Proposed Re-evaluation Decision PRVD2020-11

(S)-kinoprene and its Associated End-Use Products

Consultation Document

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Re-evaluation of (S)-kinoprene

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

(S)-kinoprene is an insect juvenile hormone analogue that inhibits insect growth during the moulting process. It is used to control aphids and whiteflies, and suppress mealybugs on greenhouse ornamental plants. It is applied as a foliar spray. Currently registered products containing (S)-kinoprene can be found in Appendix I.

This document presents the proposed regulatory decision for the re-evaluation of (S)-kinoprene including the proposed risk mitigation measures to further protect human health and the environment, as well as the science evaluation on which the proposed decision was based. All products containing (S)-kinoprene registered in Canada are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period, during which the public including the pesticide manufacturers and stakeholders may submit written comments and additional information to PMRA Publications. The final re-evaluation decision will be published taking into consideration the comments and information received.

Outcome of science evaluation

(S)-kinoprene is an insect growth regulator. It works by contact action or ingestion, interfering with pupation, and causing sterile adults and eggs. (S)-kinoprene is valued as a tool to manage aphids, mealybugs and whiteflies in greenhouse ornamentals.

With respect to human health, risks were identified for occupational workers; risks were not shown to be acceptable when used according to current label directions, or when additional mitigation measures were considered. Therefore, cancellation of all uses for (S)-kinoprene is proposed.

(S)-kinoprene was found to present potential risks to certain terrestrial and aquatic organisms. However, potential risks to the environment from (S)-kinoprene were shown to be acceptable, with additional standard precautionary label statements to protect aquatic organisms and beneficial arthropods and with updated use directions.

Proposed regulatory decision for (S)-kinoprene

Under the authority of the *Pest Control Products Act* and based on an evaluation of available scientific information Health Canada is proposing cancellation of the registration of (S)-kinoprene and all associated end-use products for sale and use in Canada.

International context

(S)-kinoprene is currently acceptable for use in other Organisation for Economic Co-operation and Development (OECD) member countries including the United States. No decision by an OECD member country to prohibit all uses of (S)-kinoprene for health or environmental reasons has been identified.

Next steps

The public, including the registrants and stakeholders, are encouraged to submit comments and information on this proposed decision during the 90-day public consultation period[1] upon publication of this proposed re-evaluation decision.

All comments received during the 90-day public consultation period will be taken into consideration in preparation of the re-evaluation decision document,[2] which could result in revised risk mitigation measures. The re-evaluation decision document will include the final re-evaluation decision, the reasons for it and a summary of comments received on the proposed re-evaluation decision with Health Canada's responses.

Additional scientific information

No additional scientific data are required at this time.

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

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

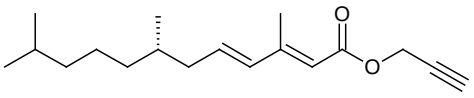
Science evaluation

1.0 Introduction

(S)-kinoprene is an insect juvenile hormone analogue that inhibits insect growth during the moulting process. It is used to control aphids and whiteflies, and suppress mealybugs on greenhouse ornamental plants. (S)-kinoprene is registered for use on greenhouse non-food crops and is applied as a foliar spray. Currently registered products containing (S)-kinoprene can be found in Appendix I.

2.0 Technical grade active ingredient

2.1 Identity

Common name		Kinoprene
Function		Insecticide
Chemical family		Alkenyl carboxylic ester
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	Prop-2-ynyl (*E*,*E*)-(*S*)-3,7,11-trimethyldodeca-2,4-dienoate
2	**Chemical Abstracts Service (CAS)**	2-Propyn-1-yl (2*E*,4*E*,7*S*)-3,7,11-trimethyl-2,4-dodecadienoate
CAS registry number		65733-20-2
Molecular formula		$C_{18}H_{28}O_2$
Structural formula		
Molecular weight		276.4
Purity of the technical grade active ingredient		94.6%
Registration number		25575

2.2 Physical and chemical properties

Properties	Value	Comments
Water solubility	0.211 ppm at 25 °C	Insoluble in water
Vapour pressure	7.19×10^{-6} mm Hg at 20 °C	Low volatility under field conditions
Octanol/water partition coefficient (log K_{ow})	log K_{ow} = 5.38	Potential for bioaccumulation
Henry's law constant (H) (calculated) **1/H**	1.254 Pa m^3/mol at 25 °C 1.97×10^3 at 25 °C	Slightly volatile from water or moist surfaces
Dissociation constant	Not applicable	(S)-kinoprene is insoluble in water
UV/visible absorption spectrum	Not available	No data available, but expected to photolyse

2.3 Description of registered (S)-kinoprene uses

Appendix II lists all the uses for which (S)-kinoprene is presently registered.

All uses were supported by the registrant at the time of re-evaluation initiation and were therefore considered in the health and environmental risk assessments of (S)-kinoprene.

