Health Canada Santé Canada

Evaluation Report for Category A, Subcategory 1.3 Application

Application Number: 2008-1306
Application: New Active Ingredient - Maximum Residue Limit (MRLs) only
Product: Danitol Technical Insecticide/Miticide
Registration Number: #####
Active ingredients (a.i.): Fenpropathrin (FDK)
PMRA Document Number 1988762

Background

The active ingredient fenpropathrin is used to control a range of insects and mites, in various fruits, vegetables, nuts, and tea. It is registered for use in the United States, and in several other countries.

Purpose of Application

The purpose of this application was to establish import maximum residue limits (MRLs) in Canada to cover residues of the active ingredient fenpropathrin in/on crop subgroup 5A, crop group 8-09, crop group 9, crop group 10, crop group 11-09, crop group 12-09, crop subgroup 13-07A, crop subgroup 13-07B, crop subgroup 13-07F, crop subgroup 13-07G, crop group 14, avocadoes, black sapote, canistel, mamey sapote, mango, olives, papaya, peanuts, pistachios, sapodilla, star apple, succulent shelled peas, tea (dried), and undelinted cotton seeds.

Chemistry Assessment

The Active Ingredient, Its Properties and Uses

Identity of the Active Ingredient

Active substance	Fenpropathrin
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	(*RS*)-α-cyano-3-phenoxybenzyl 2,2,3,3-tetramethylcyclopropanecarboxylate
2. Chemical Abstracts Service (CAS)	Cyano(3-phenoxyphenyl)methyl 2,2,3,3-tetramethylcyclopropanecarboxylate

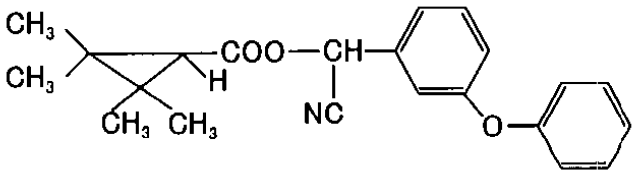
Canada

CAS number 39515-41-8

Molecular formula $C_{22}H_{23}NO_3$

Molecular weight 349.3

Structural formula



Purity of the active ingredient 92%

Physical and Chemical Properties of the Active Ingredient and End-Use Product

Technical Product—Fenpropathrin Technical

Property	Result
Colour and physical state	Yellow to brown liquid or solid
Odour	Faint characteristic odour
Melting range	45-50°C
Boiling point or range	377°C
Density	1.103 g/mL
Vapour pressure at 20°C	0.730 mPa
Ultraviolet (UV)-visible spectrum	pH — λ_{max} (nm) neutral — 277.6 acidic — 277.6 basic — 307.6
Solubility in water at 25°C	14.1 µg/mL
Solubility in organic solvents (%)	Solvent — Solubility Methanol — 1.7 n-Hexane — 16.6 Acetone, xylene, cyclohexanone — > 50 Ethyl acetate — 74.6 Acetonitrile — 76.3
n-Octanol-water partition coefficient (K_{ow})	Log K_{ow} = 6.0
Stability (temperature, metal)	Stable to heat for at least one year; stable to light at λ > 350 nm.

Methods for Analysis of the Active Ingredient

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

Health Assessments

Impact on Human and Animal Health

Toxicology Summary

Fenpropathrin, as with other synthetic pyrethroid insecticides, operates via a neurotoxic mode of action in insects and mammals. Pyrethroids delay the closing of neuronal voltage-dependant sodium channels causing the depolarization of the neuron; this interferes with the ability of the nervous system to relay nerve transmissions and results in downstream clinical effects. Affected neuronal action potentials result in repetitive activity (Type I pyrethroids) or blockage of nerve conduction (Type II pyrethroids). Type II pyrethroids are chemically classified as those with a cyano group on the alpha carbon, while Type I pyrethroids lack this functional group. Pyrethroids induce one of three different neurotoxicity syndromes. The "T syndrome" is generally induced by Type I pyrethroids and is characterized by aggressive sparing, increased sensitivity and fine whole body tremor. The "CS syndrome," generally produced by Type II pyrethroids, is characterized by initial pawing and burrowing, salivation and choreoathetosis (involuntary excessive movements progressing to sinuous writhing). Finally, a mixed Type I/ Type II neurotoxic syndrome may be observed. Fenpropathrin, a pyrethroid with an alpha-carbon cyano group, is a Type II pyrethroid which produces a mixed neurotoxic syndrome.

A detailed review of the toxicological database for fenpropathrin was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to fenpropathrin.

Following oral dosing of radiolabeled fenpropathrin in rats, absorption was similar between sexes as evidenced by the recovery of radioactivity in excreta and tissues. Absorption was slightly higher following repeated administration of a low-dose as compared to a single high or single low dose. Excretion via urine and feces was essentially complete by 72 hours. The parent compound was the major component identified in the feces; no parent compound was identified. Two different major metabolites were identified in the urine depending on the position of the radiolabel used. The glucuronic acid conjugate of 2,2,3,3-tetramethylcyclopropane-carboxylic acid (TMPA-glucuronic acid) was identified in the urine when the radioactive label was located on the acid moiety of the compound, and the sulfate conjugate of 3-(4'-hydroxyphenoxy) benzoic acid (4'-OH-PBacid sulfate) was identified when the alcohol moiety was labeled. The major fecal metabolite identified was (RS)-alpha-cyano-3-phenoxybenzyl 2-hydroxymethyl-2,2,3-trimethylcyclopropane carboxylate (CH_2OH-fenpropathrin). Very little fenpropathrin was retained in the tissues, but repeated dosing of rats indicated some potential for accumulation. Of all tissues sampled, the highest concentration of fenpropathrin was found in the fat. The proposed biotransformation pathways of fenpropathrin included oxidation at the methyl group of the acid moiety, hydroxylation at the 4'- position of the alcohol moiety, cleavage of the ester linkage and conjugation with sulfuric acid or glucuronic acid.

Technical grade fenpropathrin was of high acute toxicity following a single oral dose to the rat. Clinical signs consisted of those indicative of neurotoxicity (muscular fibrillation, decreased spontaneous activity, body tremors, salivation, ataxia, urinary incontinence, limb paralysis, irregular respiration, lacrimation and clonic convulsions). Three chemical impurities in the technical grade fenpropathrin were found to have slight to low acute toxicity following administration of a single oral dose to the rat.

