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and the environment

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humaine et l'environnement

Proposed Registration Decision

PRD2026-12

Deltamethrin, Ultratec 5SC MUP and Raid Bug Defense

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Overview

Proposed Registration Decision for Deltamethrin

Health Canada, pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Deltamethrin Technical Insecticide, Ultratec 5SC MUP, and Raid Bug Defense, containing the active ingredient deltamethrin, to control ants, cockroaches, house flies, stable flies and spiders on and around the home (outdoors only).

Deltamethrin is currently registered for use on greenhouse ornamentals, greenhouse food crops, industrial oilseed crops, terrestrial feed and food crops, roadsides, shelterbelts, indoor and outdoor surfaces of agricultural buildings and structures, turf for the control of numerous insect pests, outdoor-grown boxwood for the control of box tree moth, and for use in residential and recreational areas for the control of adult mosquitoes. For details, see the Proposed Registration Decision (PRD) document PRD2023-05, *DeltaGard SC Insecticide, containing deltamethrin*; PRD2019-07, *Deltamethrin and Annihilator PolyZone* and Registration Decision (RD) document RD2019-15, *Deltamethrin and Annihilator PolyZone*; PRD2017-05, *Deltamethrin* and RD2017-08, *Deltamethrin*; Proposed Re-evaluation Decision (PRVD) document PRVD2015-07, *Deltamethrin*, and Re-evaluation Decision (RVD) document RVD2018-27, *Deltamethrin and its Associated End-use Products*.

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

This Overview describes the key points of the evaluation, while the Science evaluation provides detailed technical information on the human health, environmental and value assessments of deltamethrin, Ultratec 5SC MUP, and Raid Bug Defense.

What does Health Canada consider when making a Registration Decision?

The primary objective of the *Pest Control Products Act* is to prevent unacceptable risks to individuals and the environment from the use of pest control products. Health or environmental risk is considered acceptable¹ if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value² when used according to the label directions. Conditions of registration may include precautionary measures on the product label to further reduce risk.

To reach its decisions, Health Canada applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children). They also consider the unique characteristics of organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how Health

¹ “Acceptable risks” as defined by subsection 2(2) of the *Pest Control Products Act*.

² “Value” as defined by subsection 2(1) of the *Pest Control Products Act*: “the product’s actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product’s (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact.”

Canada regulates pesticides, the assessment process, and risk-reduction programs, please visit the Pesticides and pest management portion of Canada.ca.

Before making a final registration decision on deltamethrin, Ultratec 5SC MUP, and Raid Bug Defense, Health Canada will consider any written comments received from the public directly related to the proposed decision in this consultation document.³ Health Canada will then publish a Registration Decision⁴ on deltamethrin, Ultratec 5SC MUP, and Raid Bug Defense, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada's response to these comments.

For more details on the information presented in this Overview, please refer to the Science evaluation of this consultation document.

What is deltamethrin?

Deltamethrin is a conventional chemical insecticide that affects the nervous system of insects, leading to death after exposure or ingestion. It is the active ingredient in the domestic class product Raid Bug Defense, which is proposed for use to control certain insect pests on and around the home (outdoors only).

Health considerations

Can approved uses of deltamethrin affect human health?

Raid Bug Defense, containing deltamethrin, is unlikely to affect human health when used according to proposed label directions.

Potential exposure to deltamethrin from the use of Raid Bug Defense may occur when handling and applying the end-use products or when coming into contact with treated surfaces. When assessing health risks, two key factors are considered: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are selected to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose level at which no effects are observed. The health effects noted in animals occur at dose levels more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals, deltamethrin was of low to high acute oral toxicity and low to moderate acute inhalation toxicity. It was of low acute dermal toxicity and was neither an eye nor a skin irritant. Exposure to deltamethrin is not expected to cause an allergic skin reaction; however, itching, tingling, or burning sensations of the skin may occur.

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

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

The acute toxicity of the end-use product Raid Bug Defense, containing deltamethrin, was low via the oral, dermal, and inhalation routes of exposure. It was minimally irritating to the eyes and skin and did not cause an allergic skin reaction.

The acute toxicity of the manufacturing concentrate product Ultratec 5SC MUP, containing deltamethrin, was low via the oral, dermal and inhalation routes of exposure. It was mildly irritating to the eyes; consequently, the signal word “CAUTION” and hazard statement “EYE IRRITANT” are required on the label. It was slightly irritating to the skin and did not cause an allergic skin reaction.

Registrant-supplied short- and long-term (lifetime) animal toxicity tests as well as information from the published scientific literature were assessed previously for the potential of deltamethrin to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. An updated review of the published scientific literature was undertaken for the current assessment. The most sensitive endpoint used for risk assessment was neurotoxicity in young animals. There was evidence that the young were more susceptible than adult animals to these effects. The risk assessment protects against the effects noted above and other potential effects by helping to ensure that the level of exposure to humans is well below the lowest dose level at which these effects occurred in animal tests.

Occupational risks from handling Raid Bug Defense

Raid Bug Defense is a domestic class end-use product and so will not be used by pest control professionals.

Health risks in residential and other non-occupational environments

Risks in residential and other non-occupational environments are not of health concern when Raid Bug Defense is used according to the proposed label directions.

Raid Bug Defense is a domestic class end-use product and is applied by adults (16+ years) to exterior structural surfaces and ant hills. As such, adults may be exposed to deltamethrin through the dermal and inhalation routes during application. No risks of concern were identified through either route of exposure for adults.

Raid Bug Defense can be applied to outdoor structural surfaces and ant mounds in residential areas; however, based on these locations of use, adult and child postapplication exposure to treated surfaces is expected to be minimal. As such, dermal and incidental oral exposures were assessed qualitatively.

Aggregate health risks from dietary and residential exposures

Deltamethrin is used on food/feed crops, so an aggregate assessment was conducted.

There is the potential for individuals to be exposed to deltamethrin via different routes and sources of exposure concurrently. Based on common affects identified in the toxicological reference values, aggregate exposure for adults may occur through inhalation exposure during application and from consuming food and drinking water (dietary exposure) resulting from the currently registered food uses of deltamethrin (PRVD2015-07). No aggregate risks of concern to deltamethrin were identified when the product is used according to label directions.

For children, aggregate exposure may occur through dermal and incidental oral exposure from treated surfaces and from the dietary route. However, aggregate exposure was not quantified as dermal and incidental oral exposure to treated outdoor surfaces is not expected.

Health risks to bystanders

Bystander risks are not of health concern when Raid Bug Defense is used according to the proposed label directions.

Label directions prohibit people (other than the applicator) and pets from being present during application. As such, bystander exposure is expected to be minimal, so health risks are not of concern.

Environmental considerations

What happens when deltamethrin is introduced into the environment?

When deltamethrin is used according to label directions, the risks to the environment have been determined to be acceptable.

Deltamethrin, when used for control of crawling and flying insect pests, will be sprayed as a spot or crack and crevice treatment onto outdoor surfaces of buildings and structures. As a result, the amount of pesticide deposited on soil and water is expected to be minimal and will be localized to the exterior surfaces of buildings and structures.

In laboratory studies, deltamethrin was found to be toxic to bees, beneficial insects, mammals, and aquatic organisms when exposed to high enough concentrations. Due to the application method, exposure to the environment is expected to be minimal, and the environmental risks to non-target terrestrial and aquatic organisms associated with the use of Raid Bug Defense are acceptable when used in accordance with the label directions.

Value considerations

What is the value of Raid Bug Defense?

Raid Bug Defense controls certain insect pests on and around the home (outdoors).

Raid Bug Defense provides control of ants, cockroaches, house flies, stable flies, and spiders. Raid Bug Defense is a new product with a new active ingredient for these uses.

Measures to minimize risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law.

The key risk-reduction measures being proposed on the labels of Deltamethrin Technical Insecticide, Ultratec 5SC MUP, and Raid Bug Defense to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Human health

The proposed label for Raid Bug Defense was amended to align with the required label statements outlined in the PMRA Guidance Document, *Structural Pest Control Products: Label Updates*, which specifies the proper use and handling of domestic class end-use products in residential areas.

Environment

Label statements are required to inform users that deltamethrin is toxic to bees, beneficial insects, and aquatic organisms, and to prevent contamination of irrigation, drinking water supplies and aquatic habitats.

Next steps

Before making a final registration decision on deltamethrin, Ultratec 5SC MUP, and Raid Bug Defense, Health Canada will consider any written comments received from the public that are directly related to this proposed decision, such as comments directed to the science evaluation, in response to this consultation document up to 30 days from the date of publication (by 16 August 2026) of this document. Please forward all comments to Pesticides Regulatory Directorate Publications, through the Public Engagement Portal (Public Engagement Portal forms – Consultation Comment). Health Canada will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and Health Canada's response to these comments.

Other information

When Health Canada makes its registration decision, it will publish a Registration Decision on deltamethrin, Ultratec 5SC MUP, and Raid Bug Defense (based on the Science evaluation section of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the Pesticides Regulatory Directorate's Reading Room. For more information or if you have questions, please contact Pesticides Information Service.

Science evaluation

Deltamethrin and Raid Bug Defense

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance Deltamethrin

Function Insecticide

Chemical name

1. International Union of Pure and Applied Chemistry (IUPAC) (*S*)- α -cyano-3-phenoxybenzyl (1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate

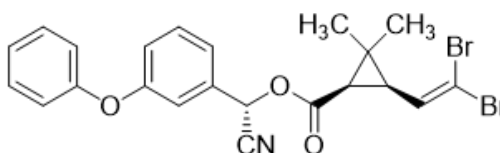
2. Chemical Abstracts Service (CAS) (*S*)-cyano(3-phenoxyphenyl)methyl (1*R*,3*R*)-3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate

CAS number 52918-63-5

Molecular formula C₂₂H₁₉Br₂NO₃

Molecular weight 505.2

Structural formula



Purity of the active ingredient 99.5%

1.2 Physical and Chemical Properties of the Active Ingredient, Manufacturing Concentrate and End-Use Product

Technical Product—Deltamethrin Technical Insecticide

Property	Result
Colour and physical state	Colourless crystals
Odour	Odourless
Melting range	100–102°C
Boiling point or range	Not applicable
Density	0.55 g/cm ³
Vapour pressure at 20°C	1.24 × 10 ⁻⁵ mPa
Ultraviolet (UV)-visible spectrum	Not expected to absorb at $\lambda > 300$ nm

Property	Result																				
Solubility in water at 20°C	< 0.2 µg/L																				
Solubility in organic solvents at 20°C	<table> <tr> <th>Solvent</th><th>Solubility (g/L)</th></tr> <tr> <td>Dioxane</td><td>900</td></tr> <tr> <td>Cyclohexanone</td><td>750</td></tr> <tr> <td>Dichloromethane</td><td>700</td></tr> <tr> <td>Acetone</td><td>500</td></tr> <tr> <td>Benzene</td><td>450</td></tr> <tr> <td>Dimethylsulfoxide</td><td>450</td></tr> <tr> <td>Xylene</td><td>250</td></tr> <tr> <td>Ethanol</td><td>15</td></tr> <tr> <td>Isopropanol</td><td>6</td></tr> </table>	Solvent	Solubility (g/L)	Dioxane	900	Cyclohexanone	750	Dichloromethane	700	Acetone	500	Benzene	450	Dimethylsulfoxide	450	Xylene	250	Ethanol	15	Isopropanol	6
Solvent	Solubility (g/L)																				
Dioxane	900																				
Cyclohexanone	750																				
Dichloromethane	700																				
Acetone	500																				
Benzene	450																				
Dimethylsulfoxide	450																				
Xylene	250																				
Ethanol	15																				
Isopropanol	6																				
<i>n</i> -Octanol-water partition coefficient (K_{ow})	Log K_{ow} = 4.6																				
Dissociation constant (pK_a)	Not applicable																				
Stability (temperature, metal)	Stable at ≤ 190°C; under UV irradiation and in sunlight, a <i>cis-trans</i> isomerization, splitting of the ester bond, and loss of bromine occur; more stable in acidic than alkaline media.																				

Manufacturing Concentrate—Ultratec 5SC MUP

Property	Result
Colour	White
Odour	Waxy smell
Physical state	Liquid
Formulation type	Solution
Label concentration	4.75%
Container material and description	Plastic jugs, totes and bulk tanker cars
Density	1.016 g/mL at 20°C
pH of 1% dispersion in water	4.45–5
Oxidizing or reducing action	Contains no strong oxidizing or reducing substances
Storage stability	Stable for 2 weeks at 54°C in commercial packaging material
Corrosion characteristics	Not corrosive to commercial packaging material
Explosibility	Contains no shock sensitive components

End-Use Product—Raid Bug Defense

Property	Result
Colour	Colourless to milky white
Odour	Odourless
Physical state	Liquid
Formulation type	Solution

Property	Result
Label concentration	0.03%
Container material and description	Plastic bottle
Density	0.9986 g/mL at 20.1°C
pH of 1% dispersion in water	5.8–6.2
Oxidizing or reducing action	Contains no strong oxidizing or reducing substances
Storage stability	Stable for 2 weeks at 54°C in commercial packaging material
Corrosion characteristics	Not corrosive to commercial packaging material
Explosibility	Contains no shock sensitive components

1.3 Directions for use

Raid Bug Defense controls ants, cockroaches, certain flies, and spiders on and around residential structures (outdoors only). The product is a ready-to-use liquid formulation packaged in a spray bottle with a trigger sprayer provided either as a manual pump or as a battery-powered automatic sprayer. The product is applied as a spot spray with 1–3 trigger pulls or 1–2 seconds spray (~1–3 g product) or as a crack and crevice treatment with approximately 7 trigger pulls or 2–3 seconds spray per linear metre using the manual pump or battery-powered automatic sprayer, respectively.

1.4 Mode of action

Deltamethrin is a sodium channel modulator in the pyrethroid chemical class (IRAC Mode of Action Group 3A). Pyrethroids cause sodium channels in neuronal axons to remain open, causing overexcitation of the nervous system, leading to paralysis and death.

2.0 Methods of analysis

2.1 Methods for analysis of the active ingredient

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

2.2 Method for formulation analysis

The methods provided for the analysis of the active ingredient in the formulations have been validated and assessed to be acceptable for use as enforcement analytical methods.

2.3 Methods for residue analysis

Not applicable.