3.0 Human health assessment

3.1 Toxicology summary

A detailed review of the toxicological database for (S)-kinoprene was conducted. The database for (S)-kinoprene consists of studies performed both with (S)-kinoprene (acute toxicity and genotoxicity studies) and the racemic (R,S) mixture of kinoprene (repeat-dose toxicity studies). The database is incomplete, consisting of only a subset of the full array of toxicity studies currently required. The database does not include toxicokinetic studies, an in vitro mammalian cell forward gene mutation study, studies investigating effects following longer-term exposure to

(S)-kinoprene, including assessment of carcinogenic potential, or studies assessing the potential for developmental and reproductive toxicity. Of the available studies, some were performed prior to the widespread use of Good Laboratory Practices and/or were considered supplemental due to limitations in study protocol and reporting.

(S)-kinoprene was of low acute toxicity in rats via the oral, dermal, and inhalation routes of exposure. It was minimally irritating to the eye and mildly irritating to the skin of rabbits, and was a dermal sensitizer in guinea pigs based on the results of a Buehler test.

In repeat-dose dietary toxicity studies conducted with (R,S)-kinoprene in rats and dogs, effects consisted of decreased body weight and increased liver weight accompanied by histopathological changes in the liver. In the 90-day dietary study in rats, findings in both sexes included decreased body weight, increased liver weight, liver hypertrophy, and increased serum alkaline phosphatase. In the 90-day dietary study in dogs, both sexes at the highest dose level tested exhibited decreased body weight, increased liver weight, histopathological changes in liver, and increased serum alkaline phosphatase. In male dogs, effects were observed down to the lowest dose level, and included decreased body weight and food consumption and histopathological alterations in the testes and prostate.

A supplemental 90-day oral capsule study in male dogs was conducted with (R,S)-kinoprene for comparative purposes with the dietary study. There were no findings that were considered to be adverse; however, histopathological examination was only conducted on the testes and prostate.

Results of the available genotoxicity studies conducted with (S)-kinoprene, including an in vivo mouse micronucleus assay, did not suggest genotoxic potential.

Prenatal developmental toxicity studies performed with (S)-kinoprene were not available. A waiver rationale was provided to bridge to the database for (S)-methoprene, another insect juvenile growth hormone analogue, for this requirement. However, it was determined that, although the compounds are structurally similar, the toxicological profiles for (S)-kinoprene and (S)-methoprene are not equivalent. Following repeated oral dosing with kinoprene, target organs were liver, testes and prostate, whereas the liver and kidney were affected in similar studies conducted with methoprene. In addition, (S)-kinoprene is a dermal sensitizer, while (S)-methoprene is not. Bridging to hydroprene, another insect juvenile growth hormone analogue, was also considered, but rejected due to dissimilarity in the toxicological profiles including differences in target organs. Therefore, the rationale provided by the registrant did not adequately support the request to waive the requirement for prenatal developmental toxicity studies conducted with (S)-kinoprene and as such, this remains as a deficiency in the toxicology database.

In addition to the lack of studies to assess prenatal toxicity, the database for (S)-kinoprene does not include studies that investigate reproductive toxicity, chronic toxicity, neurotoxicity, or carcinogenicity. As such, the potential for these effects could not be evaluated in this assessment, and the toxicology database is not considered adequate according to current standards to support continued registration.

Notwithstanding these concerns, a point of departure (POD) from the available database was selected in order to assess the human health risks associated with the current registered uses of (S)-kinoprene, with a 10-fold database uncertainty factor applied in view of these significant limitations.

Results of the toxicology studies conducted on laboratory animals in support of (S)-kinoprene are summarized in Appendix III, Table 1. The toxicology reference values for use in the human health risk assessment are summarized in Appendix III, Table 2.

3.1.1 *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.

The toxicology database for (S)-kinoprene is inadequate as it pertains to assessing the toxicity to infants and children, as no studies were conducted to investigate the potential for pre- and postnatal toxicity. As such, uncertainty remains concerning sensitivity of the young following exposure to (S)-kinoprene. Notwithstanding this fact, the 10-fold factor required under the *Pest Control Products Act* was reduced to onefold as the deficiencies in the toxicology database, and subsequent uncertainty with respect to pre- and postnatal toxicity, have been addressed through the application of a database uncertainty factor of 10-fold in the risk assessment.

3.2 Dietary exposure and risk assessment

3.2.1 Determination of acute reference dose

Establishment of an acute reference dose is not required as there are no food or feed uses and contamination of drinking water sources is not expected.

3.2.2 Acute dietary exposure and risk assessment

Acute dietary exposure to (S)-kinoprene through food is not anticipated as there are no registered food or feed uses. Therefore, an acute risk assessment is not required.

3.2.3 Determination of acceptable daily intake

Establishment of an acceptable daily intake is not required as there are no food or feed uses and contamination of drinking water sources is not expected.

3.2.4 Cancer assessment

Due to the absence of oncogenicity studies in rodents, the potential carcinogenicity of (S)-kinoprene cannot be fully assessed.

