg/kg and above:** ↓serum albumin **10 mg/kg:** vomiting, unsteadiness, lack of coordination and excessive salivation
Chronic Toxicity/Oncogenicity: Cyhalothrin			
2-yr dietary	Mice, Charles River 52/sex/dose 0, 20, 100, 500 ppm (0, 2, 10, 50 mg/kg bw/day) Four additional satellite groups of 12/sex/dose were sacrificed after 12 months	NOAEL = 2 mg/kg bw/day LOAEL = 10 mg/kg bw/day	**10 mg/kg:** piloerection and aggressive behaviour (♂); ↑ AST (♂, ♀), ↑ALT (♀). **50 mg/kg:** piloerection and aggressive behaviour (♂), hunched posture (♂,♀), slightly ↑ mortality (♂), ↓bw gain (♂), ↑ AST and ALT in plasma (♂,♀), ↓ cholesterol (♀), ↓ total plasma protein and globulin (♂) **Not oncogenic.**
2-yr dietary	Rats, Alpk/AP, Wistar derived 62/sex/dose 0, 10, 50, 250 ppm (0, 0.5, 2.5, 12.5 mg/kg bw/day) Satellite groups of 10/sex/dose sacrificed at 12 months	NOAEL = 2.5 mg/kg bw/day LOAEL = 12.5 mg/kg bw/day	**2.5 mg/kg:** ↓bw gains (♂), ↓ total protein (♀), ↓ plasma cholesterol (♂), ↓ relative adrenal wt (all considered non-adverse) **12.5 mg/kg:** slight ↑ mortality (♂), ↓ body weight (♂,♀), ↑ plasma AST (♀), ↑ total protein (♀), ↑ plasma cholesterol (♂), ↑ triglycerides (♂,♀), ↓ urine volume (♂,♀), ↑ relative liver weight (♂,♀), ↑ absolute and relative adrenal weight (♀). **Not oncogenic.**

Study	Species/Strain and Doses	NOAEL and LOAEL mg/kg bw/day	Target Organ/Significant Effects/Comments
Reproductive/Developmental Toxicity: Cyhalothrin			
3-generation reproduction, dietary	Rat, Alpk/AP Wistar derived; 30♀/dose 0, 10, 30, 100 ppm (0, 0.6, 1.7, 5.5 mg/kg bw/day)	NOAEL (maternal) = 0.6 mg/kg bw/day LOAEL (maternal) = 1.7 mg/kg bw/day NOAEL (offspring) = 0.6 mg/kg bw/day LOAEL (offspring) = 1.7 mg/kg bw/day	**1.7 mg/kg and above:** ↓bw gain in dams (10–15%) and pups (during lactation period) **5.5 mg/kg:** slight ↓ in pup viability during lactation
Teratogenicity, oral gavage	Rats, CD 24 ♀/dose 0, 5, 10, 15 mg/kg bw/day during days 6–15 of gestation.	NOAEL (maternal) = 10 mg/kg bw/day LOAEL (maternal) = 15 mg/kg bw/day NOAEL (developmental) = 15 mg/kg bw/day	Maternal toxicity: **15 mg/kg:** ↓ bw gain, uncoordinated limb movements **No evidence of teratogenicity.**
Teratogenicity, oral gavage	Rabbits, NZW 18–22♀/dose 0, 3, 10, 30 mg/kg bw/day during days 6–18 of gestation	NOAEL (maternal) = 30 mg/kg bw/day NOAEL (developmental) = 30 mg/kg bw/day	No significant effects on dams or fetuses were observed. **No evidence of teratogenicity.**
Neurotoxicity: Lambda-cyhalothrin and Cyhalothrin			
Acute neurotoxicity (lambda-cyhalothrin)	Rats, Alpk: AP_fSD 10/sex/dose 0, 2.5, 10, 35 mg/kg bw	NOAEL = 2.5 mg/kg bw LOAEL = 10 mg/kg bw	**10 mg/kg:** increased breathing rate in 5 males on day 2 and 5 females on day 1 **35 mg/kg:** Clinical signs indicative of neurotoxicity (decreased activity, ataxia, reduced stability, salivation, piloerection, tiptoe gait, upward curvature of the spine, urinary incontinence, and (or) tremors) observed in both sexes approximately 7 hours post-dose. Signs were observed in some animals from either sex on days 2 and 3. All signs were reversible by day 5. Reduced landing foot splay measurements on day 1 for males

Study	Species/Strain and Doses	NOAEL and LOAEL mg/kg bw/day	Target Organ/Significant Effects/Comments
Subchronic neurotoxicity (lambda-cyhalothrin)	Rats, Alpk: AP_fSD 12/sex/dose 25, 60, 150 ppm in diet (2.0, 4.6, 11.4 mg/kg bw/day in males, and 2.2, 5.2, 12.5 mg/kg bw/day in females)	NOAEL = 4.6/5.2 mg/kg bw/day LOAEL = 11.4/12.5 mg/kg bw/day	**11.4/12.5 mg/kg bw/day:** Decreased bw in males throughout the study period. Decreased food consumption in males and females for first half of the study.
Delayed neurotoxicity (cyhalothrin)	Hens, 10/dose Dosed singly at 0, 2500, 5000, 10 000 mg/kg bw then observed for 21 days. 10 positive controls received TOCP at 500 mg/kg bw	N/A	**5000 mg/kg and above:** treatment related decreases in bw No signs of neurotoxicity or histopathological changes in the spinal cord observed in any cyhalothrin-treated animals. Positive control animals developed ataxia and exhibited histopathological changes in the spinal cord.
Dermal absorption (cyhalothrin)	Human subjects (5) Single dermal dose of 20 mg/800 cm^2 applied to backs	N/A	All subjects reported symptoms of paraesthesia including mild to moderate tingling sensation and mild itchiness and in some cases a warm feeling over the back. Mild irritation was noted in one subject over the whole back