3.0 Impact on human and animal health

3.1 Hazard assessment

3.1.1 Toxicology summary

Deltamethrin is a broad spectrum pyrethroid insecticide. Pyrethroids are believed to induce neurotoxic effects primarily by binding to voltage-dependant sodium channels in neurons, thereby delaying the closing of sodium channels and causing the depolarization of neurons. This affects action potentials and results in repetitive activity (Type I pyrethroids) or blockage of nerve conduction (Type II pyrethroids). Deltamethrin, a pyrethroid containing a cyano group, is a Type II pyrethroid. Type II pyrethroids induce the “CS syndrome”, characterized by choreoathetosis (involuntary excessive movements progressing to sinuous writhing), sedation, salivation, dyspnoea, clonic seizures and body tremors.

An extensive toxicology database is available for deltamethrin, and the data quality is considered adequate for hazard characterization. A detailed review of this toxicology database was conducted as part of the previous re-evaluation for deltamethrin (see PRVD2015-07 and RVD2018-07). Deltamethrin was neither genotoxic nor carcinogenic, did not cause adverse effects on mating performance or fertility, and did not induce teratogenic effects in mice, rats or rabbits following gavage administration of maternally-toxic doses.

Neurotoxicity was identified as a critical endpoint in the mammalian toxicology database, which contained several studies that investigated the neurotoxic potential of deltamethrin in young and adult animals. In short-term dietary studies in adult mice, mortality and decreased body weight were the critical toxicological effects, with neurotoxicity noted at higher oral doses. In short-term oral toxicity studies in other species, the critical effects in adult animals at low oral doses were decreased body weight in rats and neurotoxicity in dogs, as indicated by tremors, posture and gait abnormalities, splayed limbs, decreased reflex reactions and paresthesia. At higher subchronic oral doses, neurotoxicity and mortality were also noted in rats. Other acute or repeat-dose oral neurotoxicity studies in adult rats demonstrated results of mortality, decreased body weight, salivation, drooping eyelids, tremors, decreased motor activity, altered posture and mobility, low arousal, decreased limb grip strength, impaired gait, muscular rigidity, piloerection, and convulsions. The neurotoxic effects of deltamethrin were not exacerbated with prolonged duration of oral exposure, likely due to the rapid metabolism and elimination of this compound. The signs of neurotoxicity in adults were largely reversible.

Neurotoxic signs were reported in adult rats following short-term (whole-body) inhalation exposure to very low concentrations of deltamethrin aerosol. However, the inhalation toxicity study was not used as a critical study for risk assessment as the clinical signs may have been attributable to a physical response to the dust (for example, blinking, licking) rather than chemical toxicity per se. Furthermore, the results of the inhalation toxicity study may have been confounded by the whole-body exposure.

No adverse toxicological effects were noted in adult rats following short-term (21-day) dermal exposure to deltamethrin in polyethylene glycol at the limit dose. However, this study did not include any assessment of neurotoxicity beyond the recording of clinical signs of toxicity.

In the mammalian toxicity studies included in the re-evaluation, the young animal was found to be more sensitive to the neurotoxic effects of deltamethrin, when compared to adult animals. In an acute oral comparative neurotoxicity study (Sheets et al., 1994; PMRA No. 1857302), pup and weanling rats were up to 16-fold more sensitive to mortality than adults, based on LD₅₀ values. Weanling and adult rats demonstrated a decrease in acoustic startle response amplitude at the lowest administered dose, resulting in a LOAEL of 1 mg/kg bw. Salivation, burrowing behavior, and spontaneous vocalizations were noted in weanlings, while similar effects were noted in adults at a higher oral dose.

In the acute oral comparative neurotoxicity study, brain tissue concentrations of deltamethrin were twofold higher in weanling rats compared to adults receiving the same dose. In toxicokinetics studies in adult rats, only a small proportion (0.1%-0.3%) of the absorbed oral dose reached the brain. Deltamethrin was eliminated slowly from the adult brain, with elimination half-lives in adult rat brain tissue ranging from 12.5 to 19.5 hours. Studies have demonstrated higher and prolonged brain concentrations in young animals, compared to adults, exposed to low oral doses of deltamethrin.

In the reproductive toxicity study in rats, there was qualitative sensitivity of the young with greater neurotoxicity and mortality in F1 offspring compared to F0 parental animals at the same dose level. Qualitative sensitivity of the young was observed in the rat developmental neurotoxicity (DNT) study, as characterized by neurotoxic signs in offspring, but not dams exposed to the same oral dose of deltamethrin.

Acoustic startle response was identified as the most sensitive neurobehavioural endpoint in the available deltamethrin database. The LOAEL of 1 mg/kg bw established for weanling rats in the acute oral comparative neurotoxicity study was determined to be the critical point of departure (POD) for assessing human health risks as part of the previous re-evaluation.⁵ However, there is some concern that this critical study assessing this endpoint may have underestimated the sensitivity of young rats. As discussed in PRVD2015-07, validation data were not presented in the study report for the “time-of-peak-effect” used to assess acoustic startle response in pups (adults and pups were both assessed 2 hours post-exposure). Indeed, the same authors used a “time-of-peak-effect” of 1.5 hours for assessment of acoustic startle response in an earlier study of deltamethrin toxicity in the same strain of adult rats. Further, the use of older pups (21 days old) in the critical study may be less than ideal for representing the most susceptible human life stage, and it has been noted that acoustic startle response may not be the best measure for juvenile sensitivity because the response itself varies with age.

For the purposes of assessing the request to expand the use of deltamethrin to outdoor residential areas, relevant studies located in the published scientific literature were incorporated into the hazard assessment. A search of the publicly available scientific literature was conducted to identify studies of potential import to the hazard characterization of deltamethrin.⁶ The results of studies identified in the literature are summarized in Appendix I, Table 2. Focus was placed on studies investigating the sensitive endpoint of neurotoxicity or demonstrating evidence of

⁵ Note that an additional uncertainty factor for lack of a NOAEL was not required since the extent of change (18% decrease) in acoustic startle response was considered to be close to the response threshold.

⁶ A search of the published literature was conducted in March 2025 by querying the PubMed database to identify studies with the keywords “deltamethrin, deltamethrin toxicity, deltamethrin toxicology, deltamethrin mammal toxicology, deltamethrin mammal toxicity, deltamethrin tox, and/or deltamethrin neurotoxicity”

sensitivity in the young, and studies showing potential effects at doses levels critical to the human health risk assessment. Critical information from relevant studies was integrated into the hazard assessment and previous conclusions with regards to established toxicology reference values (TRVs) were re-examined.

As a result of this literature search, six studies of particular interest were identified (Pitzer et al., 2019; PMRA No. 3470523; Bagherpour et al., 2019; PMRA No. 3470520; Williams et al., 2019; PMRA No. 3686295; Elbanna et al., 2023; PMRA No. 3566649; Tsakiridis et al., 2023; PMRA No. 3566636; Ouais et al., 2023; PMRA No. 3826218; Ma et al., 2024; PMRA No. 3826221). These studies reported apparent effects at dose levels lower than the established POD (the LOAEL of 1 mg/kg bw) selected during the previous re-evaluation to assess risks to human health for various exposure scenarios. Effects of note observed in these literature studies included neurotoxicity and effects on the testes and small intestine, as well as altered oxidative, inflammatory, and energy expenditure parameters. In particular, the Pitzer et al., 2019 study demonstrated apparent neurotoxic effects on young rats dosed with deltamethrin in corn oil by oral gavage from post-natal day (PND) 3 to 20 at dose levels as low as 0.25 mg/kg bw/day, and increased startle response starting at 0.5 mg/kg bw/day. In the Williams et al., 2019 study, acute oral dosing of deltamethrin to PND 15 and adult rats provided evidence of age-related sensitivity. Although there were substantial limitations with the acoustic startle response data in this study, the age-comparative time-course data for tissue concentrations, neurotoxic signs, and mortality were of sufficient quality for consideration in the assessment in a qualitative manner. Evidence of neurotoxic clinical signs, including tremors and salivation, and mortality were noted in pups at lower external doses, as well as at lower brain concentrations, compared to adults. Effects were noted at all doses tested in pups (≥ 1 mg/kg bw), increasing in severity with increased doses. Effects in adults were limited to clinical signs observed at the highest dose tested (25 mg/kg bw). Although brain concentrations were higher at a given external dose level in pups compared to adults, this study also provided indications that clinical signs of neurotoxicity and mortality were observed at lower brain concentrations in pups compared to adult animals.

The results of the studies located in the published scientific literature assessing neurotoxic effects in adult and weanling rats were generally consistent with the findings summarized in PRVD2015-07. The noted testicular effects were consistent with those observed in other studies in the toxicology database at higher dose levels. Effects in the small intestine that were noted in the literature studies were not specifically investigated in the available database, but a toxicokinetics study (PMRA No. 1549396) showed that deltamethrin distributes to small intestines following oral gavage dosing.

There were several limitations associated with the reporting in the studies located in the published literature, including certain critical data only being presented graphically, many results being grouped by sex, lack of clarity around some testing methods, as well as a lack of historical control data. These limitations precluded the use of these studies in a quantitative manner in the risk assessment but allowed for integration of the results qualitatively into the weight of evidence for hazard characterization. In particular, the results of certain studies were critical in determining the level of concern for neurotoxic effects in the young in the hazard characterization of deltamethrin, as discussed in section 3.1.2 *Pest Control Products Act* hazard characterization.

In acute toxicity studies, the end-use product Raid Bug Defense and the manufacturing concentrate product Ultratec 5SC MUP were both of low toxicity via the oral, dermal, and inhalation routes of exposure in rats. In rabbits, Raid Bug Defense was minimally irritating to the eyes and skin, while Ultratec 5SC MUP was mildly irritating to the eyes and slightly irritating to the skin. Both products were negative for skin sensitization in guinea pigs using the Buehler method.

The updated toxicology reference values for use in the human health risk assessment are summarized in Appendix I, Table 1. Results of the newly identified key studies from the published scientific literature with deltamethrin are summarized in Appendix I, Table 2, while results of the acute toxicity studies conducted with the associated end-use product and manufacturing concentrate product are summarized in Appendix I, Table 3.

3.1.2 *Pest Control Products Act* hazard characterization

For assessing risks from potential residues in 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 threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.⁷

With respect to the completeness of the toxicology database for the assessment of risk to infants and children, the required studies for risk assessment were available. The database contains a range of adequate studies including oral developmental toxicity studies in mice, rats and rabbits, a 2-generation reproductive toxicity study in rats, a comparative acute oral neurotoxicity study in rats, and a DNT study in rats. The literature also provided additional studies assessing the critical endpoint of neurotoxicity in the young.

With respect to identified concerns relevant to the assessment of risk to infants and children, there was quantitative sensitivity in weanling rats to the lethal effects of deltamethrin, compared to adults, based on LD₅₀ values in the comparative acute oral neurotoxicity study. In the reproductive toxicity study, there was qualitative sensitivity of the young with greater neurotoxicity and mortality in F1 offspring compared to F0 parental animals at the same dose level. Studies in the published scientific literature were consistent with these findings, providing further evidence of increased sensitivity of the young to the neurotoxic effects of deltamethrin. Increased sensitivity of the young was also observed in the rat DNT study, as characterized by neurotoxic signs in offspring, but not in dams exposed to the same oral dose of deltamethrin. In some developmental toxicity studies, delayed ossification in mice and decreased fetal body weight in mice and rabbits were observed in the absence of maternal toxicity, while in other studies, no developmental effects were observed. In a supplemental oral developmental toxicity study in rats, effects on the reproductive system of male offspring were observed in the absence of maternal toxicity.

Although the limitations of the literature studies preclude their quantitative utility in the assessment, several studies identified neurotoxic effects in young animals at or below dose levels used as the point of departure for the previously established toxicology reference values for oral

⁷ SPN2008-01, The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides

and inhalation risk assessments. In the previous re-evaluation, the *Pest Control Products Act* (PCPA) factor was retained but reduced to threefold due to residual uncertainty regarding the method of assessment of acoustic startle response in the critical study as well as the sensitivity and seriousness of the endpoint. At the time of the re-evaluation, the only comparative neurotoxicity study in the toxicology database was the one conducted by Sheets et al. (1994). There were several limitations identified with that study, including the uncertainty with regards to whether the acoustic startle was assessed at the time of peak effect as well as the fact that the study was conducted in older pups (PND 21) that may not represent most sensitive human life stage. Further, as the acoustic startle response varies with age, it may not be the best comparative measure of juvenile sensitivity to pyrethroid neurotoxicity. In light of the additional evidence from the literature confirming that young animals are more sensitive than adult animals to the effect of deltamethrin on the nervous system, and the concerns for the seriousness of such effects, the magnitude of the PCPA factor was revisited as part of this assessment.

For dermal risk assessments for which the 21-day dermal toxicity study in the rat may be appropriate, potential age sensitivity remained an important consideration. The 21-day dermal toxicity study in rats was conducted in adults and did not include a targeted assessment of neurotoxicity or an assessment of potential effects in the young. As the young have been demonstrated to be more sensitive than the adult animal for various endpoints, these missing assessments are notable limitations.

Overall, the database is adequate for determining the sensitivity of the young. There is a high level of concern for sensitivity of the young based on the seriousness of the endpoint (neurotoxicity) observed in the absence of toxicity to adult animals. Therefore, the full 10-fold PCPA factor was retained for scenarios in which the endpoint of neurotoxicity in the young was used to establish the point of departure for assessing human health risks to relevant vulnerable populations (that is children and people who may become pregnant or be lactating). Given the limitations noted above for the 21-day dermal study, the full 10-fold PCPA factor was also retained for scenarios in which the point of departure from this study was used to assess human health risks.

3.2 Toxicology reference values

3.2.1 Route and duration of exposure

Residential exposure to Raid Bug Defense is characterized as short- to intermediate-term in duration due to the type of pests controlled and its limited use outdoors. Applicator exposure is predominantly by the dermal and inhalation routes. Postapplication exposure for adults and children is expected to be minimal based on the use pattern of the end-use product and therefore was assessed qualitatively.

3.2.2 Occupational and residential toxicology reference values

Short-, intermediate-, and long-term dermal – Adults

For short-, intermediate- and long-term dermal risk assessment for adults, the NOAEL of 1000 mg/kg bw/day in the 21-day rat dermal toxicity study was selected. While it is noted that there was no targeted neurobehavioural assessment in the 21-day dermal toxicity study, the dermal toxicity study was considered appropriate for exposure scenarios involving adults as there was

close examination of clinical signs that could indicate neurotoxicity, and no effects were observed up to the limit dose. The 21-day dermal toxicity study also did not include assessments of in utero exposure; however, concern for prenatal exposure was partially lessened by evidence for limited absorption via the dermal route for deltamethrin and the lack of serious effects in fetuses following pre-natal exposure via the oral route. Additionally, in the dietary DNT study with deltamethrin, which examined neurotoxicity in the young following pre-natal exposure, decreases in body weight and clinical signs in offspring (vocalization, resistance to handling) occurred at the same oral dose level that resulted in body weight changes in maternal animals. Overall, the available information did not suggest an increased sensitivity of the young following in utero exposure. However, despite these considerations, some residual concern remained that potential sensitivity of the young to the neurotoxic effects of deltamethrin were not assessed in the dermal toxicity study. Therefore, as outlined in the *Pest Control Products Act* hazard characterization section, the full 10-fold PCPA factor was retained to provide an additional margin of safety to account for potential sensitivity of the young.