3.2.5 Chronic dietary exposure and risk assessment

Chronic dietary exposure to (S)-kinoprene through food is not anticipated as there are no registered food or feed uses. Therefore, a chronic risk assessment is not required.

3.3 Exposure from drinking water

Based on the registered uses for (S)-kinoprene, residues in drinking water are not anticipated. As such, a drinking water risk assessment is not required.

3.3.1 Concentrations in drinking water

Modelling of environmental concentrations in drinking water sources was not conducted for (S)-kinoprene. No water monitoring data were available for (S)-kinoprene. The currently registered use pattern (greenhouse use only) is expected to result in limited exposure to the environment. In addition, for greenhouse uses, proposed label statements would prohibit discharge of effluent containing (S)-kinoprene into water bodies.

3.4 Occupational and non-occupational exposure and risk assessment

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

3.4.1 Toxicology reference values

3.4.1.1 Short-, intermediate- and long-term dermal and inhalation

For short-, intermediate- and long-term occupational exposures via the dermal and inhalation routes, the lowest observed adverse effect level (LOAEL) of 12 mg/kg bw/day from the 90-day dietary study in dogs was selected for risk assessment. Toxicity was observed in males at all dose levels in this study in the form of decreased body weight and food consumption, and histopathological alterations in the testes and prostate. Repeat-dose dermal and inhalation toxicity studies were not available and thus, the use of a POD from an oral study was considered appropriate.

The target MOE for these scenarios is 1000, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, as well as an additional uncertainty factor of 10-fold for the overall deficiencies and limitations in the toxicology database including the use of a LOAEL.

3.4.1.2 Cancer assessment

See Section 3.2.4.

3.4.1.3 Aggregate toxicology reference values

Since residential exposure is not expected and there are no uses on food or feed crops, an aggregate risk assessment for (S)-kinoprene is not required.

3.4.1.4 Dermal absorption

The occupational toxicology reference value selected for short-, intermediate- and long-term dermal exposure is based on an oral study. Therefore, a dermal absorption factor is required for occupational risk assessment. Since dermal absorption data were not submitted to the PMRA for (S)-kinoprene, a dermal absorption factor of 100% (default value) was used in the risk assessment for (S)-kinoprene.

3.4.2 Non-occupational exposure and risk assessment

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

A residential assessment is not required since there are no domestic-class end-use products and commercial application to residential areas is not expected. In addition, since it is assumed that a homeowner would have less exposure than workers, the occupational risk assessment (Section 3.4.3) will address homeowner exposure and risk from treated retail plants.

For bystanders, the use of (S)-kinoprene in greenhouses is expected to result in minimal exposure.

3.4.3 Occupational exposure and risk assessment

Workers can be exposed to (S)-kinoprene through mixing, loading, or applying the pesticide, and when entering a treated greenhouse to conduct activities, such as hand harvesting, debudding and pruning.

3.4.3.1 Mixer, loader, and applicator exposure and risk assessment

There are potential exposures to mixers, loaders, and applicators (M/L/A). The following scenarios were assessed:

- Mixing/loading of liquids into stationary airblast/mistblower (AB/MB).
- Mixing/loading and applying to cut and potted flowers in greenhouses with:
    - mechanically pressurized handgun (MPHG);
    - manually pressurized handwand (MPHW);
    - backpack; and
    - handheld airblast/mistblower (HH AB/MB)

Based on the (S)-kinoprene use pattern, farmers and commercial applicators applying (S)-kinoprene may be exposed for a short- to intermediate-term duration.

M/L/A exposures were estimated based on the following personal protective equipment (PPE):

- Baseline PPE: long pants, long-sleeved shirts, chemical-resistant gloves, socks and shoes.
- High-level PPE: chemical-resistant coveralls over long pants, long-sleeved shirts, chemical-resistant gloves, socks and shoes.
- A respirator.

No chemical-specific handler exposure data were available for (S)-kinoprene. Therefore, dermal and inhalation exposures were estimated using data from the Pesticide Handlers Exposure Database (PHED), the Agricultural Handler Exposure Task Force (AHETF), the Non-Dietary Exposure Task Force (NDETF) and Thouvenin (2015).

The PHED, AHETF, NDETF and Thouvenin (2015) are compilations of generic M/L/A passive dosimetry data which are used for scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of PPE.

M/L/A exposure estimates are based on the best available data at this time.

Calculated dermal, inhalation, and/or combined (total exposure from dermal and inhalation routes) MOEs for M/L/A of (S)-kinoprene are less than the target MOE (with the exception of manually pressurized handwand at the low rate, and stationary airblast/mistblower). For most uses, risks are not shown to be acceptable, even with the following mitigation measures:

- Increasing the PPE to the maximum level: chemical-resistant coveralls over long-sleeved shirt, long pants, chemical-resistant gloves, shoes, socks and a respirator.
- Reducing the application rate to only the lowest efficacious rate.

Therefore, as most risks are not shown to be acceptable for M/L/A, and postapplication risks are also identified (see below), all uses of (S)-kinoprene are proposed for cancellation.