Repeat-dose dietary studies were conducted in rats, mice, and dogs. Clinical signs of neurotoxicity were noted in all species tested. At high doses of fenpropathrin, increased mortality was also noted in all species, but there was no evidence of neuropathology in any study. Increased duration of dosing did not result in an increase in the severity or the nature of the neurotoxic effects noted.

Throughout the 28-day and 90-day dosing studies, body tremors were observed in rats. At higher doses, increased mortality occurred following the observation of severe clinical signs including body tremors and general signs of hypersensitivity. Consistent changes in some hematology and clinical chemistry parameters (decreased platelets, decreased albumin and increased alkaline phosphatase) were also noted in high-dose rats. Body tremors were noted throughout the two year rat study in addition to increased mortality during the first 26 weeks of dosing; these findings were evident at lower doses for female rats than for male rats. Increased kidney, liver and pituitary weights were detected in male rats during this study; however, corroborating histopathological changes were only revealed in the liver. At high doses, testicular atrophy and medullary hyperplasia of the adrenal gland were also observed in male rats.

Clinical signs indicative of neurotoxicity in the one year study in dogs included body tremors, ataxia, languid appearance and polypnea. At the high dose, one death and altered red blood cell parameters were noted in males, and increased kidney weights and altered clinical chemistry parameters in females were also noted.

Treatment related effects in mice required much higher dosing than in all other species treated with fenpropathrin. At the high dose level of the 28-day study, clinical signs were noted primarily in male mice and included piloerection, pallor of the extremities, hunched posture, lethargy, and tremors. Increased mortality and body tremors were noted in the initial long term study (which was terminated due to excessive mortality) in both sexes; however, these effects became apparent in males at lower doses than for females. In the two-year study, increased brain weights were noted in male and female mice in addition to increased kidney weights and hyperactive behaviour in females. No corroborating histopathological findings were revealed in the brains or kidneys of these animals.

Due to the known neurotoxic mode of action of pyrethroid insecticides, the neurotoxic potential of fenpropathrin was investigated in several studies. In these studies, the functional and morphological effects on the nervous system were assessed. Acute and short term neurotoxicity studies were employed to evaluate the neurotoxic potential of fenpropathrin in adult rats. A developmental neurotoxicity (DNT) study assessed potential effects on the developing nervous system following in utero and early postnatal exposure. A range-finding DNT study was also conducted to evaluate the lactational and placental transfer potential of fenpropathrin. Clinical signs indicative of neurotoxicity were noted in all studies.

In acute neurotoxicity testing, single gavage doses of fenpropathrin induced body tremors in both sexes of adult rats. Exacerbated clinical and behavioural signs including convulsions, gait effects, extremely coarse tremors, and death were observed at high dose levels. Following single dose administration, time to peak effect was identified as three hours post-dosing. In an acute neurotoxicity study published in the peer-reviewed literature and conducted in male adult rats, motor activity (the only behavioural parameter assessed) was decreased at dose levels comparable to those producing neurotoxicity in the guideline acute neurotoxicity study (Wolansky et al., 2006).

Following repeat dietary exposure to high doses during neurotoxicity testing, adult females displayed effects such as popcorn seizures, increased startle response, abnormal gait, ataxia, tremors, altered rearing, uncoordinated righting reflex, decreased motor activity and convulsions. In adult males, clinical signs were restricted to body tremors/twitches and hypersensitivity to sound. In the DNT study, offspring in the high dose group displayed behavioural effects such as increased motor activity and auditory startle reflex amplitude as well as decreased habituation to both of these assessments. A high degree of variability in the motor activity data confounded the interpretation of these assessments. In addition, on post-natal day 21 at the highest dose level, brain weights and lengths were decreased in male offspring and some changes in brain morphometric measurements were identified in both sexes. Although brain morphometric assessments were not conducted on the low- and mid-dose pups, there was a low level of concern in light of the absence of any indication of adverse findings in the pups at these dose levels. All of the effects identified in offspring occurred in the presence of maternal toxicity; therefore, sensitivity of the young was not identified in the DNT study.

As part of a range-finding DNT study, it was determined that fenpropathrin can be transferred to offspring via the placenta and maternal milk. Maternal plasma levels of fenpropathrin were assessed and were found to increase with increasing dietary concentrations, as were fetal plasma levels on gestation day (GD) 20. Maternal milk and plasma concentrations were also found to increase with increasing dietary concentrations on lactation day (LD) 4, 10 and 16. Pup plasma concentrations of fenpropathrin increased with dietary concentration on LD 4 and 10, only, and did not increase with dose on LD 16. Concentrations of fenpropathrin were lower in pup and fetal plasma as compared to maternal plasma levels.

In the multigeneration reproduction study conducted in the rat, there was no indication of sensitivity of the young animals. Parental toxicity was evident at the mid-dose level with body tremors and mortality occurring in dams during lactation; decreased pre-mating body weight and body weight gains were noted at higher dose levels in both sexes. Toxicity to offspring was noted at the mid-dose level and above and included body tremors, mortality, and decreased testes weight. A decrease in the viability of offspring at birth and early in lactation was noted at the highest dose level tested.

The developmental toxicity of fenpropathrin was investigated in rats and rabbits. In rabbits, there was an increased number of dams displaying grooming behaviour post-dosing in all treated dose groups. It is believed that the increased grooming behaviour was likely due to animals experiencing paresthesia (due to incidental transfer of the compound during the gavage dosing procedure), a known symptom of contact with pyrethroids. Paresthesia may be described as abnormal skin sensations (such as tingling, tickling, itching, or burning of the skin) that are usually associated with altered peripheral nerve function. Paresthesia is thought to result from contact exposure and is generally believed to be a transient and reversible effect. Since the Lowest-Adverse-Effect-Level (LOAEL) in this study is likely reflective of paresthesia, the level of concern over the lack of a No-Adverse-Effect-Level (NOAEL) in the rabbit developmental toxicology study was lessened. At dose levels above the LOAEL, dams displayed other clinical signs indicative of neurotoxicity such as flicking of the forepaws, shaking movements/trembling, unsteadiness and stamping of the hind feet. In addition, abortions (total litter loss) occurred in dams at these dose levels. No other developmental effects in offspring were noted. Decreased food consumption in dams was also noted at the high dose level. Sensitivity of the young was not identified in this study.