As such, for residential scenarios, a target margin of exposure (MOE) of 1000 was derived, which includes uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 10-fold PCPA factor as outlined above. Although occupational exposure is not relevant to the proposed uses, the target MOE for occupational exposure scenarios is 1000, which includes uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 10-fold factor to account for the residual concern pertaining to potential sensitivity of the young to the neurotoxic effects of deltamethrin that were not assessed in the dermal toxicity study.

Short-, intermediate-, and long-term dermal – Children (up to 12 years old)

For short-, intermediate- and long-term dermal risk assessment for children, the LOAEL of 1 mg/kg bw/day was selected based on reduced acoustic startle response in weanling rats in the acute oral comparative neurotoxicity study (Sheets et al., 1994; PMRA No. 1857302). This LOAEL was selected since it is based on the most sensitive endpoint in the database in the most sensitive population (the young), and it is protective of other neurological and systemic effects. Furthermore, the POD from this acute study was considered appropriate for repeated exposure scenarios based on the available evidence that neurotoxicity associated with exposure to deltamethrin does not increase with increasing duration of exposure. A target MOE of 1000 was selected based on uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 10-fold PCPA factor as outlined in the *Pest Control Products Act* hazard characterization section. An additional uncertainty factor for lack of a NOAEL was not required since the extent of change (18% decrease) in acoustic startle response was considered to be close to the response threshold.

Short-, intermediate-, and long-term inhalation

The most appropriate study for short-, intermediate- and long-term inhalation risk assessment for all populations was the acute oral comparative neurotoxicity study in rats (Sheets et al., 1994; PMRA No. 1857302), in which a LOAEL of 1 mg/kg bw/day was determined in weanling rats based on reduced acoustic startle response. This LOAEL was selected since it is the most sensitive endpoint in the database in the most sensitive population (the young), and it is protective of other neurological and systemic effects. Furthermore, the POD from this acute study was considered appropriate for repeated exposure scenarios based on the available

evidence that neurotoxicity associated with exposure to deltamethrin does not increase with increasing duration of exposure. This LOAEL is supported by the results of the short-term inhalation toxicity study in adult rats in which a LOAEL of 0.78 mg/kg bw/day was derived based on minimal effects on body weight and clinical signs at the lowest tested dose. The inhalation toxicity study was not used as the critical study for risk assessment since the clinical signs may have been attributable to a physical response to the dust (for example, blinking, licking) rather than chemical toxicity per se. Furthermore, the results of the inhalation toxicity study may be confounded by the whole-body exposure.

For residential scenarios, a target MOE of 1000 was derived, which includes uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 10-fold PCPA factor as outlined in the *Pest Control Products Act* hazard characterization section. Although occupational exposure is not relevant to the proposed uses, the target MOE for occupational scenarios is 1000, which includes uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 10-fold factor for concerns relating to lack of testing in a susceptible population (the young) as well as concerns regarding the sensitivity of the measured endpoints in the dermal study (for example, motor activity and acoustic startle response were not assessed). An additional uncertainty factor for lack of a NOAEL was not required since the extent of change (18% decrease) in acoustic startle response was considered to be close to the response threshold.

Non-dietary incidental oral Ingestion (all durations)

No incidental oral exposure is expected with the proposed uses. However, as a result of this assessment, the target MOE for incidental oral exposures has been revised to reflect the change in PCPA factor. For assessment of non-dietary (incidental) oral exposure (all durations), the LOAEL of 1 mg/kg bw/day was selected based on reduced acoustic startle response in weanling rats in the acute oral comparative neurotoxicity study (Sheets et al., 1994; PMRA No. 1857302). This acute LOAEL was selected since it is the most sensitive endpoint in the database in the most sensitive population (the young). Furthermore, the POD from this acute study was considered appropriate for repeated exposure scenarios based on the available evidence that neurotoxicity associated with exposure to deltamethrin does not increase with increasing duration of exposure, and the LOAEL is protective of other neurological and systemic effects. A target MOE of 1000 was selected based on uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 10-fold PCPA factor as outlined in the *Pest Control Products Act* hazard characterization section. An additional uncertainty factor for lack of a NOAEL was not required since the extent of change (18% decrease) in acoustic startle response was considered to be close to the response threshold.

3.2.3 Acute reference dose (ARfD)

No exposure via the diet or drinking water is expected with the proposed uses. However, as a result of this assessment, the previously established ARfD, as described in PRVD2015-07, has been revised to reflect the change in PCPA factor. To estimate acute dietary risk, the acute oral comparative neurotoxicity study in rats (Sheets et al., 1994; PMRA No. 1857302) was selected for risk assessment. A LOAEL of 1 mg/kg bw was determined in weanling rats based on a reduction in acoustic startle response. This LOAEL was selected since it is based on the most sensitive endpoint available in the database, is relevant to a single exposure, is derived from the most sensitive population (the young), and is protective of other neurological and systemic

effects. Uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were used to derive the ARfD. An additional uncertainty factor for lack of a NOAEL was not required since the extent of change in acoustic startle response was considered to be close to the response threshold. As discussed in the *Pest Control Products Act* hazard characterization section, the full 10-fold PCPA factor was retained, resulting in a Composite Assessment Factor (CAF) of 1000. The ARfD is calculated according to the following formula:

$$\text{ARfD} = \frac{\text{LOAEL}}{\text{CAF}} = \frac{1 \text{ mg/kg bw}}{1000} = 0.001 \text{ mg/kg bw of deltamethrin}$$

This ARfD provides a margin of 6800 to the NOAEL for mortality in pregnant rats due to acute exposure and a margin of 1270 to the BMDL₁₀ for decreased motor activity in adult rats.

3.2.4 Acceptable daily intake (ADI)

No exposure via the diet or drinking water is expected with the proposed uses. However, as a result of this assessment, the previously established ADI, as described in PRVD2015-07, has been revised. To estimate risk following repeated dietary exposure, the acute oral comparative neurotoxicity study in rats (Sheets et al., 1994; PMRA No. 1857302) was selected for risk assessment. A LOAEL of 1 mg/kg bw/day was determined in weanling rats based on reduced acoustic startle response. This LOAEL was selected since it is based on the most sensitive endpoint in the database in the most sensitive population (the young). Furthermore, the POD from this acute study was considered appropriate for repeated exposure scenarios based on the available evidence that neurotoxicity associated with exposure to deltamethrin does not increase with increasing duration of exposure, and the LOAEL is protective of other neurological and systemic effects. Uncertainty factors of 10-fold for interspecies extrapolation as well as 10-fold for intraspecies variability were used to derive the ADI. An additional uncertainty factor for lack of a NOAEL was not required since the LOAEL was considered to be close to the response threshold. The full 10-fold PCPA factor has been retained as discussed in the *Pest Control Products Act* hazard characterization section, resulting in a CAF of 1000. The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{LOAEL}}{\text{CAF}} = \frac{1 \text{ mg/kg bw/day}}{1000} = 0.001 \text{ mg/kg bw/day of deltamethrin}$$

This ADI provides a margin of 5500 to the NOAEL for parental toxicity in the reproductive toxicity study and a margin of 3300 to the NOAEL for mortality in pregnant rats due to repeated exposure. This ADI provides a margin of 2000 to the NOAEL for reproductive effects in male rats. This also ensures a margin of 200 to the LOAEL for body weight loss and colon and intestinal effects observed in a literature study after repeated exposures.

3.2.5 Cancer assessment

There was no evidence of tumourigenicity and therefore, a cancer risk assessment is not required.

3.2.6 Aggregate toxicology reference values

Aggregate exposure is the total exposure to a single pesticide that may occur from dietary (food and drinking water), residential, and other non-occupational sources, and from all known or

plausible exposure routes (oral, dermal and inhalation). Short-, intermediate- and long-term aggregate exposure to deltamethrin may be comprised of food, drinking water and residential exposure via the dietary and dermal routes in children (up to 12 years old) and via the dermal, inhalation, and oral routes in youth and adults. For all sub-populations, the toxicology endpoint selected for aggregation was reduced auditory startle response in weanling rats.

For adults and youth, exposure via the dermal route was not aggregated since no adverse toxicological effects were noted following repeated dermal dosing. For the oral and inhalation routes, the LOAEL of 1 mg/kg bw/day from the acute oral comparative neurotoxicity study in rats (Sheets et al., 1994; PMRA No. 1857302) was selected with a target MOE of 1000.

For children, the LOAEL of 1 mg/kg bw/day from the acute oral comparative neurotoxicity study in rats (Sheets et al., 1994; PMRA No. 1857302) with a target MOE of 1000 was selected for the oral and dermal routes.

3.3 Dermal absorption

A rat in vivo dermal absorption study currently on-file was assessed in the framework of this application.

Sprague-Dawley rats were administered nominal doses of 250 or 1.18 $\mu\text{g}/\text{cm}^2$ of deltamethrin in an emulsifiable concentrate formulation and were monitored for up to 144 hours postapplication. The skin site was washed after 8 hours with sacrifice at 8, 24, 72, and 144 hours ($n = 5$). Following each sacrifice event, the saddle, cover and tape, treated skin, skin surrounding the application site (about 1 cm width), a sample of untreated dorsal skin and the carcass were collected and analyzed for recovery via liquid scintillation counting. Total recovery of the applied dose (mass balance) was acceptable and ranged from 91% to 98% for all dose subgroups.

For all dose groups, the largest proportion of the applied dose was recovered from the wash of the skin site (range from 46% to 68% of the applied dose). Several tape strippings were performed to characterize skin bound residues. Significant residues were found in this layer at 8 hours (24% and 34% of the applied high and low doses, respectively) and decreased with time until 144 hours (4% and 6% of the applied high and low doses, respectively). Total absorbed dose was calculated from the sum of residues excreted (urine, feces, cage wash) and residues in tissue (the remaining treated skin after tape stripping, untreated skin, and the carcass). Skin bound residues in treated skin were also included but not residues in the stratum corneum (tape strips) based on observations that recoveries from excreta and tissues were fairly consistent over time when compared to the marked decrease in recoveries over time from tape strips and increase over time from dose site shavings and gauze washes. In addition, urine collections indicated a general trend of peak recoveries at or around the 48 hour time point and decreased from this point onwards, indicating decreased absorption over time.

No major limitations were found in this study, and it is considered to be acceptable for determining a dermal absorption value for deltamethrin. Estimates of dermal absorption were based on the sum of residues in the excreta (urine, feces, cage wash) + skin sites (surrounding skin, untreated skin, treated skin excluding tape strips) + carcass (including blood).

A dermal absorption value of 5% was selected based on the low dose (1.18 $\mu\text{g}/\text{cm}^2$) 144 hour monitoring group, which was the subgroup of the in vivo study with the highest dermal

absorption observed. Tape strips were not included as “absorbed” since although the residues in the tape strips decreased over time, it was not accompanied by an equivalent increase in dose recovered from the tissues and excreta. In addition, the amount of the dose found in the dose site shavings and gauze washes increased over time. This indicates that the skin bound residues were not bioavailable, and were subsequently sloughed off (Appendix I, Table 4).

3.4 Occupational and residential exposure assessment

3.4.1 Acute hazards of end-use product and mitigation measures

3.4.1.1 Raid Bug Defense

The acute hazard assessment indicated that Raid Bug Defense of low acute toxicity in rats via the oral, dermal and inhalation routes of exposure. It is minimally irritating to the eyes and skin of rabbits and was not a dermal sensitizer in guinea pigs when tested using the Buehler method. Based on these acute hazards, no signal words or hazard statements are required, and personal protective equipment will not be added to the label.

3.4.2 Occupational exposure and risk assessment

Raid Bug Defense is a domestic class end-use product and so will not be used by pest control professionals. As such, an occupational risk assessment was not conducted.

3.4.3 Residential exposure and risk assessment

3.4.3.1 Handler exposure and risk assessment

Raid Bug Defense is a domestic class product. The dermal and inhalation estimates of exposure to residential applicators during spot and crack and crevice application of the ready-to-use product were calculated based on the algorithms and standard parameter values from the USEPA 2012 Residential Standard Operating Procedure (SOP). Surrogate unit exposure (UE) values representative of a trigger pump sprayer and refillable automatic sprayer were taken from the Pesticide Handler Database (PHED) and/or the Outdoor Residential Exposure Task Force (ORETF).

Using the standard values in combination with toxicological reference values, applicator exposure is not expected to result in risks of concern when deltamethrin is used according to label directions as the calculated MOEs exceeded the target MOE of 1000 (Appendix I, Table 5).

3.4.3.2 Postapplication exposure and risk assessment

A quantitative risk assessment of potential exposure to adults and children from treated outdoor surfaces was not conducted. Based on guidance from the 2012 Residential SOP, Section 3 Lawns/Turf, postapplication assessments do not need to be conducted if label directions indicate the turf use is an edging use (for example, along fence rows), a foundation perimeter treatment (for example, 1 metre (3 foot) band around the perimeter of the house), or a specific spot treatment (for example, ant hills). Exposure to treated surfaces in these areas is expected to be minimal based on limited human activity.

3.4.4 Bystander exposure and risk assessment

Label directions prohibit people (other than the applicator) and pets from being present during application. As such, bystander exposure is expected to be minimal, therefore, health risks are not of concern.

3.5 Aggregate exposure and risk assessment

There is the potential for adults to be exposed to deltamethrin via different routes and sources of exposure concurrently. Aggregate exposure for adults may occur through inhalation exposure during application and from consuming food and drinking water (dietary exposure), from currently registered deltamethrin food uses (PRVD2015-07). For children, aggregate exposure is not expected from the use of Raid Bug Defense as the dermal and incidental oral routes from outdoor treated surfaces and from the dietary route are not expected to co-occur.

The chronic dietary exposure values (food plus drinking water) for adults were aggregated with the applicator inhalation exposure values. Aggregate exposure estimates were compared to the aggregate toxicology reference value to obtain the MOE. The results of the aggregate risk assessment are presented in Appendix I, Table 6. The calculated MOE for adults exceeds the target MOE of 1000. As such, there are no health risks of concern.