Genotoxicity: **Lambda-cyhalothrin**

Study	Species/Strain or Cell Type and Concentrations/Doses Employed	Results
Reverse mutation in bacteria	*Salmonella typhimurium*, TA1535, TA1537, TA1538, TA98, TA100. 1.6, 8.0, 40, 200, 1000, 5000 µg/plate ± S9 enzyme	Negative
In vitro chromosomal aberration	Human blood lymphocytes 100, 500, 1000 µg/mL ± S9 enzyme	Negative
In vitro unscheduled DNA synthesis	HeLa cells 1, 10, 100, 1000 µg/mL ± S9 enzyme	Negative
In vivo Erythrocyte micronucleus assay	Mice (♂,♀ C57BL/6J), bone marrow 0, 22, 35 mg/kg bw/day	Negative

Study	Species/Strain and Doses	NOAEL and LOAEL mg/kg bw/day	Target Organ/Significant Effects/Comments
Genotoxicity: Cyhalothrin			
Reverse mutation in bacteria	*Salmonella typhimurium*, TA1535, TA1537, TA1538, TA98, TA100. 4, 20, 100, 500, 2500 µg/plate ± S9 enzyme		Negative
In vivo chromosomal aberration	Male rats, bone marrow sampled at 6 and 24 h after treatment 1 or 5 consecutive oral dose of 0, 1.5, 7.5 mg/kg bw		Negative
In vivo dominant lethal assay	Male mouse (CD-1) 5 consecutive daily oral (gavage) doses of 0, 1, 5, or 10 mg/kg bw		Negative
ARfD: The ARfD is 0.025 mg/kg bw, based on the NOAEL of 2.5 mg/kg bw from the acute neurotoxicity study in rats, and an uncertainty factor of 100× (10× for intraspecies variation, and 10× for interspecies variation).			
ADI: The ADI is 0.005 mg/kg bw/day based on the NOAEL of 0.5 mg/kg bw/day from the 52-week dietary dog study and an uncertainty factor of 100× (10× for interspecies extrapolation and 10× for intraspecies extrapolation). Further, the synthetic pyrethroid class of insecticides will undergo reevaluation in the near future at which time the ADI will be reassessed.			

3.2 Determination of acceptable daily intake (ADI)

The acceptable daily intake is based on the NOAEL of 0.5 mg/kg bw/day from the 52-week dog study, with an uncertainty factor of 100×. The ADI is therefore 0.005 mg/kg bw/day. Effects observed at the LOAEL in this study included severe ataxia, convulsions, salivation, muscle tremors, auditory hyperaesthesia, subdued behaviour, vomiting, diarrhoea, decreased food consumption, decreased testes weight and slightly increased liver weights. The synthetic pyrethroid class of insecticides will undergo reevaluation in the near future, at which time the ADI will be reassessed. A developmental neurotoxicity study will also be required in the future, based on the mode of action of the chemical.

3.3 Acute Reference Dose (ARfD)

The acute reference dose for lambda-cyhalothrin is 0.025 mg/kg bw, based on the NOAEL of 2.5 mg/kg bw from the acute neurotoxicity study in rats, and an uncertainty factor of 100× (10× for intraspecies variation, and 10× for interspecies variation).

3.4 Toxicological endpoint selection—occupational and bystander risk assessment

The risk assessment considered two exposure scenarios: the professional applicator and the resident bystander (adult and child). Pest control operators would treat for crack and crevice for control of crawling insects intermittently throughout the year. Perimeter treatment would be seasonal. Exposure during mixing, loading and application of lambda-cyhalothrin for crack and crevice or perimeter treatment would be intermittent, and of intermediate to long-term duration. Application is likely to be repeated several times a year, at a minimum interval of 21 days for crack and crevice. Post-application exposure for children and adults in a residential scenario would therefore be of intermediate duration.

Demand CS is of low toxicity via the oral, dermal and inhalation routes of exposure, is mildly irritating to the eyes, is slightly irritating to the skin and is considered to be a potential skin sensitizer.

Lambda-cyhalothrin is not genotoxic or oncogenic. It is not a developmental or reproductive toxicant and there was no indication of increased sensitivity of the young as a result of exposure to lambda-cyhalothrin. There is no evidence that lambda-cyhalothrin has an adverse effect on the endocrine or immune systems.

The dog was the most sensitive test species and exhibited clinical signs related to pyrethroid toxicity. The NOAEL of 0.5 mg/kg bw/day from the 52-week oral study in the dog was selected as the most appropriate endpoint for conducting an intermediate or long-term risk assessment. At the LOAEL, 3.5 mg/kg bw/day, there were treatment-related findings such as severe ataxia, convulsions, salivation, vomiting, diarrhoea, decreased food consumption and testes weight and slight increase of liver weights. For the identified toxicity endpoints, a safety factor of 100 is considered adequate.

3.5 Impact on human and animal health arising from exposure to the active substance or to its impurities

Dermal Absorption

Two in vivo dermal absorption studies of lambda-cyhalothrin have been reviewed by the PMRA. One study was conducted on rats, the other on human volunteers. The estimated dermal absorption of lambda-cyhalothrin is virtually the same for the human study and the rat study, 22% versus 21% respectively, however the individual studies are very different. The rat study used multiple doses, and can account for 99.1% of the applied dose. Typical of human in vivo studies, the total dose was not accounted for and the only measure of absorption was the urinary excretion value. In addition, the human study used a single dose and a low number of replicates. A value of 21% dermal absorption is considered appropriate for a risk assessment.

3.5.1 Operator exposure assessment

Application of Demand CS

Demand CS Insecticide, containing 100 g/L lambda-cyhalothrin, is proposed for use as a structural and surrounding soil insecticide. It is proposed for indoor application for cracks and crevices treatment or outdoors, for perimeter treatment for control of crawling insects. The minimum dilution rate which can be supported by the PMRA is 0.03% (0.3 g a.i./L).