The M/L/A assessment is outlined in Appendix IV, Table 1.

3.4.3.2 postapplication worker exposure and risk assessment

The postapplication occupational risk assessment considered exposures to workers who enter treated sites to conduct agronomic activities involving foliar contact, such as hand harvesting, debudding and pruning.

Based on the (S)-kinoprene use pattern, workers may be exposed long-term to (S)-kinoprene residues.

Activity-specific transfer coefficients (TC) from the Agricultural Re-entry Task Force (ARTF) were used to estimate postapplication exposure resulting from contact with treated foliage at various times after application. Dislodgeable foliar residue (DFR) refers to the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant. A TC is a measure of the relationship between exposure and DFRs for individuals engaged in specific activities and is calculated from data generated in field exposure studies.

TCs are specific to a given crop and activity combination (for example, hand harvesting cut flowers) and reflect standard clothing worn by adult workers. Postapplication exposure activities include (but are not limited to): hand harvesting, debudding and pruning.

For more information about estimating worker postapplication exposure, refer to PMRA's Regulatory Proposal PRO2014-02, *Updated Agricultural Transfer Coefficients for Assessing Occupational Postapplication Exposure to Pesticides*.

There were no chemical-specific DFR studies submitted to the PMRA for the re-evaluation of (S)-kinoprene. Therefore the following default values were used:

- A default peak value of 25% of the application rate and a dissipation rate of 2.3% per day were used for cut and potted flowers in greenhouses.

For workers entering a treated greenhouse, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before they can safely enter after application. An REI is the period of time that must elapse before residues decline to a level where performance of a specific activity results in acceptable exposures (greater than the target MOE).

Health Canada is primarily concerned with the potential for dermal exposure for workers performing postapplication activities in crops treated with a foliar spray. Based on the vapour pressure of (S)-kinoprene, inhalation exposure is not likely to be of concern, as the active is not volatile.

Calculated dermal MOEs for workers entering a greenhouse treated with (S)-kinoprene are less than the target MOE and risks are not shown to be acceptable on day zero. For all postapplication activities, the REIs required to reach the target MOE are not agronomically feasible. Therefore, all uses of (S)-kinoprene are proposed for cancellation.

The postapplication exposure assessment is outlined in Appendix IV, Table 2.

3.5 Aggregate exposure and risk assessment

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

Since residential exposure is not expected and there are no uses on food or feed crops, an aggregate risk assessment for (S)-kinoprene is not required.

3.6 Cumulative assessment

The *Pest Control Products Act* requires that Health Canada consider the cumulative exposure to pest control products with a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pest control products was undertaken. (S)-Kinoprene is an insect juvenile growth hormone analogue that inhibits insect growth during the moulting process. At the time of this re-evaluation, two other members of this group had been identified, namely (S)-methoprene and (S)-hydroprene. While these compounds may share some

structural similarities, they are not considered toxicologically equivalent and there is insufficient data to identify a common mechanism of toxicity. Moreover, the exposure assessment has identified health risks of concern from exposure to (S)-kinoprene, thereby requiring the proposed decision to cancel all uses. Therefore, a cumulative assessment for (S)-kinoprene is not required at this time.

3.7 Incident reports

As of 14 February 2020, no human or domestic animal incident reports involving (S)-kinoprene have been reported to the PMRA.

4.0 Environmental assessment

4.1 Fate and behaviour in the environment

Limited data were available to characterise the environmental fate of (S)-kinoprene. (S)-Kinoprene has a chemical structure similar to another juvenile insect hormone analogue, (S)-methoprene. Some fate data were available for both active ingredients and a comparison of these data indicated that the fate profiles of these chemicals are similar. Therefore, data for (S)-methoprene were considered to be relevant for characterising the environmental behaviour of (S)-kinoprene. A summary of the available physical and chemical properties (see Section 2.2) and environmental fate data in soil and water for this assessment can be found in Appendix V, Table 1.

(S)-Kinoprene is not soluble in water and has a low potential to volatilize. Hydrolysis and photolysis are expected to be important routes of transformation in the environment for (S)-kinoprene. A study conducted with fresh leaves demonstrated that when (S)-kinoprene, in liquid droplets, is exposed to sunlight on the surface of plant leaves, most of the chemical breaks down within 6 hours. (S)-Methoprene has been shown to break down rapidly when exposed to light in various media (including in water and on glass surfaces); therefore, (S)-kinoprene is expected to behave in a similar manner.

Studies of biotransformation of (S)-kinoprene in soil and water were not available; however, data for (S)-methoprene indicate it is non-persistent under these conditions (half-lives in soil and water < 14 days). Due to the structural similarities between the two molecules, (S)-kinoprene is also expected to dissipate at a similar rate and is expected to be non-persistent.

A log K_{ow} value of 5.38 is an indicator that (S)-kinoprene may bioaccumulate in organisms. The log K_{ow} for (S)-methoprene was similar, with values reported as 4.6–5.3. However, a bioconcentration study in fish with (S)-methoprene indicated a relatively low potential for bioaccumulation. The bioconcentration factor, BCF, from this study was between 457–950. Therefore, bioaccumulation of (S)-kinoprene is also not expected.