3.6 Cumulative assessment

The *Pest Control Products Act* requires the Agency to consider the cumulative effects of pest control products that have a common mechanism of toxicity. Deltamethrin belongs to a group of chemicals classified as pyrethroids. Pyrethroids, along with pyrethrins, have a common mechanism of pesticidal activity wherein they all possess the ability to interact with voltage-gated sodium channels ultimately leading to neurotoxicity. The pyrethroid cumulative health risk assessment is currently in the initial planning phase and will consist of a complex standalone quantitative assessment. As part of that assessment, an evaluation will be undertaken to confirm whether deltamethrin shares a common mechanism of mammalian toxicity with other pyrethroids, and if so, a cumulative assessment for deltamethrin and relevant pyrethroids will be conducted. The status of the pyrethroid cumulative health assessment is captured in the Cumulative Health Risk Assessment Operational Planning Framework that was published in December 2025.

Of note is that the USEPA completed a cumulative health risk assessment in 2011 for pyrethroid products registered in the United States (PMRA No. 3827824), and based on a screening level assessment, concluded that cumulative risks from uses of pyrethroids and pyrethrins were not of concern. In addition, in 2020, the European Food Safety Authority (EFSA) conducted a cumulative dietary risk assessment (PMRA No. 3827830, 3827840) on pesticides that have acute effects on the nervous system, including pyrethroids. The retrospective probabilistic risk assessment focused on two effects: brain and/or erythrocyte acetylcholinesterase inhibition, and functional alterations of the motor division. It concluded that cumulative exposure to pesticides that have these acute effects on the nervous system does not exceed the threshold for regulatory consideration.

3.7 Health incident reports

From April 2007 to 12 November 2025, 46 human and 63 domestic animal incidents involving deltamethrin were submitted to Health Canada.

In the human incidents involving deltamethrin, the reported exposure scenarios in people included accidental exposure to deltamethrin when mixing/loading or applying a deltamethrin product, postapplication exposure when living or working in treated areas, contact with treated plant material, or drift from an application site. The symptoms reported in people following deltamethrin exposure were mainly minor in severity and included effects such as nausea, skin or eye irritation, coughing, shortness of breath, throat irritation, or headache. There were 14 serious human incidents involving deltamethrin (classified as death (1 US incident) or major (11 US, 2 Canadian incidents)) that were submitted to Health Canada. These incidents were further evaluated and were considered to either have insufficient information on the reported circumstances of deltamethrin exposure (e.g., unknown how the reported deltamethrin exposure occurred) or the reported effects (e.g., stroke, slurred speech, jaundice) were not typical of deltamethrin exposure.

Deltamethrin incidents involving domestic animals were mainly serious incidents (severity classification of death or major) that occurred in the US (52 incidents). The incidents commonly involved pets (e.g., cats, dogs, reptiles) and the reported exposure scenarios included applying a deltamethrin product in the vicinity of a pet, animals coming in contact with deltamethrin product residues, animals licking treated plant material or drift/run-off from a deltamethrin application site. The symptoms reported in animals include lethargy, anorexia, excessive salivation, shortness of breath, ataxia, seizures, as well as death.

The incident report review indicates a potential for accidental exposure of people and pets to deltamethrin during product application or postapplication when products are used in residential outdoor areas. No mitigation measures are being proposed considering that the label of the proposed domestic class end-use product will include any required definitions and precautionary statements as per the PMRA Guidance Document, *Structural Pest Control Products: Label Updates*.

4.0 Impact on the environment

4.1 Fate and behaviour in the environment

The properties and environmental fate characterization of deltamethrin have been previously reviewed and reported in PRVD2015-07, *Deltamethrin*, in PRD2017-05, *Deltamethrin*, for use of deltamethrin in mosquito control, and in PRD2019-07, *Deltamethrin and Annihilator PolyZone*, for use of deltamethrin on outdoor surfaces of agricultural buildings and structures.

For control of a wide variety of crawling and flying insect pests, deltamethrin is applied as a domestic trigger-spray formulation outdoors. Applications are specified as spot or crack and crevice treatments.

Deltamethrin is expected to degrade rapidly in the air, as it is susceptible to photochemical oxidative reactions (half-life is estimated to be 16 hours). Biotransformation is a route of transformation of deltamethrin in aerobic soil (DT_{50} = 6.1–72 days) and water (DT_{50} = 4–141

days); it is non-persistent to moderately persistent in both media. Aquatic field studies indicate that deltamethrin dissipates rapidly through volatilization from water surfaces (1 hour to 35.7 hours). Deposit into aquatic and terrestrial systems from the type of application proposed for outdoor surfaces of buildings and structures is greatly reduced and exposure to the environment is expected to be minimal.

4.2 Environmental risk characterization

An environmental risk characterization of deltamethrin had been previously completed for its use as an insecticide on food and non-food crop sites with single season application rates up to 135 g a.i./ha (for further details, please see PRVD2015-07, *Deltamethrin*). Its use for control of adult mosquitoes at a maximum annual use of 15 g a.i./ha was assessed in PRD2017-05, *Deltamethrin*, and its uses for spot treatments, crack and crevice applications, and general surface applications on buildings and structures were assessed in PRD2019-07, *Deltamethrin and Annihilator PolyZone*. Current application methods include conventional aerial and ground equipment such as rotary and fixed wing aircraft, boom sprayers, airblast sprayers, mist blowers and hand held sprayers. The proposed use of Raid Bug Defense as a domestic trigger spray for control of crawling and flying insects would result in a significantly lower use rate and more localized deposition of deltamethrin than currently registered for other uses. Therefore, exposure of non-target organisms, and environmental risk are expected to be minimal.

4.2.1 Risks to terrestrial organisms

The effects of deltamethrin on terrestrial organisms (at higher rates of application) have been previously reported in PRVD2015-07, *Deltamethrin*. Based on the assessment reported in PRVD2015-07, and the low potential for exposure from hand pressurized sprayers, the environmental risks of deltamethrin to earthworms, birds, mammals, and terrestrial vascular plants are acceptable.

Deltamethrin is highly toxic to beneficial insects such as the honeybee and could pose a risk to terrestrial arthropods if they are present on the treatment area. However, based on the proposed use pattern, the potential impact on honeybees or other pollinators/beneficial insects is expected to be minimal. Precautionary label statements are required on the label to advise users that exposure of beneficial arthropods and bees may be harmful.

4.2.2 Risks to aquatic organisms

The effects of deltamethrin on aquatic organisms (at higher rates of application) have been previously reported in PRVD2015-07, *Deltamethrin*. Deltamethrin is very highly toxic to fish and aquatic invertebrates. Impact on aquatic organisms is expected to be limited in view of the application method and sites of spray application for this registration. Spray droplets may evaporate while they are suspended in the air and deposition in water bodies is expected to be limited.

Precautionary label statements instructing users to avoid contamination of aquatic environments are required.

4.2.3 Environmental incident reports

Environmental incident reports are obtained from two main sources, the Canadian pesticide incident reporting system (including both mandatory reporting from the registrant and voluntary reporting from the public and other government departments) and the USEPA Ecological Incident Information System (EIIS). Specific information regarding the mandatory reporting system regulations that came into force 26 April 2007, under the *Pest Control Products Act* can be found on the Report a Pesticide Incident page on Canada.ca.

As of 12 November 2025, one incident of environmental relevance had been submitted to Health Canada that involved deltamethrin and two incidents were obtained from the EIIS. The incidents involved multiple active ingredients or circumstances that were not attributed to the labelled use of the product. Overall, the assessment of incident reports involving deltamethrin did not identify any significant environmental effects and would not affect the environmental risk assessment.

5.0 Value

Efficacy data from three trials including direct and residual treatment of American and German cockroaches support claims for cockroaches. Efficacy data from three trials including carpenter and black ants, with both direct and residual treatment of carpenter ants, support claims for ants. Efficacy data from a trial assessing residual treatment with both house flies and stable flies, supplemented by a trial with direct treatment of black flies, supports claims for house flies and stable flies. Efficacy data from a trial including at least three genera of spiders support a claim for spiders.

Numerous domestic class products are already registered for use in and around the home to control the approved labelled pests, and the various registered products contain several different active ingredients including pyrethrins and other pyrethroids. Raid Bug Defense would provide a new product with a new active ingredient, but not a new mode of action, for use to control certain labelled insect pests on and around the home (outdoors only).

6.0 Pest Control Product Policy considerations

6.1 Assessment of the active ingredient under the Toxic Substances Management Policy

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances, in other words, those that meet all four criteria outlined in the policy: persistent (in air, soil, water, and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*. The *Pest Control Products Act* requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, deltamethrin and its transformation products were assessed in accordance with the Regulatory Directive DIR99-03⁸ and evaluated against the Track 1 criteria.

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

Health Canada has reached the conclusion that deltamethrin and its transformation products do not meet all of the TSMP Track 1 criteria.

Please refer to PRVD2015-07 for further information on the TSMP assessment.

6.2 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.⁹ The list is used as described in the Science Policy Note SPN2020-01¹⁰ and is based on existing policies and regulations, including the *Toxic Substances Management Policy* and *Formulants Policy*,¹¹ and taking into consideration the *Ozone-depleting Substances and Halocarbon Alternatives Regulations* under the *Canadian Environmental Protection Act, 1999*, (substances designated under the *Montreal Protocol*).

Health Canada has reached the conclusion that Deltamethrin Technical Insecticide, Ultratec 5SC MUP, and the end-use product, Raid Bug Defense, do not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

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

7.0 Proposed Regulatory Decision

Health Canada, pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Deltamethrin Technical Insecticide, Ultratec 5SC MUP, and Raid Bug Defense, containing the active ingredient deltamethrin, to control ants, cockroaches, house flies, stable flies and spiders on and around the home (outdoors only).

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

⁹ SI/2005-114, last amended on June 24, 2020. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

¹⁰ Science Policy Note SPN2020-01, *Policy on the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under paragraph 43(5)(b) of the Pest Control Products Act*

¹¹ DIR2006-02, *Formulants Policy and Implementation Guidance Document*

List of Abbreviations

↑	increased
↓	decreased
≥	greater than or equal to
≤	less than or equal to
±	plus-minus
♀	female
♂	male
λ	wavelength
μg	microgram
μM	micromolar
°C	degrees centigrade
abs	absolute
a.i.	active ingredient
ADHD	attention-deficit/hyperactivity disorder
ADI	acceptable daily intake
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AO	adverse outcome
AOP	adverse outcome pathway
AR	androgen receptor
ARfD	acute reference dose
ASR	acoustic startle response
AST	aspartate aminotransferase
atm	atmosphere
AUC	area under the curve
BMC	benchmark concentration
BMD	benchmark dose
BMDL	benchmark dose lower confidence limit
BDNF	brain-derived neurotrophic factor
bw	body weight
CA	Cornu Ammonis
Ca ²⁺	calcium
CAF	composite assessment factor
CaN	Calcineurin
CAS	Chemical Abstracts Service
CBI	confidential business information
CES	carboxylesterases
cm	centimetres
cm ²	centimetre square
cm ³	cubic centimetre
CNS	central nervous system
CYP	cytochrome P
D1	dopamine receptor 1
D2	dopamine receptor 2
DAI	disease activity index

DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DNT	developmental neurotoxicity
DRD1	dopamine receptor D1
DRD2	dopamine receptor D2
DT ₅₀	dissipation time 50% (the time required to observe a 50% decline in concentration)
E2	estradiol
EFSA	The European Food Safety Authority
EIIS	USEPA Ecological Incident Information System
ELISA	Enzyme-Linked Immunosorbent Assay
ER ₂₅	effective rate for 25% of the population
ER	estrogen receptor
F0	parental
F1	first filial generation
Fe ²⁺	iron
Fer-1	ferrostatin-1
FR-WAIT	fixed ratio-wait behavioral test
g	gram(s)
GD	gestation day
GGT	gamma-glutamyl transpeptidase
GI	gastrointestinal tract
GluA1	glutamate receptor ionotropic, AMPA 1
GSH	glutathione
h	hours
ha	hectare(s)
Hb	hemoglobin
Hct	hematocrit
HEK293	human embryonic kidney 293 cells
HHRA	human health risk assessment
hpf	hours post-fertilization
HPLC	high performance liquid chromatography
HPLC-ECD	high-performance liquid chromatography – electrochemical detection
HPT	hypothalamic–pituitary–thyroid
hr	hour
IATA	Integrated Approaches to Testing and Assessment
ICR	Institute of Cancer Research
IFD	induced fit docking
IL	interleukin
INF-γ	interferon-gamma
IRAC	Insecticide Resistance Action Committee
IUPAC	International Union of Pure and Applied Chemistry
IV	intravenous
IVB	in vitro testing battery
IVIVE	in vitro to in vivo
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
KC/GRO	keratinocyte chemoattractant/growth-regulated oncogene
KE	key event

KER	key event relationship
kg	kilogram
K_{ow}	<i>n</i> -octanol-water partition coefficient
L	litre
LC ₅₀	lethal concentration 50%
LD ₅₀	lethal dose 50%
LDH	lactate dehydrogenase
LMA	locomotor activity
LOAEL	lowest observed adverse effect level
MAS	maximum average score for 24, 48 and 72 hours
mg	milligram
mL	millilitre
mAChRs	muscarinic acetylcholine receptor
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume
MDA	malondialdehyde
MDCK	Madin-Darby canine kidney cell line
MIE	molecular initiating event
MIS	maximum irritation score
MK-801	dizocilpine
MOE	margin of exposure
mPa	millipascals
MPTP	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
mRNA	messenger RNA
MTT	3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide
MUP	manufacturing use product
MWM	Morris water maze
Nav	voltage gated sodium channel subunit isoform
NAM	New Approach Methodologies
NDD	neurodevelopmental disorder
n	number
NMDA	N-methyl-D-aspartate
N/A	not applicable
nm	nanometres
NOAEL	no observed adverse effect level
NR2A/B	NMDA receptor subunits
NZ	New Zealand
OECD	Organisation for Economic Co-operation and Development
ORETF	Outdoor Residential Task Force
P	parental generation
p-AKT	phosphorylated Protein Kinase B
p-GluA1	phosphorylated-GluA1
p-mTOR	phosphorylated mammalian target of rapamycin
p-TrKb	phosphorylated Tropomyosin receptor kinase B
PBK	physiologically-based kinetic
PBPK	physiologically-based pharmacokinetic