Mixing, loading and application is likely to be performed by one individual. For crack and crevice or perimeter treatment, Demand CS would be mixed with water and applied using hand-held or power-operated application equipment delivering a coarse spray. For perimeter (barrier) treatment, pest control operators would apply a continual band of insecticide solution, 3 m wide with the wall being sprayed upward to 0.9 m, around building foundations, to thoroughly and uniformly wet the foundation and band area. Windows, doors and roof overhangs may be sprayed as well. For indoor applications, Demand CS could be reapplied at 21-day intervals if necessary.

Approximately 2 L of insecticide solution may be applied per location for a crack and crevice treatment and 6 locations can be treated per day by a professional applicator, which represents a maximum of 3.6 g a.i. handled per day. For perimeter treatment, an average of 20 L is applied per location and a mixer/loader/applicator would handle a total of 120 L of formulated product per day or 36 g a.i./day.

Operator exposure

Based on the amount handled per day, mixing/loading/application for perimeter treatment is considered a worst case scenario.

The Outdoor Residential Exposure Task Force[2] (ORETF) generated several exposure studies which monitored exposure of lawn care technicians and homeowners mixing, loading and applying pest control products to turf. Mixer/loader/applicator exposure was monitored using passive dosimetry, hand washes, face/neck wipes, and personal air samplers. Exposure estimates were normalized for kilogram of active ingredient handled and unit exposures were presented on the median measure of central tendency. One of these studies, conducted to monitor exposure during application of a surrogate liquid formulation, was selected and considered appropriate for estimating exposure of pest control operators applying lambda-cyhalothrin for barrier spray using hand-held or power-operated sprayer. Dermal and inhalation exposure estimates were generated based on the following equation:

$$\textbf{Exposure } (\mu g/kg/day) = \frac{\textbf{unit exposure} \times \textbf{a.i. handled per day} \times \textbf{DA}}{\textbf{body weight}}$$

Where:

Unit exposure:	Expressed in µg/kg a.i. handled (from ORETF study)
a.i. handled per day:	Expressed in kg a.i.
DA:	Dermal absorption is 21%
Body weight:	70 kg

2 Syngenta is a member of ORETF

Table 1 Unit exposure values extracted from ORETF study

Application equipment (reference)	Unit exposure µg a.i./kg a.i. handled[a]			
	Total dermal	Dermal absorbed[b]	Inhalation exposure	Total exposure
Crack and crevice or barrier treatment: Pest control operators wearing long-sleeved shirt, long pants and gloves; liquid formulation				
Turf (low pressure nozzle gun sprayer)	838	176	4	180

[a] Median unit exposure values
[b] The dermal absorption value is 21%

Table 2 Occupational exposure for mixer/loader/applicator

Treatment type	Exposure µg a.i./kg bw/d[a]			
	Total dermal	Dermal absorbed[b]	Inhalation exposure	Total exposure
Pest control operators wearing long-sleeved shirt, long pants and gloves; liquid formulation				
Perimeter (low pressure nozzle gun sprayer)	0.431	0.0905	0.002	0.0925

[a] Based on median unit exposure values
[b] The dermal absorption value is 21%

Based on a NOAEL of 0.5 mg/kg bw/day from the 52-week dog study and an estimate of daily exposure of 0.0925 µg a.i./kg bw/d, a margin of exposure (MOE) of 5700 is obtained. This MOE is considered acceptable.

3.5.2 Bystanders

Recent evidence indicates that levels of non-target surface residues from crack and crevice treatment may not be negligible. Post-application exposure to outdoor residues as a result of a barrier treatment would be within 3 m of a wall. Exposure would not be of long duration and the area would not typically be suitable for play by children.

A quantitative assessment of residential post-application exposure was conducted for adults and children re-entering treated areas as a result of indoor application. Exposure sources in this case would include mainly dermal contact for adults, dermal contact and non-dietary ingestion from hand-to-mouth activity, for children. Exposure for this scenario is considered to be of intermediate (1–6 months) duration. The assessment supported use of Demand CS only for use in non-residential buildings and structures and non-passenger areas of modes of transport.

3.5.3 Workers

Exposure of workers to lambda-cyhalothrin when re-entering industrial and commercial areas treated for crack and crevice with Demand CS is considered to be significantly less than post-application exposure of adults or children in a residential area. This is because activities in a workplace are such that opportunities for dermal contact with treatment residues are significantly less than in a home environment. Assumptions used above for the residential post-application exposure assessment are not considered appropriate for this scenario. A qualitative assessment was performed for this scenario; exposure to workers from crack and crevice application can be adequately mitigated with improvement of label precautionary statements.

4.0 Residues

Not applicable.

5.0 Fate and behaviour in the environment

Demand CS contains 100 g a.i./L lambda-cyhalothrin in a microencapsulated form. Either hand or power application equipment will be used for application. This product is currently registered in the United States.

Lambda-cyhalothrin is currently registered in Canada as a foliar spray for the control of insects on canola and mustard and so the data for this active ingredient have already been reviewed.

The Demand CS Insecticide formulation contains solvesso 100 (aromatic hydrocarbon) as a solvent at a concentration of 6.79%. Solvesso 100 (CAS # 64742-95-6) is on the U.S. EPA Inert List 2 (potentially toxic inerts).

The following summary of the environmental fate and environmental toxicology of lambda-cyhalothrin is based on the reviews from Environment Canada (1989) and the PMRA.