As (S)-kinoprene is only used in greenhouses, exposure to the aquatic environment is expected to be minimal. No water monitoring data were available.

4.2 Environmental risk characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. (S)-Kinoprene is registered for use in greenhouse production of ornamental plants only. Due to the limited potential for environmental exposure from greenhouse uses, the environmental risk assessment was qualitative.

(S)-Kinoprene will not be released directly into the environment when used in closed greenhouses. Exposure to terrestrial organisms in the natural environment is not expected for chemicals used in greenhouse operations. (S)-Methoprene is structurally similar to (S)-kinoprene. Some aquatic toxicity data were available for both active ingredients and a comparison of these data indicated that the aquatic toxicity profile of both chemicals is similar. As (S)-kinoprene is registered for greenhouse use only, environmental exposure is limited and only a qualitative risk assessment is conducted for aquatic organisms. Ecotoxicity data requirements for greenhouses focus on acute toxicity to a few species, and only report gross effects, such as organism mortality. For these reasons, it was determined that (S)-methoprene could be used to support the assessment for (S)-kinoprene for greenhouse use. In the future, if uses of (S)-kinoprene are expanded to outdoor sites, more data for (S)-kinoprene may be required. Available toxicity data for (S)-kinoprene and (S)-methoprene used in this assessment are summarised in Appendix V, Table 2.

4.2.1 Risks to terrestrial organisms

As part of greenhouse production of ornamental plants, arthropod predators and parasitoids, used to control arthropod pests as part of an integrated pest management strategy, may be exposed to (S)-kinoprene. This may occur either directly through contact with spray solution or indirectly through contact with residues on leaf surfaces. No toxicity studies are available regarding the potential effects of (S)-kinoprene to this group of organisms. However, as the potential effects of an insect growth regulator to beneficial arthropods cannot be discounted, precautionary label statements will be required to inform users of the potential toxicity to these organisms.

Based on information provided by the registrant, bees are not used to pollinate ornamentals in greenhouses; therefore, exposure of bees from the use of (S)-kinoprene in the greenhouse is not expected. (S)-Kinoprene is not expected to be systemic in plants (in other words, move to pollen and nectar) and is expected to dissipate quickly under greenhouse conditions. Therefore, risks to bees from the use of (S)-kinoprene in greenhouse ornamentals that are moved into the outdoor environment are also not a concern.

4.2.2 Risks to aquatic organisms

(S)-Kinoprene is highly toxic to aquatic invertebrates. (S)-Methoprene is also toxic to aquatic organisms, including invertebrates and fish. The toxicity of (S)-kinoprene to fish is expected to be similar. Based on the hazard identified for aquatic invertebrates and fish, the current mitigation measures appearing on labels, to minimize effluent discharge of (S)-kinoprene from greenhouses into aquatic systems, must be maintained.

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 (United States Environmental Protection Agency) 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 at the Report a Pesticide Incident page

As of October 2019, no environmental incidents for (S)-kinoprene have been reported.

4.3 Toxic substances management policy considerations

In accordance with the PMRA Regulatory Directive DIR99-03,[3] the assessment of (S)-kinoprene against Track 1 criteria of Toxic Substances Management Policy (TSMP) under *Canadian Environmental Protection Act* was conducted. Health Canada has reached the conclusions that:

- (S)-kinoprene does not meet all Track 1 criteria, and is not considered a Track 1 substance (see Appendix V, Table 3)

4.3.1 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the technical grade active ingredient and formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette.*[4] The list is used as described in the Health Canada Notice of Intent NOI2005-01[5] and is based on existing policies and regulations including DIR99-03 and DIR2006-02,[6] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). Health Canada has reached the conclusion that (S)-kinoprene and its end-use product, Enstar EW, do not contain any formulants or contaminants identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

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

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

4 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

5 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*.

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

5.0 Value assessment

(S)-Kinoprene is an insect growth regulator used by growers to control aphids and whiteflies, and suppress mealybugs on greenhouses ornamental plants. It is typically applied using low volume misters or hydraulic sprayers. All uses are proposed for cancellation based on unacceptable risks to human health. The cancellation of (S)-kinoprene should have minimal impact on greenhouse ornamental growers as it is one of many insecticides registered to control aphids and whiteflies, or to suppress mealybugs on greenhouse ornamentals. Since the other registered insecticides represent many different modes of action, sufficient alternative active ingredients to (S)-kinoprene are available for resistance management purposes.

6.0 Conclusion of science evaluation

6.1 Human health

Based on the current use pattern of (S)-kinoprene, occupational risks were not shown to be acceptable when used according to current label directions, or when additional mitigation measures were considered. Therefore, all uses of (S)-kinoprene are proposed for cancellation.