PC12	pheochromocytoma cell line
PCPA	<i>Pest Control Products Act</i>
PCR	Polymerase Chain Reaction
PFT- α	Pifithrin- α
PHED	Pesticide Handlers Exposure Database
pKa	dissociation constant
PL-C/IP3R	Phospholipase C / Inositol 1,4,5-trisphosphate Receptor
PMRA	Pest Management Regulatory Agency
PND	postnatal day
POD	point of departure
PRD	Proposed Registration Decision
PRVD	Proposed Re-evaluation Decision
PTGS2	prostaglandin-endoperoxide synthase 2
RBC	red blood cells
RD	Registration Decision
RDW-CV	red cell distribution width - coefficient of variation
rel	relative
RNA	ribonucleic acid
RoB	risk of bias
ROS	reactive oxygen species
RT	room temperature
RVD	Re-evaluation Decision
SHBG	sex hormone-binding globulin
SLC7A11	solute carrier family 7 member 11
SOP	Standard Operating Procedures
s.s.	statistically significant
T3	tri-iodothyronine
T4	thyroxine
TBPB	1-(1'-2-methylbenzyl)-1,4'-bipiperidin-4-yl)-1H-benzo[d]imidazol-2(3H)-one
th1	T helper 1
TK	toxicokinetic
TN	thermoneutral
TRH	serum thyrotropin-releasing hormone
TSH	thyroid stimulating hormone
TSMP	Toxic Substances Management Policy
TUNEL	terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling
UE	unit exposure
US	United States
USEPA	United States Environmental Protection Agency
UV	ultraviolet
V _{1/2}	half-maximal activation
VGSC	voltage-gated sodium channel
WBC	white blood cells
WG	working group
wks	weeks
wt	weight
WT	wild type

Appendix I Tables and figures

Table 1 Updated toxicology reference values for use in health risk assessment for deltamethrin

Exposure scenario	Study	Point of departure and endpoint	CAF ¹ or Target MOE
Acute dietary	Acute oral (gavage) comparative neurotoxicity study in adult, weanling rats	LOAEL = 1 mg/kg bw Decreased acoustic startle response amplitude in weanling rats	1000
ARfD = 0.001 mg/kg bw			
Repeated (chronic) dietary	Acute oral (gavage) comparative neurotoxicity study in adult, weanling rats	LOAEL = 1 mg/kg bw/day Decreased acoustic startle response amplitude in weanling rats	1000
ADI = 0.001 mg/kg bw/day			
Short-, intermediate-, long-term dermal (adults)	21-day dermal toxicity study in rats	NOAEL = 1000 mg/kg bw/day No adverse effects up to the limit dose	1000
Short-, intermediate-, long-term dermal ² (children up to 12 years old)	Acute oral (gavage) comparative neurotoxicity study in adult, weanling rats	LOAEL = 1 mg/kg bw/day Decreased acoustic startle response amplitude in weanling rats	1000
Short-, intermediate-, long-term inhalation ³	Acute oral (gavage) comparative neurotoxicity study in adult, weanling rats	LOAEL = 1 mg/kg bw/day Decreased acoustic startle response amplitude in weanling rats	1000
Incidental oral (all durations)	Acute oral (gavage) comparative neurotoxicity study in adult, weanling rats	LOAEL = 1 mg/kg bw/day Decreased acoustic startle response amplitude in weanling rats	1000
Aggregate – children up to 12 years old: Dermal ² and oral (all durations)	Dermal and oral: Acute oral (gavage) comparative neurotoxicity study in adult, weanling rats	Common endpoint: Decreased acoustic startle response amplitude in weanling rats Dermal and oral: LOAEL = 1 mg/kg bw/day	Dermal and oral: 1000

Exposure scenario	Study	Point of departure and endpoint	CAF ¹ or Target MOE
Aggregate – youth and adults: Inhalation ³ and oral (all durations)	Inhalation and oral: Acute oral (gavage) comparative neurotoxicity study in adult, weanling rats	Common endpoint: Decreased acoustic startle response amplitude in weanling rats Inhalation and oral: LOAEL = 1 mg/kg bw	Inhalation and oral: 1000
Cancer	No treatment-related tumours were observed; therefore, a cancer risk assessment is not required		

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

MOE (margin of exposure) refers to a target MOE for occupational and residential assessments.

² Since an oral NOAEL was selected, a dermal absorption factor of 5% was used in route-to-route extrapolation.

³ Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Table 2 Summary of literature studies with deltamethrin

The studies summarized in the Table 2 were identified following a literature search conducted in November 2025 and were deemed to have some potential relevance to the human health hazard assessment of deltamethrin. These studies were screened for acceptability according to Information Note: Determining Study Acceptability for use in Pesticide Risk Assessments, the study methods described within were analyzed, and the key findings were summarized. These studies were classified as “acceptable with limitations” as they were considered supplemental in nature for various reasons, such as the study reporting was limited, the design included a single dose level only preventing the assessment of a dose response, or other limitations in the study design hindered its utility.

Effects observed in both sexes are presented first followed by sex-specific effects in males, then females, each separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to body weights unless otherwise noted.

Study type/Animal/PMRA No.	Study results
Oral toxicity (gavage) (non-guideline) Effects of post-natal exposure on behaviour, learning and memory, and neurotransmitter levels. Sprague Dawley rats Pitzer et al. 2019 PMRA No. 3470523	Acceptable with limitations Young rats were dosed PND 3 to 20 and behavioural testing was conducted starting on PND 60 in the following order: open field, elevated zero maze, straight channel swimming, Morris water maze, Cincinnati water maze, acoustic startle, conditioned freezing, amphetamine and MK-801 (dizocilpine) induced locomotor activity (LMA) in open field. Rats were sacrificed 1-2 wks after all behaviour testing was complete. Neurotransmitter levels for all groups, as well as mRNA expression and dopamine release for select groups, were assessed in brain tissue.

Study type/Animal/PMRA No.	Study results
	≥0.25 mg/kg bw/day: ↓ LMA in open field and elevated zero maze (♂/♀ combined). ≥0.5 mg/kg bw/day: ↓ bw during dosing and persisting into adulthood until the end of the study on PND 119, impaired learning in Morris water maze, ↓ norepinephrine levels in hippocampus (♂/♀ combined); ↑ acoustic and tactile startle response, ↑ freezing behaviour (♂). 1.0 mg/kg bw/day: ↓ response (s.s.) to the hyperactivity-inducing effects of MK-801, altered long-term potentiation in brain tissue (♂/♀); ↑ latency and errors in Cincinnati water maze, ↓ DRD1 mRNA expression in neostriatum, ↓ dopamine release (♂). Limitations: Critical data only presented in graphical form, no historical control data, no positive control data no habituation data, results grouped by sex (unclear if biological sex was a variable for all tests), no latency measurement for ASR, no mention of time-to-peak-effect, unclear if animals that did not demonstrate learning during acquisition phase of learning and memory test were excluded from additional phases, tester blinding status unknown, multiple tests could result in stress and fatigue.
Oral toxicity (gavage) (non-guideline) Effects of acute exposure in adult and developing rats on acoustic startle response and brain and plasma concentrations Sprague Dawley rats Williams et al. 2019 PMRA No. 3686295	Acceptable with limitations Adult (PND 90) and pup (PND 15) Sprague Dawley rats dosed with deltamethrin (in corn oil) by gavage; assessment of clinical signs, ASR and brain and plasma levels of deltamethrin. Four experiments: 1. ASR in adults (doses of 0, 2, 4, or 8 mg/kg bw); 2. ASR in adults (doses of 0, 2, 8, or 25 mg/kg bw); 3. ASR in pups (doses of 0, 1, 2, or 4 mg/kg bw); 4. Brain and plasma analyses (doses of 1, 2, or 4 mg/kg bw (PND 15) and 2, 8, or 25 mg/kg bw (adults)). Adults: 25 mg/kg bw: mild to moderate salivation and mild tremor before and after ASR testing Pups: ≥ 1 mg/kg bw: mild tremors ≥ 2 mg/kg bw: mild to moderate tremors, mortality (4-8h after administration), salivation before ASR testing Brain and plasma analyses (pups and adults):

Study type/Animal/PMRA No.	Study results
	2 mg/kg bw: Brain levels higher in PND 15 pups than adults, peak brain levels observed earlier in adults than in pups. Limitations: Unclear if pups were fasted, precise ASR group matching was conducted for adults but not pups (pups randomly assigned to treatment groups), no discussion of habituation, no rationale for 2 h “time-of-peak” for ASR in both age groups (peak ASR approximately 1.5 h in adults in literature studies), discrepancies in reporting of raw ASR data (for example treatment allocation information missing and unidentified litter numbers), limited reporting of results in general. Overall, the ASR data were determined to be unreliable due to limitations noted.
28-day oral toxicity (gavage) Effects on thyroid and behaviour in adolescent mice ICR mice (♀) Zhang et al. 2020 PMRA No. 3470524	Acceptable with limitations Three week old female ICR mice exposed to deltamethrin in corn oil (8/group) at dose levels of 3, 6, or 12 mg/kg bw/day for 28 days. Estrous period of mice determined, and behavioural tests (open field test, light/dark box test, nest building test) administered between Day 21-28. Circadian activity test performed on 3 mice/group on Day 28 (observed for 4 days). Mice (5/group) sacrificed on Day 29, blood was collected hypothalamus, pituitary, thyroid, and striatum were removed and examined. Evaluation of serum TSH, TRH, T3 and T4, RNA in hypothalamus, pituitary and thyroid, and protein levels in striatum. Histopathological examination of thyroid. ≥3 mg/kg bw/day: ↑ nocturnal activity in last 3 days (3 mg/kg bw and 6 mg/kg bw only). ≥6 mg/kg bw/day: ↑ total distance, average speed, and total running time open field and circadian activity tests, ↑ immobility time and ↓ swimming time in forced swimming test, ↑ TRH, ↓ TSH, T3 and T4, ↓ expression of levels of HPT-axis-related genes in hypothalamus, pituitary and thyroid, expanded thyroid follicles, scanty colloid and hyperplastic thyroid cells noted upon histological examination, ↓ expression level of tyrosine hydrolase protein and ↑ dopamine transporter protein expression in striatum. Limitations: Purity of test material and dosing volume were not stated, limited reporting of results.

Study type/Animal/PMRA No.	Study results
30-day oral toxicity (gavage) Effects on hippocampus and learning and memory in adult mice C57BL/6 mice (♂) Hossain et al. 2020 PMRA No. 3470521	Acceptable with limitations Ten week old C57BL/6 male mice were administered 3 mg/kg bw/day deltamethrin dissolved in corn oil (1 mL/kg bw dosing volume) by gavage every 3 days for 30 days. Three days after final dosing day, novel object recognition test was conducted (12 mice/group). Morris water maze was conducted. Six mice/group sacrificed 24 hr after last dose, brains removed and used for neurogenesis study (cell proliferation, total cell counts). 3 mg/kg bw/day: significant deficits in novel object recognition and learning and memory (Morris water maze), hippocampal ↓ cell proliferation, ↓ nestin-positive neural progenitor cells, disruption of neurogenesis, ↓ granule cells. Limitations: Only one dose level tested, limited reporting of results in general.
Oral toxicity (gavage) (non-guideline) Effects of post-natal exposure on hippocampus Sprague Dawley rats Pitzer et al. 2022 PMRA No. 3516195	Acceptable with limitations Rats dosed with 1.0 mg/kg bw/day in corn oil on PND 3-20 (dosing volume 5 mL/kg bw). Dopamine markers, glutamatergic markers, glutamate release by microdialysis, apoptosis, cytokines in hippocampus measured at different time points (mostly PND 21 and 60). Specific endpoints measured: pro-caspase-3 expression via western blot analysis on PND 21; cleaved caspase-3 via western blot analysis on PND 3, 9, 15, 20; DNA fragmentation via TUNEL staining on PND 21 (♂ only); cytokines on PND 20 (♂ only); long-term potentiation on PND 60; western blot analysis for various markers on PND 60; hippocampal glutamate microdialysis on PND 60 (♂ only). 1.0 mg/kg bw/day: ↑ cell death in hippocampus and neostriatum via TUNEL staining PND 21, ↑ cytokines PND 20 (INF-γ in striatum, IL-13 in dorsal hippocampus, IL-1 β in nucleus accumbens, KC/GRO in dorsal hippocampus) ↑ NMDA-NR2A levels in the hippocampus, ↓ NMDA-NR2B levels in hippocampus, ↑ long-term potentiation (excitatory post-synaptic field potentials) in dorsal hippocampus following tetanizing stimulus on PND 60 (♂).

Study type/Animal/PMRA No.	Study results
30-day oral toxicity (gavage) (non-guideline) Effects on brain antioxidant levels, oxidative stress, serum neurotransmitters, and behaviour Rats (♂) (strain not specified) Khalifa et al. 2022 PMRA No. 3470522	Limitations: Only one dose level tested, age of rats not known at start of study, group sizes not always clear, limited reporting of results in general. Acceptable with limitations Rats dosed with 3.855 mg/kg bw/day deltamethrin in corn oil or 8.795 mg/kg bw/day silica-loaded deltamethrin, or 30.44 mg/kg bw/day chitosan encapsulated deltamethrin (15/group). Behavioural tests conducted (6 rats/group) to examine LMA, anxiety-like behaviours, exploration, and short-term memory (Y-maze). Measurement of brain antioxidant/oxidant levels, serum neurotransmitters, and protein expression. 3.855 mg/kg bw/day (deltamethrin): ↓ activity in open field, ↑ anxiety-like behaviour, impaired short-term memory, ↑ lipid peroxidation, ↑ oxidative stress, ↑ neurotransmitter levels and expression level of neurogenic genes, severe multifocal histological lesions in cerebral cortex (degenerative changes and necrosis of neurons). Nano-formulations of deltamethrin: Rats treated with the two nano-deltamethrin forms exhibited behaviour that was similar to that of controls. Moderate to severe multifocal histological lesions in cerebral cortex (degenerative changes and necrosis of neurons). Limitations: Only one dose level tested, strain of rats not known, limited reporting of results in general.
Developmental neurotoxicity (gavage) (non-guideline) Developmental pyrethroid exposure and age influence phenotypes in a Chd8 haploinsufficient autism mouse model Chd8V986*/* and C57BL/6J mice Jimenez et al. 2022 PMRA No. 3826210	Acceptable with limitations Chd8V986*/* ♂ and C57BL/6J (WT) ♀ mice bred, and 1 animal/sex/genotype per litter selected. Dams dosed with 0 or 3 mg/kg bw deltamethrin in oil/peanut butter every 3 days until PND 22. ♂ offspring used in behavioural tests (10 control (WT), 10 control haploinsufficient, 10 deltamethrin (WT), 12 deltamethrin haploinsufficient) Genotyping, behavioural testing twice (elevated plus maze, open-field, social approach in three-chamber choice task) at 6 months, then at 12 months. Another cohort tested with open-field at 6 weeks for anxiety assessment. Histopathology analyses conducted. 3 mg/kg bw: ↑ anxiety-like behaviour, ↑ sociability, ↓ elevated plus maze open-arm time, ↓ total arm entries, ↑