In rats, developmental toxicity consisted of an increased incidence of incompletely and asymmetrically ossified sternebrae. These findings occurred at a dose level which also elicited maternal toxicity consisting of decreased body weight gain and food consumption; therefore, there was no evidence of increased sensitivity of the young in this study. At the highest dose level tested in a developmental toxicity study, increased mortality, body weight loss and clinical signs indicative of neurotoxicity (such as ataxia, sensitivity to external stimuli, tremors, spastic jumping, prostration and convulsions) were also noted in the dams. Mortalities in dams occurred on gestation day (GD) 7-13; two deaths occurred on GD 7 following administration of the second dose. Due to mortality observed at lower doses in pregnant (developmental toxicity study) versus non-pregnant (acute neurotoxicity study) rats, there may be an indication of sensitivity of pregnant and lactating females in this database. The use of different strains in the developmental toxicity and acute neurotoxicity studies, however, complicates this comparison.

Despite a lack of evidence of increased sensitivity of the offspring in any of the submitted studies, residual uncertainty remains regarding susceptibility of the young. Literature studies indicate that pharmacodynamic and pharmacokinetic factors, notably age-dependent maturation of key metabolic processes, may lead to increased susceptibility of the young to pyrethroid toxicity. Young animals have incomplete maturation of the enzyme systems that detoxify pyrethroids, particularly the carboxylesterases and cytochrome P450s. Consequently, pyrethroid concentrations in target tissues (e.g. brain) may be higher in young animals than in adults given the same dose. Pyrethroid neurotoxicity is correlated to peak concentrations of the compound, with gavage dosing patterns resulting 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 the DNT study does not consider time-to-peak-effect and may miss the window of peak toxicity for the pyrethroids (US EPA, 2010).

Behavioural assessments were conducted at the time-to-peak-effect (3 hours) in adults in acute neurotoxicity studies with fenpropathrin; however, behavioural assessments were not conducted at the time-to-peak-effect in offspring. The only neurobehavioural assessments performed in offspring were those assessed in the DNT study. Since the design of the DNT study does not

consider a time-to-peak effect as noted above, an adequate comparison of the sensitivity of the young animal to an adult animal is not available. A comparative oral gavage neurotoxicity study considering time-to-peak-effect in pups, weanling and adult animals, which could address this uncertainty, was also not available. Therefore this uncertainty has been reflected in the form of a database uncertainty factor.

Fenpropathrin was not considered to be genotoxic, based on the overall weight of evidence from *in vivo* and *in vitro* genotoxicity testing. Negative results were obtained in a battery of *in vitro* and *in vivo* genotoxicity studies, with the exception of an equivocal response for gene mutations in mouse lymphoma cells. The increase in small colony size noted in this study, in the presence of metabolic activation, was considered slight relative to responses seen with positive controls. Two-year combined chronic/carcinogenicity studies were conducted in the rat and mouse. Due to high mortality in both sexes, the initial mouse carcinogenicity study was terminated at 90 days, and a second mouse carcinogenicity study was conducted at lower doses. No evidence of carcinogenicity was identified in either the rat or mouse.

Results of toxicology studies conducted on laboratory animals with fenpropathrin, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Tables 1 and 2 of Appendix I.

Incidents Reports

Since April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the PMRA website. Incidents from Canada and the United States were searched and reviewed for fenpropathrin.

The PMRA has not received any human or domestic incident reports related to fenpropathrin.

A Registration Review Docket summary document on fenpropathrin, available from the US EPA (June, 2010) notes that twelve incidents were reported between 2002 and 2010. Causality was established for six of these incidents, and three out of these six incidents were related to occupational application; the remaining three did not involve pesticide application and no further details were available. The health effects noted included dermal, neurological and ocular effects. The US EPA determined that, based on the low severity and low number of incident cases, there did not appear to be a concern that would warrant further investigation. A search of the California Department of Pesticides Regulation incident report database, from 1993-2007, describes 250 agricultural incidents. Only two of the 250 incidents were specific to fenpropathrin exposure (all other incidents involved exposure to a mixture of pesticides) and involved field workers who experienced symptoms of itching, burning, and prickling skin sensations following exposure to fenpropathrin. These symptoms are reflective of paresthesia, and are consistent with the mode of action of fenpropathrin.

PCPA Hazard Characterization

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

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, extensive data were available for fenpropathrin. The database contained the full complement of required studies including developmental toxicity studies in rats and rabbits, a rat reproductive toxicity study, a rat DNT study, and a pilot rat DNT study which examined placental and lactational transfer of fenpropathrin to pups.

The prenatal developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of rat or rabbit fetuses to *in utero* exposure of fenpropathrin. There was no indication of increased susceptibility in the offspring compared to parental animals in the reproduction study or the DNT study. Despite these findings, residual uncertainty remains regarding susceptibility of the young in light of findings noted in the peer-reviewed literature. Literature studies indicate that pharmacodynamic and pharmacokinetic factors, notably age-dependent maturation of key metabolic processes, may lead to increased susceptibility of the young to pyrethroid toxicity. This information, coupled with the absence of comparative testing for neurological endpoints in the young and adult animal, results in residual uncertainty concerning susceptibility of the young. These concerns have been reflected through the use of a database uncertainty factor (UF_{DB}). Consequently, the 10-fold factor required under the *Pest Control Products Act* was reduced to 1-fold.