6.2 Environment

When used according to the revised label directions (such as updated use directions and precautionary statements), the environmental risks associated with the use of (S)-kinoprene Technical and its associated end-use product, Enstar EW, are acceptable.

6.3 Value

(S)-Kinoprene is an insect growth regulator and the only Insecticide Resistance Action Committee MoA group 7A insecticide registered in Canada. It works by contact action or ingestion, interfering with pupation, and causing sterile adults and eggs. Alternative active ingredients to (S)-kinoprene are sufficient for resistance management purposes and it is unlikely that the discontinuation of this active would lead to loss of effective pest control for growers.

List of abbreviations

↑	increased
↓	decreased
♂	male
♀	female
µg	micrograms(s)
A	applicator
AB/MB	airblast/mistblower
a.i.	active ingredient
AHETF	Agricultural Handlers Exposure Task Force
ALP	alkaline phosphatase
ANSES	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail
ARTF	Agricultural Re-entry Task Force
ATPD	area treated per day
BAF	bioaccumulation factor
BCF	biconcentration factor
bw	body weight
ºC	degrees in Celcius
CEPA	Canadian Environmental Protection Act
cm^2	square centimeter
CR	chemical-resistant
Crl:CD	Charles River Laboratories:Caesarean-Derived
d	day(s)
DACO	Data Code
DFR	dislodgeable foliar residue
DIR	Directive
EIIS	Ecological Incident Information System
fc	food consumption
h or hr	hour
H	Henry's law constant
ha	hectare
HDT	highest dose tested
HH	handheld
HPCP	Heavy Population Control Program
ICR	Institute of Cancer Research
K_{ow}	octanol water partition coefficient
kg	kilogram(s)
L	litre(s)
Log	logarithm
LC_{50}	concentration estimated to be lethal to 50% of the test population
LD_{50}	dose estimated to be lethal to 50% of the test population
LOAEL	lowest observed adverse effect level
M/L	mixer and loader
M/L/A	mixer, loader and applicator
mg	milligram(s)
MAS	maximum average score for 24, 48 and 72 hours

MIS	maximum irritation score
mm	milimeter
MOE	Margin of Exposure
MPHG	mechanically pressurized handgun
MPHW	manually pressurized handwand
NA	not available
NDETF	Non-Dietary Exposure Task Force
NOAEL	no observed adverse effect level
Pa	pascal
PACR	Proposed Acceptability for Continued Registration
PHED	Pesticides Handlers Exposure Database
PMP	Preventative Maintenance Program
PMRA	Pest Management Regulatory Agency
POD	point of departure
PPE	personal protective equipment
Reg. No.	registration number
REI	restricted entry interval
RTI	retreatment Interval
$t_{½}$	half-life
TC	transfer coefficient
TSMP	Toxic Substances Management Policy
ULV	ultra-low volume
USEPA	United States Environmental Protection Agency
wks	weeks
wt	weight
µg	microgram

Appendix I Registered (S)-kinoprene products in Canada

Table 1 Registered (S)-kinoprene products in Canada[1]

Registration number	Marketing class	Registrant	Product name	Formulation type	Active ingredient *(%, g/L)*
25575	Technical Grade Active Ingredient	Wellmark International	(S)-Kinoprene Technical	Solution	(S)-Kinoprene 95.8%
29661	Commercial		Enstar® EW Insect Growth Regulator	Emulsifiable Concentrate	(S)-Kinoprene 18.42%

[1] as of 20 February 2020, excluding discontinued products or products with a submission for discontinuation

Appendix II Registered uses of (S)-kinoprene as of 20 February2020 excluding discontinued products or products with a submission for discontinuation

Table 1 Registered uses of (S)-kinoprene as of 20 February2020 excluding discontinued products or products with a submission for discontinuation

Site	Pest(s)	Formulations	Application method and equipment	Maximum single application rate (g a.i./100 M^2)	Maximum cumulative application rate per year	Maximum number of applications per year	Minimum interval between applications (days)
USC 6 – Greenhouse Non-Food Crops							
Greenhouse ornamentals	Control of whiteflies and aphids, and suppression of mealybugs (Preventative maintenance program)	Emulsifiable concentrate or emulsion	Low volume mister or hydraulic sprayer.	5.99	34.18 g a.i./100 m^2 per year	4 at the preventative rate or up to 2 preventative applications and 2 applications at the heavy population control rate	14
	Control of whiteflies and aphids, and suppression of mealybugs (Heavy population control program)	Emulsifiable concentrate or emulsion	Low volume mister or hydraulic sprayer.	11.1		2 applications at the heavy population control rate and up to 2 preventative applications.	7

Appendix III

Table 1 Toxicity profile of (S)-kinoprene technical

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. Unless otherwise noted, studies were conducted with (S)-kinoprene.