Study type/Animal/PMRA No.	Study results
	open-field test anxiety (haploinsufficient); ↑ elevated plus maze open-arm time (WT); ↑ interest in social novelty at 6 months, ↓ rearing movements (haploinsufficient and WT). Less exploration and rearing behaviour could be a result of motor deficits. Generally bigger changes between WT and haploinsufficient mice in deltamethrin exposed groups, compared to control, but no overall treatment effect observed. Limitations: Only one dose level tested, limited reporting of results in general.
Developmental neurotoxicity (gavage) (non-guideline) C57BL6/J or C57BL6/CR mice Curtis et al. 2023 PMRA No. 3826211	Acceptable with limitations Dams dosed with 0 or 3 mg/kg bw/day deltamethrin in peanut butter/corn oil every 3 days for 2 weeks prior to mating, through mating, pregnancy, and lactation (from Day 0 to Day 63) up to weaning of pups (PND 21). ♂ and ♀ pups tested for ultrasonic vocalization (PND 6-7). ♂ pups tested for marble burying, self-grooming, fear acquisition and recall, and operant acquisition. Juvenile play tested at PND 21, adult behaviour tested on study Day 98. Behaviourally-naïve animals selected for brain dissection. 3 mg/kg bw: ↓ ultrasonic vocalizations, ↑ repetitive behaviours, impaired fear, and operant conditioning, ↓ action potential duration, more pronounced inward rectifier current in nucleus accumbens core, ↑ dopamine and dopamine metabolites in dorsal and ventral striatum (♂). Limitations: Only one dose level tested, no dosing volume reported, limited reporting of results in general.
Developmental neurotoxicity (gavage) (non-guideline) C57BL6/J mice Curtis et al. 2024 PMRA No. 3826212	Acceptable with limitations ♀ mice dosed with 0 or 3 mg/kg bw deltamethrin in peanut butter/corn oil every 3 days from 2 weeks before pairing with ♂ to weaning. Adult ♂ offspring brain tissue underwent untargeted high-resolution, whole-brain metabolomics. 3 mg/kg bw: significantly altered metabolites for folate biosynthesis, retinol metabolism, and tryptophan metabolism (similarities to folate synthesis inhibitors) and altered molecular pathways for dopaminergic synapses.

Study type/Animal/PMRA No.	Study results
	Limitations: Purity not reported, only one dose level tested, no dosing volume reported, limited reporting of results in general.
Developmental neurotoxicity (gavage) (non-guideline) and epidemiological study C57BL6/J mice Richardson et al. 2015 PMRA No. 3690139	Acceptable with limitations Eight week old pregnant mice dosed with 0, 0.3, 1, or 3 mg/kg bw/day deltamethrin in peanut butter/corn oil every 3 days during gestation and lactation until PND 22. Testing of offspring included LMA (all doses), impulsive behaviour (FR-WAIT procedure, control, and high-dose group), and Y-maze (control and high-dose group). LMA measured recorded every 2 weeks from Week 6-12 for 3 mg/kg bw group. Biochemical and molecular assay conducted at 6 weeks of age. HPLC, microdialysis, and fast-scan cyclic voltammetry. After 30 minutes of habituation, select mice were administered methylphenidate or SKF82958, and LMA was measured for 60 minutes. At 24 hours prior to testing, select mice administered reserpine as well as α-methyl-p-tyrosine 1 hour before apomorphine administration. D1/D2 antagonists and agonists were also administered. Epidemiology nested-case study conducted to assess ADHD and pyrethroid metabolite level association in US school children age 6-15 (n = 2123). ≥ 0.3 mg/kg bw: $\uparrow$ LMA (after 30 minute habituation σ), $\uparrow$ striatal dopamine transporter levels. 3 mg/kg bw: $\uparrow$ impulsive behaviour, $\downarrow$ attention, MPTP toxicity (striatal dopamine loss) (σ/η); $\downarrow$ working memory, $\uparrow$ striatal dopamine D1 receptors, $\downarrow$ nucleus accumbens extra cellular dopamine levels (σ); $\uparrow$ D2 receptor binding (η). Most effects were more pronounced in σ. Methylphenidate, D1/D2 antagonists, and D2 agonist administration stopped the deltamethrin-associated increases in LMA. D1 agonist increased LMA, especially for deltamethrin group. Apomorphine restores LMA after dopamine depletion, but effect potentiated in deltamethrin σ group. Urinary 3-phenoxybenzoic acid levels associated with ADHD diagnosis (2.3 odds ratio).

Study type/Animal/PMRA No.	Study results
	Limitations: Purity not reported, dose volume not known, several limitations with data in epidemiology component (cross-sectional, one metabolite measurement only, covariates and confounders not adjusted for), limited reporting of results in general.
Developmental neurotoxicity (gavage) (non-guideline) Wistar rats Huang et al. 2025 PMRA No. 3826229	Acceptable with limitations Dams dosed with 0, 1, 4, or 10 mg/kg bw/day in corn oil on GD 0 to PND 21 (20-22 pregnant dams/group, 5 mL/kg bw). ♀ offspring selected for assessment. Behavioural tests (6 pups/group/test) included T-Maze and shuttle box experiments conducted on PND 20-21. PND 21 pups sacrificed and hippocampus isolated for further analyses (Nissl staining to count neurons, ferrous ion concentration, Western blot analysis, hippocampal GSH content, HT-22 cells, MDA content, ROS levels in HT-22 cells, intracellular Ca²⁺ concentration in hippocampus and HT-22 cells. ≥ 1 mg/kg bw/day: ↓ number of Nissl stained neurons in CA1 and CA3 regions, ↑ PTGS2 protein expression, ↓ SLC7A11 and GPX4. ≥ 4 mg/kg bw/day: ↓ T-Maze correct response rate, ↑ shuttle box rate of passive avoidance response, ↓ number of Nissl stained neurons in dentate gyrus region, ↑ ferrous content, ↑ GSH and MDA content, ↑ p53 protein, ↑ PL-C, IP3R and CaN protein expression, ↑ intracellular Ca²⁺. Administration of Fer-1 improved cell survival. Fe²⁺ and PTGS2 protein higher in deltamethrin group, lower when deltamethrin and then Fer-1 administered. p53 inhibition restored deltamethrin effects on ferroptosis in HT-22 cell, and PFT-α restored PL-C/IP3R pathway and calcium homeostasis effects. Limitations: Data were only presented in graphical form, no historical control data, no positive control data, no habituation data, no mention of time of peak effect for behavioural tests, limited reporting of results in general.
Developmental neurotoxicity (gavage) (non-guideline) Wistar rats	Acceptable with limitations Dams dosed with 0, 1, 4, or 10 mg/kg bw/day in corn oil on GD 0 to PND 21 (20-22 pregnant dams/group, 5 mL/kg bw). ♂ offspring assessed for forelimb grip strength on PND 14,

Study type/Animal/PMRA No.	Study results
Hao et al. 2024 PMRA No. 3826231	balance beam and rotarod assessment on PND 21, and Morris Water Maze (MWM) on PND 35 (6 pup/group/test). Hippocampi and cerebellums from each group obtained on PND 21. Immunofluorescence protocol used to assess cerebellums, Golgi-Cox staining to assess dendritic morphology, Sholl analysis assessed dendritic branching, Western blotting conducted to assess expression of proteins. PC12 cells cultured and exposed to deltamethrin (0, 10, 40, 100, 400, 700, 1000 µM) for 24 or 48 hours and cell activity measured. ≥ 1 mg/kg bw/day: altered dendritic branching of Purkinje cells. ≥ 4 mg/kg bw/day: ↓ forelimb grip strength, ↑ time on balance beam, ↓ time on rotarod, ↑ MWM escape latency, ↓ time in platform quadrant, ↓ number of platform crossings, ↓ density of dendritic spines in CA1 hippocampal region, ↓ hippocampal mushroom, ↓ dendritic length, ↓ Purkinje cell complexity, ↓ M1 mAChRs, ↓ p-AKT, ↓ p-mTOR, ↓ p-GluA1, ↓ membrane GluA1 protein, ↓ BDNF and p-TrKb proteins, ↓ p-stathmin protein. TBPB (a common M1 mAChRs agonist) administration restored deltamethrin effects on mAChR-mediated signaling pathway and PC12 cell decrease (deltamethrin exposure led to concentration dependent decrease in cell viability). Limitations: Data were only presented in graphical form, animal housing conditions not described, no historical control data, no positive control data, no habituation data, no mention of time of peak effect for behavioural tests, limited reporting of results in general.
Prenatal placental transcriptome study (gavage) (non-guideline) Effects of prenatal pesticide exposure on the fetal brain and placenta transcriptomes in a rodent model C57BL/6J mice Lesseur et al. 2023	Acceptable with limitations Eight week old ♀ mice were dosed 2 weeks prior to breeding (every 3 days) until GD 17 with 0 or 3 mg/kg bw/day deltamethrin in corn oil. Maternal animals were sacrificed on GD 17, fetal brain and placental samples were obtained. RNA sequencing was conducted to obtain transcriptomes. Weighted gene co-expression networks, differential expression, and pathway analyses were conducted, and 14 brain gene co-expression modules were identified.

Study type/Animal/PMRA No.	Study results
PMRA No. 3613501	3 mg/kg bw: genes involved in calcium signaling, spliceosome, and extracellular matrix interaction pathways were disrupted. Limitations: Purity not reported, dosing volume not known, only one dose level tested, limited reporting of results in general.
28-day oral toxicity (gavage) (non-guideline) Effects on testes BALB/c mice (♂) Bagherpour et al. 2019 PMRA No. 3470520, 3557048	Acceptable with limitations Mice received 0 or 0.6 mg/kg bw/day in corn oil by gavage. Animals were sacrificed at the end of the dosing period and testes were removed for examination (sperm parameters, histopathology, biochemical evaluation). Serum testosterone levels were measured. 0.6 mg/kg bw/day: ↓ sperm count, ↓ sperm motility, ↑ abnormal spermatozoa, histopathological changes in testicular tissue, ↓ serum testosterone, ↑ lipid peroxidation, enhanced caspase-3 expression and apoptosis in testicular tissue. Limitations: Limited information regarding study conduct, only one dose tested, lack of analytical dose accuracy, strain of mouse is known to have variable sperm abnormalities, limited reporting of results in general.
14-day oral toxicity study of relevant biomarkers (gavage) (non-guideline) Biomarkers of oral subacute toxicity Albino rats (♂) Elbanna et al. 2023 PMRA No. 3566649	Acceptable with limitations Rats received 0, 0.874, or 8.740 mg/kg bw/day deltamethrin in corn oil by gavage. Blood samples obtained from the peripheral vein 24 hours after the last dose. Hematological, clinical chemistry, and oxidative stress biomarkers were analyzed for. Histopathological analysis of relevant organs was conducted. ≥0.874 mg/kg bw/day: ↑ Hb, ↓ Hct, ↑ RBC, ↓ MCV, ↑ MCH, ↑ MCHC, ↑ platelets, ↓ WBC, ↑ RDW-CV, ↑ total protein, ↑ ALT, ↓ ALP, ↑ LDH, ↑ thiobarbituric acid reactive substances (kidney, liver, brain), ↓ glutathione peroxidase (kidney, liver, brain), ↓ superoxide dismutase (kidney, liver, brain), ↓ catalase (kidney, liver, brain), liver inflammation, hemorrhage and necrosis, dilated kidney tubules, brain vacuolation, brain necrosis, brain hemorrhage, testicular vacuolation and sloughing, epididymal necrosis, ↑ aggregate index of systemic inflammation, ↑ globulin, ↑ monocytes ↓ basophils, ↑ monocyte-to-lymphocyte, ↓ neutrophil-to-

Study type/Animal/PMRA No.	Study results
	lymphocyte platelet ratio, ↑ systemic immune inflammation index, ↑ systemic inflammation response index, ↑ albumin, ↓ uric acid. 8.74 mg/kg bw/day: kidney fibrosis and hemorrhage, epididymis inflammation and hemorrhage, testicular hemorrhage, ↓ eosinophil, ↑ platelet-to-lymphocyte ratio. Many clinical chemistry and hematological changes either did not elicit a clear dose-response or were of marginal magnitude. Limitations: No analytical verification of doses or homogeneity, age of rats not known, dosing volume not known, limited reporting of results in general.
16-week oral toxicity (diet) (non-guideline) Effects of the pesticide deltamethrin on high fat diet-induced obesity and insulin resistance in male mice C57BL/6J mice (♂) Tsakiridis et al. 2023 PMRA No. 3566636	Acceptable with limitations Mice received 0, 0.01, 0.1, or 1.0 mg/kg bw/day deltamethrin in the diet. One group tested under thermoneutral (TN) conditions (29°C) to better mimic human metabolic disease, one group under room temperature (RT) (21°C). Glucose and insulin tolerance tests were conducted, along with metabolic cage analysis. Animals were sacrificed and tissues were collected. 0.01 mg/kg bw/day: ↑ physical activity, ↑ energy expenditure (TN and RT); ↓ fat mass, ↓ abs. gonadal and inguinal white adipose tissue depot weight (TN); ↑ glucose tolerance (RT). 0.1 mg/kg bw/day (TN): ↑ energy expenditure. 1.0 mg/kg bw/day (RT): ↓ rel. liver wt. Limitations: Lack of dose response for several findings, no analytical confirmation of dose accuracy/homogeneity, limited reporting of results in general.
In vitro investigation of developmental sensitivity of VGSC (non-guideline) <i>Xenopus laevis</i> oocytes Meacham et al. 2008 PMRA No. 3367617	Acceptable with limitations Rat Nav1.2 and Nav1.3 VGSC subunits were expressed in <i>Xenopus laevis</i> oocytes alone, or with β1 or β3 subunit. Oocytes were exposed to deltamethrin concentrations of 10⁻⁵ to 10⁻⁹ M. Sodium current responses were measured via and voltage-clamp recordings.