Determination of Acute Reference Dose

To estimate acute dietary risk, the rat developmental toxicity study was selected for risk assessment with a NOAEL of 3.3 mg/kg bw/day. At the LOAEL of 6.5 mg/kg bw/day, a decrease in body weight gain and food consumption was noted in dams between gestation days six and eight (the first two days of treatment). Since the decrease in body weight gain and food consumption occurred after the dams received the first two doses of the chemical, these effects are considered relevant for the establishment of an acute reference dose. Although the LOAEL in this study was not based on a neurotoxic effect, it is comparable to the LOAEL of 4 mg/kg bw/day for increased grooming behaviour (considered to be likely due to paresthesia) in the rabbit developmental toxicity study as well as the NOAEL for decreased motor activity from the non-guideline published acute neurotoxicity study (4 mg/kg bw). Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. As discussed in the PCPA Hazard Characterization section, residual uncertainty regarding susceptibility of the young has been captured as an UF_{DB} of 3-fold. Consequently, the PCPA factor was reduced to 1-fold. **The composite assessment factor (CAF) is 300.**

The ARfD is calculated according to the following formula:

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{3.3 \text{ mg/kg bw}}{300} = 0.011 \text{ mg/kg bw of fenpropathrin}$$

Determination of Acceptable Daily Intake

To estimate the dietary risk of repeat exposure, the ADI was determined on the basis of findings from two co-critical studies: the NOAEL of 3.1 mg/kg bw/day in female rats from the reproduction study and the NOAEL of 3.1 mg/kg bw/day in the 1-year dog study. Neurotoxic effects were noted at the LOAELs, and these studies represented the lowest NOAELs in the database following extended exposure. In female rats, body tremors and mortality were noted at the LOAEL of 9.1 mg/kg bw/day. In dogs, tremors were noted in both sexes and decreased body weight gain, and increased glucose and serum creatinine were noted in females at the LOAEL of 8.14/7.68 mg/kg bw/day. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. As discussed in the PCPA Hazard Characterization section, residual uncertainty regarding susceptibility of the young has been captured as an UF_{DB} of 3-fold. Consequently, the PCPA factor was reduced to 1-fold. **The composite assessment factor (CAF) is 300.**

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{3.1 \text{ mg/kg bw/day}}{300} = 0.010 \text{ mg/kg bw/day of fenpropathrin}$$

Cancer Assessment

There was no evidence of carcinogenicity and therefore, no cancer risk assessment is necessary.

Dietary Exposure

The nature of the residue in plants is adequately understood based on metabolism studies conducted on apples, cabbages, pinto beans, and tomatoes. Further studies were conducted in abscised plant leaves (apple, cabbage, kidney bean, mandarin orange, tomato) to study the nature of the conjugates in plant material, which confirmed that a large proportion of minor metabolites occurred in conjugated forms. The residue definition in plants for enforcement purposes and dietary risk assessment is fenpropathrin.

Residues of fenpropathrin were quantified in plant matrices using gas chromatography with electron capture detection (analytical method RM-22-4). The method was modified slightly as needed to address matrix-specific characteristics. The method was independently validated and deemed adequate as an enforcement method for plant commodities.

To support the establishment of MRLs on the various fruits, vegetables and nuts, residue trials conducted in United States were reviewed. Residue trials conducted in/on tea in South Asia were

also reviewed. Based on the residue data provided, MRLs to cover residues of fenpropathrin in the various commodities will be recommended as shown in Table 3, Appendix 1.

The acute and chronic dietary exposure assessments have demonstrated that consumption of the above listed commodities will not pose a concern to human health for any segment of the population, including infants, children and seniors.

Environmental and Value Assessments

Environmental and value assessments were not required for this application.

Conclusion

The toxicology database submitted for fenpropathrin is adequate to define the majority of toxic effects that may result from exposure to fenpropathrin. There was no evidence of carcinogenicity in rats or mice following longer-term dosing. In acute and chronic studies conducted with laboratory animals, the primary effect of fenpropathrin was neurotoxicity characterized by clinical signs. There was no evidence of increased susceptibility of the young in the guideline studies submitted; however, residual uncertainty remains concerning this matter. Literature studies indicate that young animals have pharmacodynamic and, especially, pharmacokinetic differences (such as the age-dependant maturation of key metabolic processes) that may lead to increased susceptibility of the young to pyrethroid toxicity. The risk assessment protects against the toxic effects noted by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Following the review of all available data, import MRLs are recommended as 75 ppm in citrus oil, 12 ppm in/on caneberries (crop subgroup 13-07A), 10 ppm in/on raisins, 5.0 ppm in/on small fruit (vine climbing), except fuzzy kiwifruit (crop subgroup 13-07F), pome fruits (crop group 11-09), cherries, olives, 3.0 ppm in/on cotton seed oil, head and stem *Brassica* (crop subgroup 5A), bushberries (crop subgroup 13-07B), 2.0 ppm in/on citrus fruits (crop group 10), low growing berry (crop subgroup 13-07G), tea (dried), 1.4 ppm in/on stone fruits, except cherries (crop group 12-09), 1.0 ppm in/on fruiting vegetables (crop group 8-09), avocadoes, black sapote, canistel, mamey sapote, mango, papaya, sapodilla, star apple, undelinted cotton seeds, 0.5 ppm in/on cucurbit vegetables (crop group 9), 0.1 ppm in/on tree nuts (crop group 14), pistachios, 0.02 ppm in/on succulent shelled peas, and 0.01 ppm in/on peanuts.

No further data are required at this time to support the recommended MRLs. The database eficiency could be addressed with the following:

Human Health

- Comparative neurotoxicity testing in pups, weanling and adult animals (DACO 4.8)

List of Abbreviations

λ	wavelength
µg	microgram(s)
AD	administered dose
ADI	acceptable daily intake
a.i.	active ingredient
ALK	alkaline phosphatase
ARfD	acute reference dose
bw	body weight
bwg	body weight gain
CAF	composite assessment factor
CAS	Chemical Abstract Service
DNT	developmental neurotoxicity
F1	first generation
F2	second generation
FC	food consumption
FE	food efficiency
FOB	functional observational battery
g	gram(s)
GAP	good agricultural practices
GD	gestation day
ha	hectare(s)
HAFT	highest average field trial
I.V.	intravenous
kg	kilogram(s)
K_{ow}	*n*-octanol-water partition coefficient
L	litre(s)
LD	lactation day
LD_{50}	lethal dose to 50%
LOAEL	lowest observed adverse effect level
LLOQ	lower limit of quantification
mg	milligram(s)
mL	millilitre(s)
MRL	maximum residue limit(s)
nm	nanometre(s)
NOAEL	no observed adverse effect level
PCPA	*Pest Control Product Act*
PHI	pre-harvest interval
PMRA	Pest Management Regulatory Agency
PND	postnatal day
ppm	parts per million
RAC	raw agricultural commodity
UF_{DB}	database uncertainty factor
US EPA	United States Environmental Protection Agency
WBC	white blood cell count
wt	weight

Appendix 1 Tables and Figures

Table 1 Toxicity Profile of Technical Fenpropathrin

(Effects are known or assumed to occur in both sexes unless otherwise noted; organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted.)