Study type/animal/PMRA #	Study results
Acute toxicity studies	
Acute oral toxicity Crl:CD(SD) rats PMRA# 1132384	LD_{50} = 6800 mg/kg bw (♂/♀) Clinical signs of toxicity included abnormal body carriage, abnormal gait, lethargy, decreased respiratory rate, pallor of extremities and diuresis. **Low acute toxicity**
Acute dermal toxicity Crl:CD(SD) rats PMRA# 1132385	LD_{50} > 2000 mg/kg bw (♂/♀) **Low acute toxicity**
Acute inhalation toxicity (whole body) Sprague Dawley (SD) rats PMRA# 1132386	LC_{50} > 5.36 mg/L (♂/♀) Clinical signs of toxicity during exposure included partial closing of eyes, wet snout, exaggerated respiratory movements. Following exposure, animals had matted fur, exaggerated respiratory movements, and brown staining. **Low acute toxicity**
Eye irritation New Zealand White rabbits PMRA# 1132387	MAS = 0.089, MIS = 8.67 (at 1 h) **Minimally irritating**
Skin irritation New Zealand White rabbits PMRA# 1132388	MAS = 2.53, MIS = 2.8 (at 48 h) **Mildly irritating**
Dermal sensitization (Buehler) Dunkin/Hartley Albino guinea pigs PMRA# 2720616	Positive **Potential dermal sensitizer**

Study type/animal/PMRA #	Study results
Short-term toxicity studies	
90-day oral toxicity (dietary) (R,S)-kinoprene Sprague Dawley rats PMRA# 2720619	NOAEL = 68/75 mg/kg bw/day (♂/♀) **374/390 mg/kg bw/day:** ↓ bw, ↓ fc, ↑ liver wt, liver histopathology (hypertrophy), ↑ serum ALP (♂/♀)
90-day oral toxicity (dietary) (R,S)-kinoprene Beagle dogs PMRA# 2720618	NOAEL = Not established ♂/38.5 mg/kg bw/day ♀ **≥ 12 mg/kg bw/day:** ↓ bw, ↓ fc, testes (spermatozoa and spermatids scant or absent) and prostate (cystic dilation) histopathology (♂) **75.7/80.5 mg/kg bw/day:** ↑ liver wt, liver histopathology (foci of lymphocytes, fibrosis, cirrhosis), ↑ serum ALP (♂/♀), mortality (♀), ↓ bw (♀)
90-day oral toxicity (capsule) (R,S)-kinoprene Beagle dogs (male) PMRA# 2720620	Supplemental No effects observed up to 40 mg/kg bw/day (♂) (HDT). This study was considered supplemental due to limitations in study protocol and reporting. Only males were included in the study, and histopathological examination was only conducted on testes and prostate.
Genotoxicity studies	
Bacterial reverse mutation assay S. typhimurium TA98, TA100, TA1535, TA1537, TA1538 PMRA# 1132391	**Negative ± metabolic activation** Tested up to a cytotoxic concentration.
In vitro unscheduled DNA synthesis assay Hepatocytes from adult male Fischer 344 rat PMRA# 1132393	**Negative** Tested up to a cytotoxic concentration.
In vivo micronucleus assay (gavage) ICR mice PMRA# 1132392	**Negative** **1200 mg/kg bw/day:** Two ♂ died 48 h after dosing. One ♀ died 71 h after dosing.

Table 2 Toxicology reference values for use in health risk assessment for (S)-kinoprene

Exposure scenario	Study	Point of departure and endpoint	Target MOE[3]
Short-, intermediate-, and long-term dermal[1]	90-day dietary in dogs	LOAEL = 12 mg/kg bw/day Based on body weight loss and histopathological changes in testes and prostate	1000
Short-, intermediate-, and long-term inhalation[2]	90-day dietary in dogs	LOAEL = 12 mg/kg bw/day Based on body weight loss and histopathological changes in testes and prostate	1000

[1] Since an oral LOAEL was selected, a dermal absorption factor of 100% (default value) was used in a route-to-route extrapolation.
[2] Since an oral LOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.
[3] Margin of Exposure (MOE) refers to a target MOE for occupational assessments.

Appendix IV

Table 1 Occupational dermal and inhalation exposure risk assessment

Application method	Greenhouse ornamentals	Rate[a] (kg a.i./ha)	ATPD[b]	Exposure (µg/kg bw/day)[c]		MOE (target = 1000)		Combined MOE[e] (target = 1000)
				Dermal	Inhalation	Dermal[d]	Inhalation[d]	
CR coveralls over single layer (M/L); CR coveralls with hood over single layer, CR gloves and respirator (A)								
HH AB/MB	Cut and potted flowers	1.11	2 ha	904.3	109.4	13	110	12
		0.599		488.8	59.01	25	203	22
Single layer and CR gloves (M/L)								
Stationary AB/MB	Cut and potted flowers	1.11	2 ha	1.62	0.017	7390	686 000	7310
		0.599		0.88	0.009	13700	1 270 000	13 600
CR coveralls over single layer, and CR gloves (M/L/A)								
MPHG	Cut and potted flowers	1.11	2 ha	50.70	4.19	237	2864	219
		0.599		27.36	2.26	439	5307	405
Backpack	Cut and potted flowers	1.11	2 ha	56.26	1.72	213	6960	207
		0.599		30.36	0.93	395	12 900	384
MPHW	Cut and potted flowers	1.11	2 ha	19.25	1.25	623	9570	585
		0.599		10.39	0.68	1160	17 700	1090