Study type/Animal/PMRA No.	Study results
	Summary of key findings: Study demonstrated ↑ sensitivity in juvenile VGSC vs adult at all concentrations of deltamethrin. Sensitivity to modification of VGSC kinetics for all subunit combinations at all deltamethrin concentrations (concentration-related increases) in Rat Embryonic Nav1.3 vs Rat Nav1.2, especially with β-subunits present. Limitations: Study does not provide information regarding endpoints for use in quantitative risk assessment.
In vitro electrophysiology (non-guideline) HEK293 cells James et al. 2017 PMRA No. 3681111	Acceptable with limitations Acute deltamethrin exposure to Nav isoforms. Patch-clamp electrophysiology assessment measuring sodium currents encoded by Nav1.1 or Nav1.6 channels stably expressed in HEK293 cells. Summary of key findings: ≥1 μM: persistent and tail current densities potentiated, no effect on peak transient current densities (Nav1.1). 10 μM: persistent and tail current densities potentiated, no effect on peak transient current densities (both isoforms). Both isoforms ↑ window currents (more pronounced for Nav1.1). Impact on activation slope and steady state inactivation for peak currents $V_{1/2}$ (Nav1.6). Persistent current activation $V_{1/2}$ hyperpolarization (Nav1.1). Potentiation of persistent and tail current densities (both, only use-dependent in Nav1.6). Human Nav1.1 (present during neurodevelopment and in adults) was more sensitive than human adult Nav1.6 to deltamethrin using a mammalian HEK293 cell expression system. Limitations: Study does not provide information regarding endpoints for use in quantitative risk assessment, purity not reported, does not test β-subunits in conjunction (which would better reflect native mammalian channels).
Physiologically based kinetic (PBK) model	Acceptable with limitations To compare human fetal brain concentrations to in vitro DNT benchmark concentration, PBK model created by PK-

Study type/Animal/PMRA No.	Study results
Considering developmental neurotoxicity in vitro data for human health risk assessment using physiologically-based kinetic modelling: deltamethrin case study Maass et al. 2023 PMRA No. 3613499	Sim (version 9). Deltamethrin properties sourced from literature, internal company data, and in vivo and in vitro rat data. Model was then translated to human in vivo exposure based on the ADI established by the JMPR. Human fetal brain exposure after maternal exposure to deltamethrin was estimated. Read-across approach used to estimate blood-placenta partitioning range. Summary of key findings: Deltamethrin transfer across blood brain barrier is limited, maternal plasma/brain concentration ratio ≈ 0.06 determined from species extrapolation of rat data. Worst-case scenario of fetal/maternal transfer was estimated to be 1.2, with a median value of 0.2. Human fetal brain concentrations were far below benchmark concentrations. Worst-case scenario (no blood-brain or blood-plasma barrier) at gestational age 20 and 40 weeks, margin of safety approaches in vitro BMC of 0.5 μM at dose of 0.9 mg/kg/day (90$\times$ higher than ADI). When dosing at the JMPR ADI, margin of is 80-244 (still far below in vitro benchmark) indicating a simulated fetal brain deltamethrin concentration orders of magnitude lower than the in vitro benchmark. Limitations: Not a primary study, study does not provide information regarding endpoints for use in quantitative risk assessment.
Physiologically based pharmacokinetic (PBPK) model Evaluation of deltamethrin kinetics and dosimetry in the maturing rat using a PBPK model Tornero-Velez et al. 2010 PMRA No. 3686217	Acceptable with limitations Existing PBPK model of deltamethrin in adult σ rats was modified to assess and accurately predict blood and target organ dosimetry during maturation (PND 10, 21, 40 and 90). Age-specific organ weights and age-dependent changes in oxidative and hydrolytic clearance of deltamethrin modelled using generalized Michaelis–Menten model for growth and summary equations. Summary of key findings: The model predicted juvenile TK sensitivity. Predicted PND 10 and 21 pup brain concentrations were 3.8-fold and 2.5-fold higher than adults

Study type/Animal/PMRA No.	Study results
	(PND 90), respectively, suggesting that pups require lower doses to achieve the same brain concentration. Limitations: Not a primary study, study does not provide information regarding endpoints for use in quantitative risk assessment.
Determination of potential toxicodynamic differences of pyrethroid insecticides on native voltage-sensitive sodium channels in juvenile versus adult rat brain (non-guideline) Symington et al. 2023 PMRA No. 3686298	Acceptable with limitations Juvenile and adult rat brain neurolemma fragments were microtransplanted into <i>X. laevis</i> oocytes (to study multiple CNS VGSC isoforms in their native configuration and lipid environment) and were treated with deltamethrin. Automated western blotting was used to assess VSSC expression. Summary of key findings: Juvenile neurolemma demonstrated 2.5× greater sensitivity to modification of VGSC kinetics compared to adult neurolemma at all deltamethrin concentrations tested. Nav1.2. was the predominant isoform in adults and pups, but the level noted in the adult isoform was 2.8-fold greater than in pups. The Nav1.6 isoform was also significantly higher level (2.2-fold) in adults. Concentration-dependent increases in in-ward tetrodotoxin-sensitive current in the presence of niflumic acid were noted in both adult and juvenile tissues following a pulsed depolarization of the oocyte plasma membrane. Limitations: Study does not provide information regarding endpoints for use in quantitative risk assessment.
Physiologically based kinetic (PBK) model with in vivo toxicokinetic testing (gavage and IV) (non-guideline) Rat and human diffusion-limited model Long Evans rats Godin et al. 2010 PMRA No. 3684088	Acceptable with limitations A PBK model was used to describe gastrointestinal absorption (mediated by phase III efflux transporters pumping deltamethrin out of enterocytes into GI tract). In vivo analyses of dose-dependence of absorption and bioavailability were conducted to assess predictions of the PBK model. The model was optimized, sensitivity analysis was conducted, and then predictions were extrapolated to humans. Doses of 0.3 and 3.0 mg/kg bw administered in corn oil (1 mL/kg bw, 4 ♂/group). Animals were sacrificed; histopathological analyses were conducted. Another group received 1 mg/kg bw deltamethrin via IV. Bioavailability was calculated by comparing the oral administration and IV

Study type/Animal/PMRA No.	Study results
	groups. Deltamethrin sources from the literature and in vitro data were used to translate human in vivo exposure based on a dose level of 1 mg/kg bw/day. Human fetal brain exposure after maternal exposure to deltamethrin was estimated. Read-across approach was used to estimate blood-placenta partitioning range. Summary of key findings: There was no difference in bioavailability between both dose levels. Dose-dependence of oral absorption was not observed in vivo, unlike what the PBK model predicted. Biphasic distribution in the blood and brain was apparent following IV administration. Diffusion-limited model predicted rapid decrease of liver concentrations and brain concentrations for the 3.0 mg/kg bw dose level. Predicted brain AUC of deltamethrin in humans was threefold greater than in rats. Limitations: Not a primary study but rather review and integration of various in vivo and in vitro studies to evaluate specific parameters of a PBPK model, study does not provide information regarding endpoints for use in quantitative risk assessment.
In vitro to in vivo (IVIVE) extrapolation based physiologically based pharmacokinetic (PBPK) model Evaluation of age-related pyrethroid pharmacokinetic differences in rats Sprague-Dawley rats (♂) Song et al. 2019 PMRA No. 3686292	Acceptable with limitations IVIVE extrapolation based PBPK model. In vitro metabolism data collected for deltamethrin via liver microsomes and cytosol. Plasma prepared from PND 15, 21, and 90 rats. Various metabolic parameters biologically scaled to in vivo parameters for use in the age-specific PBPK model. Age-dependent changes in target tissue exposure simulated across ages using the model. Summary of key findings: Age-dependent increases in hepatic and plasma intrinsic clearance. CYP enzymes are the major contributor to hepatic metabolic clearance, but CES also plays a role. Both in vitro and in vivo data showed progressive increases in CYP- and CES-mediated metabolism of deltamethrin. Study authors noted that humans lack plasma CES and argued therefore that younger humans may not be susceptible to reduced metabolic clearance observed in juvenile rats.

Study type/Animal/PMRA No.	Study results
	Limitations: Not a primary study but rather review and integration of various in vivo and in vitro studies to evaluate specific parameters of a PBPK model, all data appear to only be obtained from ♂ rats, study does not provide information regarding endpoints for use in quantitative risk assessment.
Case study for the integration of in vitro data in the developmental neurotoxicity hazard identification and characterization using deltamethrin as a prototype chemical OECD 2022 PMRA No. 3826214	Acceptable with limitations Deltamethrin was used as a case study in the development of an AOP. The report included a systematic literature review of in vivo and in vitro experimental evidence and human observational studies. Quantitative analysis of uncertainty was conducted along with the DNT-IVB covering basic neurodevelopmental key events. An AOP network was developed, applied as a framework to develop IATA to structure all the evidence gathered and characterize the individual biological and toxicological relevance of the DNT-IVB in predicting an adverse effect. Summary of key findings: A complex putative AOP network for the adult brain was developed to assess the KEs (including altered brain network function) that lead to behavioural impairment (adverse outcome) with 2 MIEs (VGSC or Ryanodine receptor binding). The model assumed monotonic dose-response. The DNT-IVB concluded that deltamethrin is a developmental neurotoxicant. Overall, the case study demonstrated the applicability of the DNT-IVB and the usefulness of the AOP in hazard characterization. Limitations: Not a primary study, but rather review and integration of various other studies, study does not provide information regarding endpoints for use in quantitative risk assessment.
Development of Integrated Approaches to Testing and Assessment (IATA) case studies on developmental neurotoxicity (DNT) risk assessment EFSA 2021 PMRA No. 3681072	Acceptable with limitations Deltamethrin was used as a case study in the development of an IATA for DNT. The report included a systematic literature review of in vivo and in vitro experimental evidence, NAMs, and human observational studies. The IATA development included expert knowledge elicitation and a probabilistic approach to an uncertainty analysis, followed by integration of evidence using the AOP framework.

Study type/Animal/PMRA No.	Study results
	Summary of key findings: A more complex putative AOP Network for adult brain was developed to assess the KEs (including altered brain network function) that lead to behavioural impairment (adverse outcome) with 2 MIEs (VGSC or Ryanodine receptor binding). The model assumed monotonic dose-response. The DNT-IVB concluded that deltamethrin is a developmental neurotoxicant. EFSA acknowledged that potentially important KEs may still be missing from this putative AOP, and recommended testing additional pyrethroids in the DNT-IVB. Bayesian network analysis (to determine the probability of causal associations for KEs) was used to determine the probability of downstream KEs. KE5 (↓ oligodendrocyte differentiation) is a sensitive endpoint for which specificity is still uncertain; additional characterization is needed. Causal association of deltamethrin exposure with all DNT outcomes <66% (principally due to “probably” or “definitively high” RoB for exposure measurements). Human evidence of deltamethrin prenatal exposure linked with NDD, consistent with animal data and biology of NDDs and available evidence structured in the AOP. A knowledge gap was noted for the final two KERs. Limitations: Not a primary study, but rather review and integration of various other studies, study does not provide information regarding endpoints for use in quantitative risk assessment.
A developmental neurotoxicity adverse outcome pathway (DNT-AOP) with voltage-gated sodium channel (VGSC) inhibition as a molecular initiating event (MIE). EFSA 2024 PMRA No. 3681074	Acceptable with limitations An ad hoc EFSA working group (WG) was put together to complete a systematic literature review of empirical evidence to assess developmental neurotoxicity AOP effectiveness, in particular the key event relationships (KERs). The OECD DNT-IVB assays cover several KEs mapped by this AOP. Previous (2021) deltamethrin case study by EFSA contained weak or moderate empirical support for downstream KERs. Literature review tools applied stepwise to identify additional KEs, and broad search to identify additional empirical evidence. Two major uncertainties in

Study type/Animal/PMRA No.	Study results
	initial AOP: potential limitations of some KEs being overlooked due to only deltamethrin being assessed, knowledge gap for last two KERs in AOP. WG aimed to close knowledge gap linking KE4 to AO, and reduce uncertainties by evaluating information from additional stressors. Summary of key findings: AOP (#442) was developed by EFSA in collaboration with various experts to provide a structured approach for evaluating DNT. AOP focus was on the hippocampus due to its critical role in cognitive function and vulnerability during development. Limitations: Systematic review that does not directly inform quantitative HHRA, aims to broaden scope of DNT-AOP beyond just deltamethrin.
Developmental neurotoxicity (non-guideline) Zebrafish Kung et al. 2015 PMRA No. 3681114	Acceptable with limitations Fertilized embryos exposed at 3 hpf (512-cell stage) to 0, 0.25, 0.33, 0.50 µg/L concentrations of deltamethrin dissolved in 0.01% dimethylformamide (30-50 embryos). Reverse-transcriptase quantitative PCR, high-performance liquid chromatography – electrochemical detection (HPLC-ECD), activity monitoring of 2-week-old larvae performed. Summary of key findings: No mortality or acute toxicity observed. 0.25 µg/L: ↑ th1 transcript level at 72 hpf. ≥ 0.33 µg/L: ↑ swim activity (all time bins after larval transition to darkness), ↓ DRD1 transcript levels at 72 hpf (and larval stage for 0.50 µg/L). 0.50 µg/L: ↓ DRD2 transcript levels. Swim activity effects restored when knocking out dopamine transporter, and also ↓ swim activity after methylphenidate administration. Limitations: Lack of standardization of the assays leading to difficulty with comparisons across studies, difficult to discern if behavioral effect observed is present in conjunction with other toxicity, limited reporting of results in general.

Study type/Animal/PMRA No.	Study results
30-day toxicity study (nasogastric gavage) (non-guideline) Effects on rat testis structure Sprague Dawley rats (♂) Ouais et al. 2023 PMRA No. 3826218	Acceptable with limitations Adult rats dosed with 0.6 mg/kg bw/day deltamethrin in corn oil for 2-weeks or 1 month (5 ♂/group). Note: Other groups received vitamin E + deltamethrin (results not reported here). Animals were sacrificed at the end of the dosing period and blood samples were analyzed for testosterone levels, antioxidants, and oxidative stress markers. Histopathological and biochemical analysis of testes structure was conducted. 0.6 mg/kg bw/day: ↓ testosterone, ↓ glutathione, ↓ catalase activity, ↑ malondialdehyde, ↓ seminiferous tubular diameter and thickening, ↑ interstitial tissue spacing (2-weeks and 1 month); ↓ rel. seminiferous tubules size, rel. atrophy of interstitial tissue, ↓ eosinophilic sperm tails in tubular lumen, irregular seminiferous tubule basement membrane, loss of germinal epithelium lining with cystic alterations, ↓ number of Sertoli and Leydig cells, abnormally shaped cells in spermatid threads, testicular basement membrane irregularity, rounded/abnormal spermatids, early vacuolations, lack of mature sperm in lumen (2-weeks); “bizarre” shaped and collapsed seminiferous tubules, generally no sperm tails, interstitial tissue hemorrhagic exudate, scanty germinal epithelium, lack of Sertoli cells and spermatogonia, pale and chromin-lacking rounded spermatids, lack of sperm in lumen, abnormally shaped interstitial Leydig cells, hemorrhagic exudate in the interstitial tissue (1-month). Electron microscopy showed that there was damage to the cell membrane with no clear boundaries between cells, degenerative changes in primary spermatocytes, corrugation in the nuclear membrane, vacuolated cytoplasm, and swollen mitochondria after 2 weeks of exposure. In the 1-month group, there were marked degenerative changes in most of the seminiferous tubules and the whole cells, Sertoli cells had hyperchromatic nuclei, rarified cytoplasm with wide space between cells and scattered electron-dense granules similar to lysosomes. Limitations: Only one dose level tested, no dosing volume, no purity reported, limited reporting of results in general.