Study Type/ Animal / PMRA #	Study Results[a] (mg/kg/day in ♂/♀)
Acute Oral SD rat PMRA # 1782547	LD_{50} (♂) = 70.6 mg/kg bw LD_{50} (♀) = 66.7 mg/kg bw High Toxicity
Acute Oral SD rat PMRA # 1782548	LD_{50} (♂) = 54.0 mg/kg bw LD_{50} (♀) = 48.5 mg/kg bw High Toxicity
Acute Oral **Impurity: Para-fenpropathrin** ddY mouse PMRA # 1580162	LD_{50} > 5000 mg/kg bw Low Toxicity
Acute Oral **Impurity: Benzoin ester** ddY mouse PMRA # 1580162	LD_{50} > 5000 mg/kg bw Low Toxicity
Acute Oral **Impurity: TMPA-AH** dd mouse PMRA # 1580163	LD_{50} (♂) = 1450 mg/kg bw LD_{50} (♀) = 1880 mg/kg bw Slight Toxicity
28-day dietary SD rat PMRA # 1782556	A NOAEL and LOAEL were not established as this was a dose range-finding study. Adverse effects noted at 42.8 mg/kg bw/day in females included: ↓WBC.

Study Type/ Animal / PMRA #	Study Results[a] (mg/kg/day in ♂/♀)
28-day dietary SD rat PMRA # 1782557	A NOAEL and LOAEL were not established as this was a dose range-finding study. Adverse effects noted at 44.1/51.3 mg/kg bw/day and above in males/females included: deaths/sacrifices (as early as day 3, preceded by severe clinical signs); body tremors; general signs of hypersensitivity; ↓ bw/bwg (♀);↓ food consumption (♂); ↓ tot/diff WBC, ↓ platelets; ↓ total protein, &↓ albumin (♀); ↓ globulin (♂);↓ β-globulin
90-day dietary Rat PMRA # 1580167	A NOAEL and LOAEL were not established as this study was considered supplemental due to limited reporting. Adverse effects noted at the highest dose of 30 mg/kg bw/day included: tremors (beginning wk 5, 1 ♂& 9 ♀); ↓ bw; ↓ food consumption;↓ bwg (♀); ↑ ALK; ↑ potassium (♂); ↓chloride (♀)
90-day dietary Rat PMRA # 1782549	NOAEL: 28.8/25.2 LOAEL: not established/36.1 Based on effects in ♀ only: 1 death day 46; ↓ bw (7-10%); ↓ overall bwg (24%); ↓ food conversion efficiency (21% overall); ↓ platelets (9%); ↑ ALK (31%). No adverse effects were noted in male rats.
28-day dietary CD-1 mouse PMRA # 1782562	A NOAEL and LOAEL were not established as this was a dose range-finding study. No treatment-related effects were noted.
28-day dietary CD-1 mouse PMRA # 1782561	A NOAEL and LOAEL were not established as this was a dose range-finding study. No adverse effects were noted at 63/69 mg/kg bw/day. Adverse effects noted at 123/142 mg/kg bw/day included: piloerection (2 ♂); dark eyes (1 ♂); pallor of the extremities (1 ♀); ↓ overall bwg (♂); ↓ food conversion efficiency (♂); ↑relative liver weight (♂; 14%).
1-year dietary Beagle dog PMRA # 1782551	NOAEL: 3.09 LOAEL: 8.14/7.68 Based on tremors noted sporadically (week 2 onward); ♀ only: ↓ overall bwg, ↑ glucose, ↑ serum creatinine (week 26 only).

Study Type/ Animal / PMRA #	Study Results[a] (mg/kg/day in ♂/♀)
Chronic/ Carcinogenicity (2-year dietary) CD-1 mouse PMRA # 1782563	A NOAEL and LOAEL were not established as this study was considered supplemental. The study was terminated early at 90 days due to excessive mortality. No adverse effects were noted at 4.9/5.7 mg/kg bw/day. Adverse effects were noted at 24.7 mg/kg bw/day and above: ♂ only: 4 mortalities with one displaying tremors, ↑bwg and ↑food consumption.
Chronic/ Carcinogenicity (2-year dietary) CD-1 mouse PMRA # 1580178-1580187	NOAEL (♀): 16.2 LOAEL (♀): 65.2 Based on hyperactivity, ↑brain wt, ↑ kidney wt NOAEL (♂): 4.9 LOAEL (♂): 24.7 The male NOAEL/LOAEL was established based on mortality observed at 24.7 mg/kg bw/day in the initial 2-year mouse study, listed above.
Chronic/ Carcinogenicity (2-year dietary) SD rat PMRA # 1782553	NOAEL: 5.7/7.1 LOAEL: 17.0/21.9 Based on↑ cholesterol (♀); tremors (♀); ↑ mortality first 26 weeks (♀);↑ kidney weight (♂; week 52); dark subcapsular areas of the liver (♂; week 104); dilated congested sinusoids of the liver (♂; week 104).
Two-generation reproduction BR rat PMRA # 1782565	**Parental toxicity**: NOAEL: 2.6/3.1 LOAEL: 7.8/9.1 Based on body tremors (♀) and mortality (♀) during lactation; ↓ pre-mating bw (F1) and bwg (F1 ♀). **Offspring toxicity:** NOAEL (♀):3.1 LOAEL (♀):7.8 Based on effects noted in three F2 females: body tremors, mortality 2/3 ♀ (LD 19-21, following observation of tremors) NOAEL (♂):9.1 LOAEL (♂):23.3 Based on ↓pup viability LD4-21; ↓ bw **Reproductive toxicity:** NOAEL: 2.6/3.1 LOAEL:7.8/9.1 Based on ↓ testes wt (F1). This finding was not statistically significant and no histopathological changes were noted.