5.1 Physical and chemical properties relevant to the environment

Lambda-cyhalothrin is practically insoluble in water (4 µg/L) and hence, this compound should have a low potential for leaching. Lambda-cyhalothrin has a low vapour pressure in the liquid phase at high temperatures (0.2–3.0 mPa at 60–80°C). The vapour pressure of the solid phase at 20°C was estimated to be 2×10^{-4} mPa. An estimated Henry's Law Constant (1/H) of 1.1×10^{5} at 20°C indicates that lambda-cyhalothrin will be non-volatile from water surfaces and moist soil. Based on the values for vapour pressure and Henry's Law Constant, and the strong adsorption of lambda-cyhalothrin to soil and sediment, volatilization is not expected to be an important route for dissipation under field conditions. The octanol/water partitioning coefficient of lambda-cyhalothrin (log K_{ow} = 7) indicates that this compound has a high potential for bioconcentration/bioaccumulation.

5.2 & 5.3 Abiotic and biotic transformation

Hydrolysis is not an important route of lambda-cyhalothrin's transformation at pH 5 and pH 7. No hydrolysis or isomerization occurs at pH 5, however a slow isomerization of this compound occurs at pH 7. Results of a laboratory study indicate that almost half of lambda-cyhalothrin isomerized by day 30. At pH 9, lambda-cyhalothrin rapidly transforms with a half-life of 7 days. At this pH, lambda-cyhalothrin is hydrolyzed via ester cleavage to yield a cis-cyclopropanecarboxylic acid moiety and a phenoxybenzyl moiety.

Laboratory studies have demonstrated that lambda-cyhalothrin is stable to phototransformation on soil surfaces. In water, however, phototransformation of lambda-cyhalothrin was evident with an estimated half-life of 23 days. In illuminated river water, the half-life of lambda-cyhalothrin was approximately 20 days. Two major phototransformation products[3] and three isomers of lambda-cyhalothrin were detected in water. The major phototransformation products were identified as (1RS)-cis-3-(ZE-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid (14% of applied) and 3-phenoxybenzoic acid (25% of applied). It is anticipated, therefore, that phototransformation may be an important route for the transformation of lambda-cyhalothrin within the photic zone of aquatic environments. As the potential use pattern of lambda-cyhalothrin involves indoor and outdoor residential (structure, surrounding soil, ornamental and residential outdoor), and this molecule is not highly mobile in the soil, it is unlikely that lambda-cyhalothrin will migrate from the treated area to the open water where aqueous photolysis could occur. Consequently, under the proposed use pattern, the formation of phototransformation products is unlikely.

In laboratory biotransformation studies, lambda-cyhalothrin transformed in sandy loam soil under aerobic conditions with DT_{50} values ranging from 21 to 42 days at 20°C to 56 days at 10°C, and under anaerobic conditions with the DT_{50} value of 74 days at 20°C. These values indicate that lambda-cyhalothrin is moderately persistent in soils under aerobic and anaerobic conditions. Under aerobic soil conditions, lambda-cyhalothrin transformed by hydrolytic (up to 7% of applied as (1RS)-cis-3-(ZE-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid) and oxidative (up to 11% of applied as (RS)-α-cyano-3-(4-hydroxyphenoxy)benzyl (1RS)-cis-3-(Z-2-chloro-3,3,3,-trifluoroprop-1-enyl)-2,2,dimethylcyclopropanecarboxylate) pathways. The transformation products were extensively mineralized to CO_2 (up to 70% of the applied by week 25 of incubation). After 25 weeks of

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3 A major transformation product is defined as a transformation product that is present at 10% or more of the initial parent chemical concentration or a transformation product whose concentration increases steadily during a study of transformation in the laboratory.

incubation, up to 32% of the applied remained unextracted from the soil. No data on the aerobic or anaerobic water/sediment biotransformation of lambda-cyhalothrin was provided.

5.4 Mobility

Laboratory studies on adsorption/desorption and leaching of lambda-cyhalothrin and its transformation products in different soils (sandy clay loam, sandy loam, silt and sandy loam) indicated that lambda-cyhalothrin was strongly adsorbed (K_d = 1200–3200 and K_{oc} = 70,000–430,000), and that residues (lambda-cyhalothrin and transformation products) were not detected in the leachate or below the 5 cm soil depth. Results of a thin-layer chromatography (TLC) study also indicated that lambda-cyhalothrin (with a mean Reference factor (Rf) value of 0.03) is immobile in soil, according to Helling and Turner's mobility classification scheme (1968). Therefore, lambda-cyhalothrin and its transformation products are expected to have limited mobility in soil under field conditions.

5.5 Dissipation and accumulation under field conditions

Under Canadian field conditions [St-Amable, Quebec (loamy soil); and Speers, Saskatchewan (clay loam)], lambda-cyhalothrin was moderately persistent in soil (DT_{50} = 53–59 days). Residues were detected only in the top 5 cm of soil. With a single application rate of 53 g a.i./ha, lambda-cyhalothrin was carried over in measurable amounts (12% of the initial amount) into the next spring. These results indicate that repeated applications of lambda-cyhalothrin every year may result in carry-over and sustained residue levels in soil. Transformation products were not detected at more than 10% of the applied amount and no isomerization was reported.

5.6 Bioaccumulation

Data are not relevant to the proposed use category.

5.7 Summary of fate and behaviour in the terrestrial environment

Terrestrial fate endpoints and transformation products detected in terrestrial fate studies are summarized in Tables 5.6.1 and 5.6.2, respectively.