Study type/Animal/PMRA No.	Study results
8 to 12-week toxicity study (intragastric gavage) (non-guideline) Purpose to assess injury to small intestine BALB/c mice (♀) Ma et al. 2024 PMRA No. 3826221	Acceptable with limitations Four-week old mice dosed with 0.2 mg/kg bw/day deltamethrin for 8-weeks or 10 to 12-weeks (5 ♀/group). Body weights, disease activity index (DAI) scores recorded. Colon tissues were collected hematoxylin-eosin, immunofluorescence and immunohistochemistry staining were conducted. RNA sequencing performed to assess. Note: Other groups received other compounds and various durations of combinations of deltamethrin with other compounds, but results of those groups are not reported here. 0.2 mg/kg bw/day: deltamethrin accumulation in the intestines (even after stopping dosing for 1-2 weeks), weight loss, ↑ disease activity index score, colitis, apoptosis of colonic epithelial cells, ↓ colon length, senescence of colon tissue, ↑ p21 and p26, ↑ p53 activation. Limitations: Purity not reported, only one dose level tested, not explicitly stated that deltamethrin was dissolved in the vehicle, no dosing volume reported, limited reporting of results in general.
Application of the Integrated Approach to Testing and Assessment (IATA) for evaluating endocrine disruption potential Human H295R adenocarcinoma, hERα-HeLa-9903, and 22Rv1/MMTV_GR-KO cell lines Ortiz et al. 2025 PMRA No. 3826232	Acceptable with limitations Deltamethrin dissolved in DMSO and incubated with cell lines for 24 hours at different concentrations. 3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide (MTT) assay used to assess cell viability. ELISA kits used to assess 17β-estradiol (E2) and testosterone (T) levels via ER and AR transactivation, respectively, and H295R steroidogenesis assay used with human H295R cells. Summary of key findings: Slight ↓ in E2 levels but significantly ↓ testosterone levels in steroidogenesis assay. In the ER transactivation assay, deltamethrin showed strong ER agonist activity but not antagonist activity. In the AR transactivation assay, weak but positive AR agonist activity was noted along with clear AR antagonistic activity. Limitations: Study does not provide information regarding endpoints for use in quantitative risk assessment.
14-day oral study (gavage) (non-guideline)	Acceptable with limitations

Study type/Animal/PMRA No.	Study results
Investigation into protective effects of essential oils against deltamethrin-induced hematological and biochemical toxicity in ♀ adult rabbits Rabbits (Crossbred INRA 2666 strain X a local strain; ♀) Chaouchi et al. 2025 PMRA No. 3826236	Four month old rabbits dosed with 1.28 mg/kg bw/day deltamethrin in corn oil. Note: Other groups received corn oil, essential oils alone, or essential oils with deltamethrin (results of other groups not reported here). Behaviour, body weight, and blood parameters analyzed. In silico analyses conducted to assess toxicokinetics. Summary of key findings: In silico results suggested 0.50 probability of neurotoxicity, low intestinal absorption, low MDCK permeability, and suboptimal Caco-2 permeability, inhibition of CYP enzymes (CYP1A2, CYP2C9, CYP2C19, CYP2C8, and CYP3A4), no permeation of blood-brain barrier. 1.28 mg/kg bw/day: tremors, signs of agitation, unusual hyperactivity, and stereotyped movements, ↓ RBC, ↓ lymphocytes, ↓ Hct, ↑ MCH, ↑ platelets, ↑ ALT, ↑ AST, ↑ creatinine, ↑ glucose, ↓ GGT, ↓ ALP. Limitations: Several limitations with reporting, no purity reported, no dosing volume, only one dose level tested, no details on specific behavioural changes (such as incidence, duration, severity).
Androgen receptor signaling simulation study (non-guideline) Sheikh et al. 2023 PMRA No. 3826213	Acceptable with limitations Schrodinger's induced fit docking approach used to characterize structural binding of deltamethrin to steroid SHBG ligand-binding pocket, followed by molecular dynamics simulations. Binding interactions, binding energy, docking score, and IFD score were determined and compared to dihydrotestosterone (native ligand) binding. Summary of key findings: Deltamethrin demonstrated tight binding into the SHBG pocket, high commonality % of SHBG residues with native ligand, higher binding energy values than native ligand, higher stability than cypermethrin-SHBG complex. Deltamethrin had stable binding to the AR ligand-binding pocket, 80-90% commonality with testosterone in the interacting amino acid residues lining the binding pocket and similar binding energy. Limitations: Study does not provide information regarding endpoints for use in quantitative risk assessment.

Table 3 Toxicity profile of end-use product and manufacturing concentrate product containing deltamethrin

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

Study type/Animal/ PMRA No.	Study results
Raid Bug Defense (end-use product)	
Acute Oral Toxicity (Up and Down) Sprague Dawley rats PMRA No. 3014520	LD ₅₀ > 5000 mg/kg bw (♀) No clinical signs of toxicity. Low acute oral toxicity
Acute Dermal Toxicity Sprague Dawley rats PMRA No. 3014521	LD ₅₀ > 5000 mg/kg bw (♀) No clinical signs of toxicity. Low acute dermal toxicity
Acute Inhalation Toxicity (nose-only) Wistar rats PMRA No. 3014522	LC ₅₀ > 5.49 mg/L Clinical signs of toxicity included irregular respiration in all animals, but this returned to normal after Day 1. One male from the 2.40 mg/L test group exhibited corneal opacity on Days 13 and 14. Low acute inhalation toxicity
Eye Irritation NZ Albino rabbits PMRA No. 3014523	MAS = 1.56/110 MIS = 6/110 at 1 hour All scores zero by 72 hours. Based on persistence of irritation at 24 hours, the hazard was increased one category to “Minimally irritating”. Minimally irritating
Dermal Irritation NZ Albino rabbits PMRA No. 3014524	MAS = 0.33/8 MIS = 1/8 at 1 hour Very slight erythema was observed at all three treated sites within 30-60 minutes after patch removal. All animals were free of erythema by 72 hours. Minimally irritating
Dermal Sensitization (Buehler) Hartley Guinea Pigs PMRA No. 3014525	Negative

Study type/Animal/ PMRA No.	Study results
Ultratec 5SC MUP (manufacturing concentrate product)	
Acute Oral Toxicity (Up and Down) Sprague Dawley rats PMRA No. 3014123	LD ₅₀ > 5000 mg/kg bw (♀) No clinical signs of toxicity. Low acute oral toxicity
Acute Dermal Toxicity Sprague Dawley rats PMRA No. 3014124	LD ₅₀ > 5000 mg/kg bw Erythema in 1 ♀ on Day 1 only. Low acute dermal toxicity
Acute Inhalation Toxicity (nose-only) Sprague Dawley rats PMRA No. 3014125	LC ₅₀ > 5.12 mg/L All rats exhibited irregular respiration, anogenital staining, and/or hunched posture. All signs resolved by Day 3. Low acute inhalation toxicity
Eye Irritation NZ Albino rabbits PMRA No. 3014126	MAS = 12.67/110 MIS = 23.67/110 at 24 hours Conjunctivitis in all of treated eyes from 1-hour post-instillation, persisted until Day 7 in two animals. Corneal opacity and iritis observed in one treated eye starting at 24 hours, with iritis clearing by 48 hours and corneal opacity clearing by 72 hours. All animals free from all irritation by Day 10. Mildly irritating to the eye
Dermal Irritation NZ Albino rabbits PMRA No. 3014127	MAS = 0.8/8 MIS = 1/8 at 1 and 24 hours Very slight erythema on all three treated sites within 30-60 minutes. By 24 hours, very slight edema on one treated site. All rabbits were free from erythema and edema by Day 7 and 48 hours, respectively. Desquamation observed at two dose sites on Day 7. Slightly irritating
Dermal Sensitization (Buehler) Hartley Guinea Pigs PMRA No. 3014128	Negative

Table 4 Rat in vivo dermal absorption study demonstrating the amount of deltamethrin in each matrix at the specified hour (skin wash at 8 hours)

Residues in matrix (% of applied dose) ^a								
Matrix analysed	Dose							
	250 µg/cm ²				1.18 µg/cm ²			
	8h	24h	72h	144h	8h	24h	72h	144h
Dose site swabs (8 hours)	59.94	58.07	68.44	64.56	45.59	49.98	46.95	51.27
Gauze wash (8 hours)	8.20	2.57	3.72	4.28	9.52	2.67	7.04	7.82
Gauze wash (sacrifice)	N/A	7.48	8.02	8.82	N/A	2.13	7.26	10.73
Dose site shavings	N/A	5.54	7.11	12.85	0.00	13.50	12.08	11.92
Scissor wash	0.10	0.05	0.03	0.04	0.08	N/A	0.00	0.00
Total non-absorbed dose^b	68.24	73.71	87.33	90.55	55.20	68.29	73.33	81.74
Surface tape strip	1.53	4.14	2.65	1.16	4.34	8.12	3.34	1.73
Tape strips (>1)	22.50	12.91	5.11	2.76	30.09	14.27	9.32	4.19
Total tape strips residues^c	24.03	17.05	7.76	3.92	34.43	22.39	12.66	5.92
Urine	0.16	0.55	1.17	1.70	0.14	1.08	3.03	3.58
Feces	0.00	0.16	0.33	0.54	0.00	0.10	0.68	0.86
Cagewash	0.11	0.34	0.50	0.84	0.06	0.19	0.33	0.11
Total excreta^d	0.24	1.06	2.00	3.08	0.20	1.36	4.04	4.55
Surrounding Skin	0.20	2.19	0.68	0.67	0.14	0.08	0.09	0.11
Untreated Skin	0.01	0.00	0.02	0.01	0.00	0.00	0.00	0.00
Treated skin (excluding tape strips)	1.62	1.07	0.30	0.18	1.91	1.37	0.74	0.35
Carcass (including blood)	0.38	0.08	0.06	0.08	0.00	0.01	0.01	0.00
Total Tissues and Carcass^e	2.20	3.34	1.07	0.94	2.05	1.46	0.84	0.47
Dermal absorption^f	26.47 ± 3.39	21.45 ± 1.63	10.83 ± 2.92	7.94 ± 2.56	36.69 ± 4.00	25.21 ± 3.44	17.54 ± 3.47	10.94 ± 0.34
Dermal absorption without tape strips^g	2.44 ± 0.19	4.40 ± 1.78	3.07 ± 1.00	4.02 ± 1.11	2.25 ± 0.73	2.83 ± 1.00	4.88 ± 0.98	5.02 ± 1.44
Overall recovery^h	94.71	95.16	98.15	98.49	91.89	93.50	90.87	92.68

^a mean of 5 animals/group.

^b Total non-absorbed dose: Based on sum of Dose site swabs (8 hours) + Gauze washes + Dose site shavings + scissor wash.

^c Total Tape Strip Residues: Based on sum of all tape strips.

^d Total excreta: Based on sum of Urine + Feces + Cagewash.

^e Total Tissues and Carcass: Based on sum of Surrounding skin + Untreated Skin + Treated skin (excluding tape strips) + Carcass (including blood).

^f Dermal absorption: Based on sum of Total Excreta + absorbed dose Subtotal + Total tape strips.

^g Dermal absorption without Tape strips: Based on sum of Total Excreta + absorbed dose Subtotal.

^h Overall Recovery: Based on sum of Total non-absorbed dose + Dermal absorption.

Table 5 Residential applicator dermal and inhalation exposures to Raid Bug Defense

Scenario	Application equipment	Application rate (kg a.i./bottle) ¹	Amount handled daily (bottle)	Unit exposure (mg/kg a.i.)		Exposure (mg/kg bw/day) ²		MOE ³	
				Dermal	Inhalation	Dermal	Inhalation	Dermal	Inhalation
Outdoor structures and ant hills	Trigger-spray bottle	0.000195	1	187.61	0.13	4.6E-04	3.2E-07	2.2E+06	3.2E+06
Outdoor structures and ant hills	Automatic Sprayer ⁴	0.0015	1	130.1	0.149	2.4E-03	2.8E-06	4.1E+05	3.6E+05
PHED open mix/load liquid		0.0015	1	6.5	0.0016	1.2E-04	3.0E-08	8.3E+06	3.3E+07
Combined mix/load and application to outdoor structures for an automatic sprayer		0.0015	1	136.6	0.151	2.6E-03	2.8E-06	3.9E+05	3.5E+05

¹ The amount of end-use product per bottle was assumed to be 650 mL for the manual trigger sprayer and 5 L for the automatic sprayer. The latter is the maximum net contents.

² Exposure (mg/kg bw/day) = Application rate (kg a.i./bottle) × Amount handled per day (Fraction of bottle) × Unit Exposure (mg/kg a.i.) ÷ Body Weight (kg)

³ MOE = Dermal NOAEL (mg/kg bw/day) or Inhalation LOAEL (mg/kg bw/day) ÷ Exposure (mg/kg bw/day)

⁴ Unit exposure values from the ready-to-use pump sprayer were used as a surrogate exposure scenario for the automatic sprayer.

Table 6 Aggregate exposure and risk estimates for adults (16+ years)

Life stage	Exposure (mg/kg bw/day)			Aggregate MOE ⁴
	Inhalation ¹	Chronic dietary ²	Aggregate ³	
Adults (16+ years)	2.8E-06	0.000321	0.000324	3090

¹ Inhalation exposure for adults from application to exterior structural surfaces from Table 5, Residential Applicator Dermal and Inhalation Exposures to Raid Bug Defense.

² Chronic dietary (food + drinking water) exposure estimates for the general population from PRVD2015-07; Appendix VI, Table 2

³ Aggregate exposure = Inhalation Exposure + Chronic Dietary Exposure

⁴ Aggregate MOE = LOAEL of 1 mg/kg bw/day ÷ Aggregate Exposure; Target MOE = 1000 (see Table 1 for the Toxicological Reference Values).

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A. List of Studies/Information Submitted by Registrant

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1.0	Chemistry
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3014511	2018, Storage stability, DACO: 3.5.10 CBI
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B. Additional Information Considered

i) Published Information

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