Study Type/ Animal / PMRA #	Study Results[a] (mg/kg/day in ♂/♀)
Developmental toxicity-gavage F-344 rat PMRA # 1782570	**Maternal:** NOAEL: 3.3 LOAEL: 6.5 Based on ↓bwg GD 6-8; ↓food consumption GD 6-8 **Developmental:** NOAEL: 3.3 LOAEL: 6.5 Based on ↑incidence of incompletely ossified 5th /6th sternebrae and asymmetrically ossified sternebrae (fetal and/or litter basis)
Developmental toxicity-gavage NZW rabbit PMRA # 1580220	A NOAEL and LOAEL were not established as this was a dose range-finding study, and only non-pregnant female rabbits were dosed. The results of this study, listed below, were reported within the main rabbit developmental study. Adverse effects were noted in females at the lowest dose of 15 mg/kg bw/day and above, including: grooming and flicking of forepaws post-dosing observed at all dosages with the incidence increasing with increasing dosage.
Developmental toxicity-gavage NZW rabbit PMRA # 1782571	**Maternal:** NOAEL: Not established. Adverse effects were noted at the lowest dose tested. LOAEL: 4 Based on ↑ grooming behaviour **Developmental:** NOAEL: 4 LOAEL: 12 Based on total litter loss in one dam at 12 mg/kg bw/day who aborted on Day 19.
Acute neurotoxicity – gavage SD rat PMRA # 1580201 & 1580202	A NOAEL and LOAEL were not established as this was a dose range-finding study. Adverse effects were noted at the lowest dose tested, 6 mg/kg bw, and included the following which was noted 3-5 hours post dosing: Slight tremors (1 ♂), slight tremors and hunched appearance (1 ♀)
Acute neurotoxicity – gavage SD rat PMRA # 1580209	A NOAEL and LOAEL were not established as this was a dose range-finding study. No treatment-related effects on survival, FOB parameters, or motor activity were noted.
Acute neurotoxicity – gavage SD rat PMRA # 1580205	NOAEL (♀): 6 LOAEL (♀): 15 Based on slight tremors day 0 NOAEL (♂): 15 LOAEL (♂): 30 Based on slight tremors & clonic convulsions day 0

Study Type/ Animal / PMRA #	Study Results[a] (mg/kg/day in ♂/♀)
Acute neurotoxicity – gavage Long-Evans rat **Published in peer-reviewed literature**: M.J. Wolansky, et al. (2006) Toxicological Sciences 89 (1) 271-277.	NOAEL (♂): 4 LOAEL (♂): 8 Based on ↓ motor activity
28-day Neurotoxicity – dietary SD rat PMRA # 1580210	A NOAEL and LOAEL were not established as this was a dose range-finding study. No adverse effects were noted at the low dose of 5/6 mg/kg bw/day. Adverse effects were observed at the next highest dose level of 26 mg/kg bw/day in females, and included: ↓bw and ↓ bwg. At 53/60 mg/kg bw/day, following effects were noted: ↓bw; ↓ bwg; ↑ tremors; ↑ hypersensitivity to sound; ↑ head and/or body twitches. In females only**:** ↑popcorn seizures, dried red material (ventral abdominal and urogenital areas), dried yellow material (ventral abdominal area), wet yellow material (ventral abdominal area), abnormal gait (walking on tiptoes, hindlimbs splayed or dragging, ataxia), ↑ slight to moderately-coarse tremors, ↓ rearing, ↓ air righting reflex (lands on back), ↑ startle response (2 ♀), ↓ total and ambulatory motor activity.
90-day Neurotoxicity – dietary SD rat PMRA # 1580212	NOAEL (♀):5 LOAEL (♀): 15 Based on 3 ♀ with abnormal gait (walking on toes, hunched body posture, ataxia), and tremors (1 ♀) observed at week 12. NOAEL (♂): 13 LOAEL (♂): 38 Based on ↓bw; ↓bwg; ↓FC; ↓ FE; body tremors; hypersensitivity to sound.

Study Type/ Animal / PMRA #	Study Results[a] (mg/kg/day in ♂/♀)
Developmental Neurotoxicity- dietary SD rat PMRA # 1580216, 1580217 & 1580218	A NOAEL and LOAEL were not established as this was a dose range-finding study. Adverse effects were noted as follows, and dose levels represent mg/kg bw/day intake during gestation/lactation: **Maternal toxicity** No adverse effects were noted at the low dose of 4/6-8 mg/kg bw/day. Adverse effects were noted at the next highest dose level: *Milk collection group* **13/23 mg/kg bw/day:** Body tremors (1♀, LD3-21); ↓ bwg (GD 6-9); ↓ FC (LD1-7). *Blood collection group* **13/23 mg/kg bw/day:** ↓ bwg (GD 6-9). **Offspring toxicity** *Milk collection group* No adverse effects were noted at the low dose of 4/6-8 mg/kg bw/day. Adverse effects were noted at the next highest dose level: **13/23 mg/kg bw/day:** ↓ bw; ↓ bwg (♂). *Blood collection group* No adverse effects were noted at the low dose of 13/23 mg/kg bw/day. Adverse effects were noted at the next highest dose level: **27/44 mg/kg bw/day:** ↑pup deaths (PND 7-21); ↓litter size on PND 0; ↑ cool bodies; ↓ bw; ↓ bwg; bw loss (♀); ↑ total and ambulatory motor activity; ↓ habituation to motor activity. **Additional Assessments:** *Placental Transfer Phase* Maternal plasma levels increased with increasing dietary concentration of fenpropathrin on GD 20. Concentrations of fenpropathrin were lower in fetal plasma (<LLOQ – 0.0770 ppm) than in maternal plasma (0.111 - 0.268 ppm) at all dietary concentrations on GD 20. *Lactational Transfer Phase* On LD 4, 10 and 16, across groups, maternal plasma concentrations increased with increasing dietary concentration, as did pup plasma concentration on LD 4 and 10 (44-64% of maternal concentrations). On LD16, pup plasma concentrations were similar in 50 ppm and 160 ppm pups (70-85% of maternal concentrations); however, plasma concentrations decreased in 360 ppm pups to 30-33% of maternal plasma concentrations.