Table 5.6.1 Summary of transformation and mobility data

Transformation	Value	Interpretation
Hydrolysis	No hydrolysis at pH 5 – pH 7 DT_{50}: 7 d at pH 9	Not a route of dissipation in the environment at pH 5–pH 7. An important route of dissipation in the environment at pH 9
Phototransformation	No photolysis on soil DT_{50} in water: 20–23 d	Phototransformation on soil will probably not be a route of dissipation in the environment. Phototransformation may be a route of dissipation in aquatic systems.
Soil aerobic biotransformation	DT_{50} : 21–42 d at 20°C DT_{50} : 56 d at 10°C	Moderately persistent in aerobic soil (Goring et al., 1975).
Soil anaerobic biotransformation	DT_{50} : 74 d at 20°C	Moderately persistent in anaerobic soil (Goring et al., 1975).
Adsorption/desorption	$K_{d\text{-}ads}$: 1200–3200 $K_{oc\text{-}ads}$: 70,000–430,000	Limited potential for mobility (McCall et al., 1981).
Unaged and aged soil column leaching	No residues (lambda-cyhalothrin or transformation products) were detected in the leachate or below 5 cm soil depth.	Limited potential for leaching (McCall et al., 1981).
Soil TLC leaching	Rf: 0.03	Limited potential for mobility (Helling and Turner, 1968).
Canadian field studies	DT_{50} : 53–59 d	Moderately persistent under Canadian environmental conditions (Goring et al., 1975). Residues were detected only in the top 5 cm of soil.

Table 5.6.2 Summary of transformation products formed in terrestrial fate studies

Transformation	Major transformation products (% of applied)
Phototransformation in water	(1RS)-cis-3-(ZE-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid (14% of applied) and 3-phenoxybenzoic acid (25% of applied).
Soil aerobic biotransformation	(1RS)-cis-3-(ZE-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid), (up to 7% of applied) and (RS)-α-cyano-3-(4-hydroxyphenoxy)benzyl (1RS)-cis-3-(Z-2-chloro-3,3,3,-trifluoroprop-1-enyl)-2,2,dimethylcyclopropanecarboxylate), (up to 11% of applied.
Canadian field dissipation	Not detected.

5.8 Summary of fate and behaviour in the aquatic environment

Data are not relevant to the proposed use category.

5.9 Expected environmental concentration (EEC)

Based on the proposed use pattern (spot, band application on indoor and outdoor structural and surrounding soil), the estimation of EEC is not applicable.

6.0 Effects on non-target species

6.1 Effects on terrestrial organisms

6.1.1 Invertebrates

Lambda-cyhalothrin applied at rates of 25 and 250 g a.i./ha had no observed adverse effects on populations of individual species, total numbers, or weight of earthworms in the field.

Acute contact toxicity tests indicated that lambda-cyhalothrin is highly toxic to honeybees. Lambda-cyhalothrin is toxic to most insects and related arthropods, including parasitic and predatory insects and mites that may be used in Integrated Pest Management (IPM) programs.

6.1.2 Wild birds

Lambda-cyhalothrin is practically non-toxic to the mallard duck on an acute oral basis with LD_{50} and no observed effect level (NOEL) values of > 3792 and 3792 mg a.i./kg bw, respectively. It is practically non-toxic to slightly toxic to bobwhite quail and mallard duck, respectively, based on dietary basis. Cyhalothrin did not affect the reproductive performance of the bobwhite quail at dietary concentrations of up to 46 mg a.i./kg diet, the highest dose tested. The early onset of laying eggs and elevated incidence of egg-yolk peritonities and significant reduction in egg production (no observed effect concentration (NOEC) of 5 and 4.6 mg a.i./kg diet, respectively) in mallard duck indicate the possibility of effect on the reproductive system of mallard ducks.

6.1.3 Wild mammals

Data are not relevant to the proposed use category.

6.1.4 Vascular plants

No information was available on the toxicity of lambda-cyhalothrin to terrestrial vascular plants, however the risk to terrestrial vascular plants is expected to be low, based on knowledge of the phytotoxicity of other pyrethroid insecticides.

6.2 Effects on aquatic organisms

6.2.1 Freshwater

6.2.1.1 Invertebrates

Lambda-cyhalothrin is very toxic to the water flea (*Daphnia magna*). The LC_{50} and NOEL for *Daphnia* were 0.36 and 0.06 µg a.i./L, respectively.

6.2.1.2 Fish

Lambda-cyhalothrin is very highly toxic to freshwater fish. The 96-hour LC_{50}s for rainbow trout (*Oncorhyncus mykiss*) and bluegill sunfish (*Lepomis macrochirus*) were 0.24 and 0.21 µg a.i./L, respectively. The corresponding NOEL values were 0.03 and 0.11 µg a.i./L.

6.2.1.3 Algae

No effects were noted on cell density or growth rate of the green alga, *Selenastrum capricornutum*, at concentrations up to 0.58 mg a.i./L.

6.2.1.4 Vascular plants

No information was available on the toxicity of lambda-cyhalothrin to aquatic vascular plants, however the risk to aquatic vascular plants is expected to be low, based on knowledge of the phytotoxicity of other pyrethroid insecticides.

6.3 Effects on biological methods of sewage treatment

Not applicable for the proposed use.

6.4 Risk characterization

The insecticide, lambda-cyhalothrin, is used in the formulation of the end-use product Demand CS (Submission number 99-2153). Demand CS contains 100 g a.i./L lambda-cyhalothrin, in a microencapsulated form, and is proposed for the control of structural and surrounding soil pests (non-food, non-feed areas, non-residential settings), and non-passenger areas of modes of transport. Either hand or power application equipments will be used for application. This product is currently registered in the United States (EPA registration number 10182-361).

Lambda-cyhalothrin (Registration number 24567) is currently registered in Canada as a foliar spray for the control of insects on canola and mustard. This active ingredient is also in the process of registration for seed treatment (Submission number 1998-1749). The use of this active ingredient as a structural insecticide represents a major new use (Category A). The data for this active ingredient have already been reviewed for use as an insecticide for foliar application and seed treatment by Environment Canada in 1989, the Canadian Wildlife Service in 1989, and the Environmental Assessment Division in 1996 and 2002.

The following summary of the environmental fate and environmental toxicology of lambda-cyhalothrin is based on the reviews from Environment Canada (1989), and the PMRA Environmental Assessment Division (1996, 2002).