Study Type/ Animal / PMRA #	Study Results[a] (mg/kg/day in ♂/♀)
Developmental Neurotoxicity- dietary SD rat PMRA # 1782568	**Maternal:** NOAEL: 8/16 (gestation/lactation) LOAEL = 19/40 (gestation/lactation) Based on body tremors (lactation); ↓bw, ↓bwg and ↓FC (LD 17-21); ↑ grooming (GD 10, LD 10) **Offspring:** NOAEL= 8/16 in ♂/♀ LOAEL= 19/40 in ♂/♀ Based on ↓ bw; ↓ bwg; ↑ number pups small in size; ↓ hindlimb grip strength; ↓ forelimb grip strength;↑ motor activity; ↓ habituation to motor activity (PND 17, 21); ↑ auditory startle reflex (♀; PND 60); ↓ habituation to auditory startle (PND 60); ↓auditory startle latency (♀; PND 60); ↓brain length (♂); ↓brain wt (♂); ↓ base of cerebellar lobule 9 (♂); ↑ length of the ventral limb of the dentate hilus (♀)
Gene mutations in bacteria Salmonella typhimurium PMRA # 1782573	Negative: Precipitate at 5000
Gene mutations in mammalian cells Mouse lymphoma L5178Y PMRA # 1782574	Equivocal, with activation. A significant increase in small diameter colonies was noted at ≥ 119.4 µg/mL; no corresponding increase in large diameter colonies. Increase is slight relative to response seen with positive control.
Sister chromatid exchanges Chinese hamster ovary cell (CHO-K1) PMRA # 1782575	Negative: Tested to limit of solubility.
Chromosome aberrations in vitro Chinese hamster ovary cells PMRA # 1580221	Negative

Study Type/ Animal / PMRA #	Study Results[a] (mg/kg/day in ♂/♀)
Chromosome aberrations in vitro Chinese hamster ovary cells PMRA # 1782576	Negative
Micronucleus assay (in vivo) ICR mice PMRA # 1580221	Negative
Metabolism rat PMRA # 1782579	This study was considered supplemental. **Absorption:** Approximately 46-74% of the administered dose (AD) was absorbed. **Excretion:** Excretion was rapid in both sexes, with approximately 97% AD eliminated by 48 hours post-dosing. Excretion occurred primarily via the urine. **Distribution:** Less than 1% of the AD was retained in the tissues at 8 days post-dosing. The highest levels of radioactivity were detected in the intestines (0.2% AD), skin (0.2-0.3% AD), carcass (0.4% AD), and fat (0.05-0.09% AD). When corrected for tissue mass, the highest levels of radioactivity were detected in the fat, followed by the liver, kidney, blood, muscle and brain.

Study Type/ Animal / PMRA #	Study Results[a] (mg/kg/day in ♂/♀)
Metabolism SD rat PMRA # 1782578	**Absorption** Absorption was similar between sexes and for both radiolabel positions. Absorption was slightly higher (54-58% AD) for the repeated low dose group compared to the single low (31-40% AD) and single high (29-36% AD) dose groups. **Distribution** Distribution was similar between sexes and for both radiolabel positions. The amount of radioactivity retained in tissues was less than 2% AD. For all groups, the fat contained the highest amount of radioactivity (0.3-1% AD). The repeated low dose group retained slightly more radioactivity (0.8-1.9% AD) compared to the other two dose groups (0.3-0.7% AD), indicating some potential for bioaccumulation. **Excretion** Excretion was similar between sexes and for both radiolabel positions. For the repeated dose group, roughly the same amount of radioactivity (50% AD) was excreted in the urine and the feces. For the single low dose and single high dose experiments, the urinary excretion accounted for approximately 28-40% AD while fecal excretion accounted for 65-69% AD. For all groups, most of the radioactivity excreted in the urine was recovered within the first 24 hours after dosing (76-90% AD). Urinary excretion was more than 97% complete by 72 hours. Fecal excretion was at least 75% complete by 24 hours and essentially more than 97% complete by 48 hours post-dosing. The half-lives of elimination for the time period of 0 to 72 hours were 11-16 hours for urinary excretion and 7-9 hours for fecal excretion. **Metabolism** The metabolites identified were similar between the sexes and dose groups. Fecal metabolites were similar for the two radiolabels, but different urinary metabolites were generated for the two radiolabels, with the acid label generating more metabolites (nine peaks in total) than the alcohol label (four peaks). The parent molecule was not identified in the urine. The major urinary metabolite after administration of the alcohol label was the sulfate conjugate of 3-(4'-hydroxyhenoxy) benzoic acid (22-44% AD). The major urinary metabolite identified after administration of the acid label was the glucuronic acid conjugate of 2,2,3,3-tetramethylcyclopropane-carboxylic acid (11-26% AD). In the feces, the parent molecule accounted for the majority of the radioactivity (13-33% AD). The major fecal metabolite was (RS)-alpha-cyano-3-phenoxybenzyl 2-hydroxymethyl-2,2,3-trimethylcyclopropane carboxylate (9-20% AD). Fenpropathrin underwent oxidation at the methyl group of the acid moiety, hydroxylation at the 4'- position of the alcohol moiety, cleavage of the ester linkage and conjugation with sulfuric acid or glucuronic acid. No I.V. administration, no assessment of plasma kinetics, and no assessment of biliary absorption/ excretion were performed.

Table 2 Toxicology Endpoints for Use in Health Risk Assessment for fenpropathrin

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1]

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1]
Acute Dietary, general population	Rat developmental toxicity study	NOAEL: 3.3 mg/kg bw/day Decrease in body weight gain and food consumption was noted in dams between gestation days six and eight (the first two days of treatment).	300
	ARfD = 0.011 mg/kg bw		
Repeat Dietary, general population	Rat reproduction study and 1-year dog study	NOAEL: 3.1 mg/kg bw/day In female rats: body tremors and mortality were noted. In dogs: tremors were noted in both sexes and decreased body weight gain, and increased glucose and serum creatinine were noted in females.	300
	ADI = 0.010 mg/kg bw/day		

[1] CAF (composite assessment factor) refers to a total of uncertainty factors and PCPA factors for dietary assessments.

Table 3 Summary of Supervised Residue Trials and Recommended MRLs.