6.4.1 Environmental behaviour

Lambda-cyhalothrin has a low potential for leaching owing to its low solubility in water and strong adsorption to soil. It is not likely to volatilize from moist soil and water surfaces based on its low vapour pressure and Henry's Law Constant. Lambda-cyhalothrin is stable to hydrolysis at pHs $\leq$ 7; at pHs greater than 7, hydrolysis becomes more important as a route of transformation. Phototransformation of lambda-cyhalothrin on soil will not be a route of transformation in the environment, however in the photic zone of aquatic systems, phototransformation may be important. Based on a log K_{ow} of 7 and bioassays that showed that 22% of bioaccumulated residues (parent or transformation products) remained in fish tissues after 28 days of depuration, lambda-cyhalothrin and/or its transformation products have a high potential for bioconcentration/bioaccumulation.

Laboratory and field studies indicated that lambda-cyhalothrin is moderately persistent in soil under field conditions with a potential for carry-over and accumulation from repeated applications. Lambda-cyhalothrin is also persistent in the sediments of aquatic systems. Biotransformation products of lambda-cyhalothrin were identified as (1RS)-cis-3-(ZE-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid and (RS)-α-cyano-3-(4-hydroxyphenoxy)benzyl (1RS)-cis-3-(Z-2-chloro-3,3,3,-trifluoroprop-1-enyl)-2,2,dimethylcyclopropanecarboxylate. The transformation products were extensively mineralized to CO_2 (up to 70% of the applied by week 25 of incubation). At the same time, up to 32% of the applied remained unextracted from the soil.

As determined in adsorption/desorption, leaching and TLC studies, lambda-cyhalothrin and its transformation products are expected to have limited mobility in soil under field conditions.

6.4.2 Terrestrial and aquatic organisms

Lambda-cyhalothrin applied at rates of 25 and 250 g a.i./ha had no observed adverse effects on populations of individual species, total numbers, or weight of earthworms in the field.

Acute contact toxicity tests indicated that lambda-cyhalothrin is highly toxic to honeybees. Lambda-cyhalothrin is toxic to most insects and related arthropods, including parasitic and predatory insects and mites that may be used in integrated pest management (IPM) programs. Lambda-cyhalothrin is very toxic to the water flea (*Daphnia magna*). The LC_{50} and NOEL for *Daphnia* were 0.36 and 0.06 μg a.i./L, respectively.

Lambda-cyhalothrin is very highly toxic to freshwater fish. The 96-hour LC_{50}s for rainbow trout (*Oncorhyncus mykiss*) and bluegill sunfish (*Lepomis macrochirus*) were 0.24 and 0.21 μg a.i./L, respectively. The corresponding NOEL values were 0.03 and 0.11 μg a.i./L.

No effects were noted on cell density or growth rate of the green alga, *Selenastrum capricornutum*, at concentrations up to 0.58 mg a.i./L. No information was available on the toxicity of lambda-cyhalothrin to aquatic vascular plants, however the risk to aquatic vascular plants is expected to be low, based on knowledge of the phytotoxicity of other pyrethroid insecticides.

No information was available on the toxicity of lambda-cyhalothrin to terrestrial vascular plants, however the risk to terrestrial vascular plants is expected to be low, based on knowledge of the phytotoxicity of other pyrethroid insecticides.

The end-use product, Demand CS Insecticide, contains Solvesso 100 (6.79%), which is a heavy aromatic solvent. This solvent is a mixture of C-10 alkyl benzenes (CAS # 64742-95-6) that is included on EPA List 2 (List 2 consists of formulants identified by the U.S. EPA as potentially toxic, based on structural similarity to List 1 formulations or on data suggestive of toxicity). A recent PMRA review (EAD review, M. Saner and S. Liu, February 2000) concluded that Solvesso 100 is highly toxic to aquatic organisms and practically non-toxic to bobwhite quail. Solvesso 100 is expected to be rapidly removed from aquatic and terrestrial environment through volatilization, and abiotic and biotic transformation. It is therefore not expected to persist in the environment. However, because of the toxicity of Solvesso 100 to aquatic organisms, a label statement should be included on all the labels of products containing Solvesso formulants (see Risk mitigation section).

As the proposed outdoor uses of Demand CS (use as a general or residual surface, crack and crevice or spot treatment in, on, and around buildings and structures and their immediate surroundings and on modes of transport) are relatively controlled, they pose only limited potential for environmental impact. The proposed label indicated some precautionary statements under “ENVIRONMENTAL PRECAUTIONS” to protect the surrounding environment. The label statements should be revised (see Risk mitigation section).

6.5 Risk mitigation

The proposed label indicated some precautionary statements under “ENVIRONMENTAL PRECAUTIONS” to protect the surrounding environment. The label statements should be revised as follows:

> “This product is very toxic to fish and aquatic organisms. It is also contains a petroleum distillate which is moderately to highly toxic to aquatic organisms. Do not contaminate ponds, lakes, streams, rivers or any bodies of water by direct application, during sprayer filling or rinsing operations or while spraying. Drift and runoff from treated areas may be hazardous to aquatic organisms in neighbouring areas. Do not apply when weather conditions favour drift from the target area. When making applications, care should be used to avoid exposure of household pets, particularly fish and reptile pets. This product is highly toxic to bees.”

7.0 Efficacy

7.1 Effectiveness

7.1.1 Intended use

Demand CS Insecticide is proposed for use in controlling pests in and (or) around buildings and transport vehicles. The proposed uses include control of cockroaches and ants which cause damage to buildings and food and may act as mechanical vectors for disease, and control of other arthropods such as centipedes, crickets, firebrats, millipedes, and sowbugs that may be considered a nuisance in and (or) around buildings or vehicles. Demand CS is proposed as a crack and crevice and perimeter, barrier treatment.

The product is proposed for application at a concentration of 0.03%. For indoor uses, the recommended re-treatment interval is 21 days.