Head and stem *Brassica* - CG5A U.S. GAP: 0.896 kg a.i./ha/season; PHI = 7 days								1580253 1580254	1881890
Crops	Total Rate (kg a.i./ha)	PHI (days)	Residue Levels (ppm)					Recommended MRL (ppm)	
			n	Min	Max	HAFT	Median		
Broccoli	0.896	7	14	0.11	0.58	0.52	0.39	3.0	
Cabbages with wrapper leaves	0.896	7	12	0.20	2.80	2.75	0.43		
Cabbages without wrapper leaves	0.896	7	18	0.01	0.19	0.14	0.02		
Cauliflowers	0.896	7	4	0.01	0.47	0.40	0.17		
Fruiting Vegetables - CG8-09 U.S. GAP: 0.896 kg a.i./ha/season; PHI = 3 days								1580241 1580259 1580261	1782595 1782597 1782599
Bell peppers	0.896	3	12	0.12	0.70	0.67	0.37	1.0	
Non-bell peppers	0.896	3	8	0.23	0.44	0.40	0.33		
Tomatoes	0.896	3	70	0.01	0.64	0.55	0.13		
Cucurbit Vegetables – CG9 U.S. GAP: 0.896 kg a.i./ha/season; PHI = 7 days								1580252 1782588	1782593
Cantaloupes	0.896	7	20	0.06	0.31	0.27	0.16	0.5	
Cucumbers	0.896	6-8	20	0.01	0.06	0.05	0.01		
Summer squash	0.896	6-8	14	0.01	0.04	0.03	0.01		
Citrus Fruits – CG10 U.S. GAP: 0.896 kg a.i./ha/season; PHI = 1 day								1782590 1782591	1782592 1580260

Grapefruits	0.896	1	14	0.11	0.57	0.47	0.30	
Lemons	0.896	1	10	0.21	1.03	0.88	0.74	2.0
Oranges	0.896	1	36	0.04	1.20	1.20	0.28	
Citrus oil	Citrus oil will have a separate MRL from the RAC MRL.							75
Pome Fruits - CG11-09 U.S. GAP: 0.896 kg a.i./ha/season; PHI = 14 days								1580240 1782582 1782583 1782584 1782585
Apples	0.896	14	8	0.36	1.40	1.13	0.61	5.0
Pears	0.896	14	8	0.27	2.00	1.80	0.71	
Stone Fruits - CG12-09 U.S. GAP: 0.896 kg a.i./ha/season; PHI = 3 days								1580243 1580244 1580257
Cherries	0.861-0.933	3	12	1.43	3.53	3.38	1.90	5.0
Peaches	0.861-0.933	3-4	20	0.39	1.10	1.03	0.71	
Plums	0.861-0.933	3-4	12	0.18	0.58	0.55	0.24	1.4
Dried plums	Dried plums will be covered by RAC MRL.							
Caneberries – CG13-07A U.S. GAP: 0.672 kg a.i./ha/season; PHI = 3 days								1782598
Caneberries	0.890-0.963	2-3	14	1.00	7.10	5.80	2.10	12

Crops	Total Rate (kg a.i./ha)	PHI (days)	Residue Levels (ppm)					Recommended MRL (ppm)	
			n	Min	Max	HAFT	Median		
Bushberries – CG13-07B U.S. GAP: 0.672 kg a.i./ha/season; PHI = 3 days U.S. GAP: 0.896 kg a.i./ha/season; PHI = 21 days (currants only)								1782586	1782589
Blueberries	0.650-0.694	3	18	0.73	2.77	2.75	1.66	3.0	
Currants	0.896	20-21	4	1.22	1.51	1.42	1.42		
Small Fruit Vine Climbing, except fuzzy kiwifruit - CG13-07F U.S. GAP: 0.896 kg a.i./ha/season; PHI = 21 days								1580256	1580258
Grapes	0.896	21	26	0.31	3.30	3.10	1.30	5.0	
Raisins	Raisins will have a separate MRL from the RAC MRL.							10	
Low Growing Berry - CG13-07G U.S. GAP: 0.896 kg a.i./ha/season; PHI = 2 days								1782594	
Strawberries	0.896	2	37	0.20	1.50	1.45	0.56	2.0	
Tree Nuts - CG14 U.S. GAP: 0.896 kg a.i./ha/season; PHI = 3 days								1580245	1580249
Almonds	0.896	3	10	0.01	0.03	0.03	0.01	0.1	
Pecans	0.896	3	10	0.01	0.05	0.05	0.02		
Other Crops									
Tropical Fruits - U.S. GAP: 0.896 kg a.i./ha/season; PHI = 1 day								1580251	
Avocadoes	0.894-0.914	1	12	0.14	0.58	0.55	0.41	1.0	
Avocado data to be translated to black sapote, canistel, mamey sapote, mango, papaya, sapodilla, and star apple.									
Undelinted Cotton Seed- U.S. GAP: 0.896 kg a.i./ha/season; PHI = 21 days								1782587	1782588
Cotton seed	1.68	21	14	0.01	0.29	0.28	0.04	1.0	
Cotton seed oil (refined)	Cotton seed oil (refined) will have a separate MRL from the RAC MRL.							3.0	
Olives - U.S. GAP: 0.896 kg a.i./ha/season; PHI = 7 days								1881859	
Olives	0.897-0.949	7-8	6	1.80	3.70	3.60	2.20	5.0	
Olive oil	Olive oil will be covered by RAC MRL.								
Peanuts - U.S. GAP: 0.896 kg a.i./ha/season; PHI = 14 days								1580262	
Peanuts	1.25	16-23	14	0.01	0.01	0.01	0.01	0.01	

Peanut oil	Peanut oil will be covered under the RAC MRL.							
Peas - U.S. GAP: 0.896 kg a.i./ha/season; PHI = 7 days								1782596
Succulent shelled peas	0.896	6-7	8	0.02	0.02	0.02	0.02	0.02
Tea - South Asia GAP: 0.05-0.06 kg a.i./ha; PHI = 7 days								1848576
Tea, green, black	0.05-0.06	7	15	0.05	1.44	1.38	0.17	2.0

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A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

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2.0 Human and Animal Health

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B. Additional Information Considered

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