7.1.2 Mode of action

Cyhalothrin-lambda is a synthetic pyrethroid insecticide which acts as an axonic poison on both the peripheral and central nervous systems of the insect. Initially, nerve cells are stimulated due to a blocking action on the nerve-membrane sodium channel and eventually paralysis results. A non-systemic, contact or stomach poison with some repellent properties, cyhalothrin-lambda has a rapid knockdown and long residual activity.

7.1.3 Crops

Not applicable.

7.1.4 Effectiveness against pests

Ants
Three studies were submitted to support use claims for control of ants in and around buildings. Demand CS was applied at a rate of 0.03% (g a.i./L water) on different substrates (vinyl, plywood, pinewood and concrete). These substrates were exposed to natural temperature and humidity conditions and were exposed to field conditions without protection from sunlight and rainfall. Both cornfield ants and carpenter ants were tested by exposing them to the treated substrates for a short period. Knockdown rate and mortality rate were assessed after the exposure. The data showed that the substrates treated with Demand CS can have a knockdown rate between 77.6% and 100% up to 3 weeks after treatment depending on type of substrate, and can result in 70–100% mortality for up to 4 weeks. However, residual effect of substrates without protection from sunlight and rainfall diminished 4 weeks after the

treatment. It is concluded that the data support the use claims for control of ants, although some modifications to label use directions are required.

Cockroach, German

Four studies were submitted to support control of German cockroaches. One “operational” trial was conducted in apartments in Florida in 1993 on a “wild” population of German cockroaches. Demand CS was applied at concentrations of 0.015 and 0.03% (g a.i./L water), but the amount of spray solution applied in each apartment was not reported. There were 15 apartments per treatment. Demand CS used at 0.03% controlled cockroaches for 8 weeks after treatment (76–79% reduction of population relative to controls on same date), whereas it had no effect at 0.015% 8 weeks after treatment. Three laboratory trials were conducted to determine the residual efficacy of Demand CS on various substrates and the length of time to knockdown. These trials were conducted using non-resistant adult German cockroaches. Demand CS, applied at a concentration of 0.03% in 54 mL spray solution/m^2, controlled 96–100% of adult cockroaches (relative to controls) for at least 6 weeks after treatment on plywood and vinyl tiles. On the day of application, Demand CS knocked down all cockroaches exposed to a treated surface within 14 minutes.

Crickets

Two laboratory studies were submitted to support the control of crickets. These trials were conducted using house crickets on various types of substrates, under various ambient conditions of temperature, humidity and light. Demand CS, applied at 0.03% (g a.i./L water) in 54–108 mL spray solution/m^2 (depending on the porosity of the substrate), knocked down 98–100% of crickets one hour after being exposed to a treated surface for 1–5 minutes, and killed 100% of crickets 24 hours after exposure. Control lasted for at least 3 weeks after treatment.

Centipede

One laboratory study was submitted to support label claims for control of centipedes. Centipedes were in direct contact with a treated vinyl surface throughout the trial. Eighty percent control was achieved after 1.5 hours with 100% control at 6 hours, for both tested rates (0.03% and 0.06%). The centipedes commonly found in buildings are house centipedes (*Scutigera coleoptera* (Linnaeus)), which live their entire life cycle within buildings (Bennet *et al.*, 1997). The results support the label direction “Treat baseboards, storage areas, and other locations.”

Firebrats and Silverfish

Firebrats control using Demand CS at the proposed rate range (0.03% to 0.06%), as a crack and crevice spray, is supported by the study provided. Control on unpainted plywood was more effective than on painted plywood, however both maintained over 80% control for over four weeks. The author of the study suggested that the interaction between the product and the painted surface is not unusual, insecticides or formulants may be adsorbed or bound to the paint or otherwise affected. Firebrats and silverfish are very similar in appearance and biology, therefore, silverfish can be added to the label. The life cycles of firebrats and silverfish are consistent with the use pattern suggested on the label. Crack and crevice treatment is supported.

Millipedes

Millipedes were tested in a manner consistent with the proposed use as a barrier treatment at a concentration of 0.03%. The millipedes were placed on treated surfaces for 1 or 5 minutes. Knockdown at one hour after treatment was low but 80% to 100% mortality was seen for the residual studies at 3 weeks after treatment. The results of the study support the label directions for this pest.

Sow bugs

Sow bugs had low knockdown rates but 100% mortality was observed in all trials regardless of substrate type or time interval after treatment with a concentration of 0.03% Demand CS. Results from the provided study support the label directions for this insect.

7.2 Phytotoxicity to target plants (including different cultivars), or to target plant products

Not applicable to proposed use sites.

7.3 Observations on undesirable or unintended side effects

See Section 7.5.2 for a discussion of effects on non-target beneficials.

7.4 Economics

7.5 Sustainability

7.5.1 Survey of alternatives

7.5.1.1 Non-chemical control practices

7.5.1.2 Chemical control practices

Many active ingredients have been registered to control the pests identified on the draft label. They include, but may not be limited to, organophosphates (e.g., chlorpyrifos, diazinon, malathion), carbamates (e.g., bendiocarb, carbaryl, propoxur), insect growth regulators (e.g., methoprene), synthetic pyrethroids (e.g., d-trans allethrin, permethrin, pyrethrins, tetramethrin), boric acid and silicon dioxide.

7.5.2 Compatibility with current management practices including IPM

Of the numerous insecticides registered for use against the pests listed on the draft label, many contain synthetic pyrethroids (e.g., allethrin, d-trans allethrin, d-phenothrin, permethrin, pyrethrins, resmethrin, tetramethrin), and registration of Demand CS Insecticide will add another synthetic pyrethroid formulation to the market for this use site. The potential of lambda-cyhalothrin to induce resistance in the arthropods listed on the draft label is not known.

7.5.3 Contribution to risk reduction

7.5.4 Information on the occurrence or possible occurrence of the development of resistance

See Section 7.5.2 for a discussion on resistance.

7.6 Conclusions

Sufficient efficacy data have been provided to support claims that crack and crevice and barrier treatment of structures and vehicles with Demand CS, at a concentration of 0.03%, will control cockroaches, ants (including carpenter ants), centipedes, millipedes, sowbugs, crickets, firebrats and silverfish.

7.6.1 Summary

Table 7.6.1 Summary of label proposals and recommendations

Demand CS, Submission No. 1999-2153, for use in structures (USC 20)

Accepted uses		Comments
Pests	Rate/method of application	The 0.03% application rate effectively controlled all proposed pests when applied as a crack and crevice treatment. To obtain a concentration of a.i. of 0.03%, mix 3.0 mL of Demand 10 CS per litre of water. Apply evenly to sufficiently wet surfaces without puddling.
Ants, centipedes, cockroaches (German), crickets, firebrats, silverfish, millipedes, sowbugs.	0.03% Indoor crack and crevice: re-treat if necessary after a minimum interval of 21 days. Perimeter, barrier treatment: control of ants, crickets, millipedes and sowbugs at 0.03% is supported.	

8.0 Toxic substances management policy (TSMP) considerations

During the review of lambda-cyhalothrin, the PMRA has taken into account the federal Toxic Substances Management Policy[4] and has followed its Regulatory Directive DIR99-03[5]. It has been determined that this product does not meet TSMP Track-1 criteria because:

- Although lambda-cyhalothrin has a potential for accumulation in sediments of aquatic systems, the product will not enter the general environment under normal use conditions.

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4 The federal Toxic Substances Management Policy is available through Environment Canada's Web Site at: http://www.ec.gc.ca/toxics.

5 *The PMRA's Strategy for Implementing the Toxic Substances Management Policy*, DIR99-03, is available through the Pest Management Information Service: Phone 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); Fax (613) 736-3798; E-Mail pminfoserv@hc-sc.gc.ca or through our Web Site at http://www.hc-sc.gc.ca/pmra-arla.

- Lambda-cyhalothrin has a high potential for bioconcentration/bioaccumulation, as indicated by the octanol-water partition coefficient (log K_{ow}) value of 7, which is above the TSMP Track 1 cut-off criterion of $\geq$ 5.0. Under normal use conditions, however, the product will not enter the general environment.

- On the basis of expert judgement, the concentration of lambda-cyhalothrin in any environmental medium is due largely to the quantities of the substance used or released as a result of human activity relative to contributions from natural sources. Therefore, lambda-cyhalothrin meets the criterion for being predominantly anthropogenic.

- The half-lives for the major transformation products of lambda-cyhalothrin were not determined, however the transformation products were extensively mineralized to CO_2 (up to 70% of the applied by week 25 of incubation). In addition, under normal use conditions the product will not enter the general environment.

- The end-use product, Demand CS, contains Solvesso 100 (6.79%), which is a heavy aromatic solvent. This solvent is a mixture of C-10 alkyl benzenes (CAS # 64742-95-6) that is included on the EPA List 2. (List 2 consist of formulants identified by the U.S. EPA as potentially toxic, based on structural similarity to List 1 formulations or on data suggestive of toxicity).

- Demand CS does not contain any formulants or microcontaminants known to be TSMP Track 1 substances, as identified in Appendix II of DIR99-03.

9.0 Proposed regulatory decision

The end-use product Demand CS, containing the insecticide active ingredient lambda-cyhalothrin, is proposed for registration for the control of structural pests (e.g., cockroaches, ants, carpenter ants) as a perimeter treatment around buildings (e.g., residential, farm, office and commercial structures) and as a crack and crevice treatment in non-residential buildings and non-passenger areas of transport vehicles (e.g. aircraft, boats, trailers, train cars, trucks) under Section 13 of the Pest Control Product Regulations.

This proposed regulatory decision document provides a summary of data reviewed and the rationale for the proposed Section 13 registration of this product. The Pest Management Regulatory Agency (PMRA) will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to the Publications Coordinator at the address below.

List of abbreviations

a.i.	active ingredient
ADI	acceptable daily intake
AFC	antibody-forming cell
AP	alkaline phosphatase
ARfD	acute reference dose
ALT	alanine aminotransferase
AST	aspartate aminotransferase
bw	body weight
bwg	body-weight gain
B cells	bursa derived lymphocytes
CD	cluster of differentiation (for naming cell surface molecules expressed on lymphocytes in immunology)
d	day(s)
DA	dermal absorption
DNA	deoxyribonucleic acid
EEC	expected environmental concentration
FOB	functional observational battery
F0	parental animals
F1	1st generation offspring
F2	2nd generation offspring
GIT	gastro-intestinal tract
GSD	geometric standard deviation
h	hour(s)
K_{ow}	octanol water partition coefficient
K_d	adsorption quotient
K_{oc}	adsorption quotient normalized to organic carbon
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LPS	lipopolysaccharide
MIS	maximum irritation score
MAS	maximum average score (at 24, 48 and 72 hours)
MMAD	mass median aerodynamic diameter
MOE	margin of exposure
NK	natural killer cell
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
PFC	plaque-forming cell
PC	positive control
PHED	Pesticide Handlers' Exposure Database

PMA	phorbol myristate acetate
ppm	parts per million
SER	smooth endoplasmic reticulum
sRBC	sheep red blood cell preparation (T-cell dependent antigen)
T cells	thymic derived lymphocytes
T3	tri-iodothyronine
T4	thyroxine
TBC	thyroxine binding capacity
TGAI	technical grade active ingredient
TLC	thin-layer chromatography
TOCP	tri-ortho-cresyl phosphate
TSH	thyroid stimulating hormone
TS	test substance
TSMP	toxic substances management policy
UDPGT	uridine 5′-diphosphatase-glucuronyl transferase
UDS	unscheduled deoxyribonucleic acid synthesis
μg	micrograms
μL	micro litre
yr	year

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