ATPD = Area Treated Per Day, MOE = Margin of Exposure, M/L = Mixer/Loader, A = Applicator, CR = Chemical-Resistant; Single layer = long-sleeved shirt, long pants; MPHW = manually pressurized handwand; MPHG = mechanically pressurized handgun; AB/MB = airblast/mistblower; HH AB/MB = handheld airblast/mistblower.
[a] Based on additional information received from the registrant clarifying application rates, frequency and method.
[b] Based on the 95th percentile of total area of 2.2 ha for greenhouses across Canada (Statistics Canada, 2016).
[c] Exposure (µg/kg bw/day) = unit exposure (µg/kg bw/day) × application rate (kg a.i./ha) × ATPD (2 ha/day) × dermal absorption (100%)/body weight (80 kg).
[d] Based on short-, intermediate- and long-term oral LOAEL of 12 mg/kg bw/day from a 90-day dietary toxicity study in dogs and a target MOE of 1000. Shaded cells (in grey) indicate MOEs that are less than the target MOE.
[e] Combined MOE = 1 / ((1/MOE_{Dermal}) + (1/$MOE_{Inhalation}$)). Shaded cells (in grey) indicate MOEs that are less than the target MOE.

Table 2 Postapplication exposure and risk assessment for (S)-kinoprene

Activity	TC[a] (cm^2/hr)	Rate (kg a.i./ha)	No. of appl	DFR – day 0[c] (µg/cm^2)	Dermal exposure[d] (µg/kg bw/day)	MOE[e] (target = 1000)
• Cut Flowers: Hand harvesting, debudding and pruning	4000	HPCP–1.11	2	5.13	2.05	6
		PMP–0.599	4	3.92	1.57	8
			2	2.58	1.03	12
		Combined Program[b]	4	6.98	2.79	4
• Cut Flowers: All other activities	230	HPCP–1.11	2	5.13	0.118	102
		PMP–0.599	4	3.92	0.0902	133
			2	2.58	0.0593	202

Activity	TC[a] (cm^2/hr)	Rate (kg a.i./ha)	No. of appl	DFR – day 0[c] (µg/cm^2)	Dermal exposure[d] (µg/kg bw/day)	MOE[e] (target = 1000)
• Greenhouse Potted flowers: All activities		Combined Program [b]	4	6.98	0.160	75

HPCP = Heavy Population Control Program; PMP = Preventative Maintenance Program; No. of Apps = Number of Applications

Day zero = day of application, after sprays have dried.

[a] TC = transfer coefficient.

[b] Combine Program of two PMP applications at a 14 day retreatment interval (RTI) followed by 2 HPCP applications at a 7 day RTI as per the registrant. This combination of applications rates generates the highest DFR value.

[c] DFR= dislodgeable foliar residues determined using the default peak DFR of 25% of the application rate and a daily dissipation rate of 2.3%.

[d] Dermal exposure (µg/kg bw/day) = DFR (µg/cm^2) × TC (cm^2/hr) × Duration (8 hrs/day) × dermal absorption (100%)/body weight (80 kg).

[e] Based on short-, intermediate- and long-term oral LOAEL of 12 mg/kg bw/day from a 90-day dietary toxicity study in dogs and a target MOE of 1000. Shaded cells (in grey) indicate MOEs that are less than the target MOE on day zero.

Appendix V

Table 1 Environmental fate data for analogues (S)-kinoprene and (S)-methoprene

Parameter	(S)-kinoprene	(S)-methoprene	Reference
Hydrolysis	Half-life ($t_{1/2}$) 20 °C: 161 h at pH 4, 249 h at pH 7, 271 h at pH 9 in buffered solutions Half-life ($t_{1/2}$) 40 °C: 19 h at pH 4 and 7, 12 h at pH 9 in buffered solutions. Half-life ($t_{1/2}$) 50 °C: Approximately 9 h at pH 4, 7, and 9 in buffered solutions. No major transformation products were detected; trace amounts of (S)-kinoprene acid were detected in buffer at pH 9.	Half-life ($t^{1}/_{2}$) > 4 wks at pH 5, 7 or 9 Not susceptible to hydrolysis.	PMRA# 2824058 ((S)-kinoprene) PMRA# 1384851 ((S)-methoprene)
Photolysis in water	Not available	4-5 d (sterile water at 20 °C)	PMRA# 2720626
Photolysis on leaf surfaces (applied in water droplets)	Enstar II[1] (65.1% (S)-kinoprene); holly leaves Half-life ($t_{1/2}$) estimated at 2 h in semi-qualitative study; most (S)-kinoprene gone (3.2% remaining) on leaf surfaces after 6 h.	Diacon II (33.6% (S)-methoprene); shumard oak leaves, *Quercus shumardi* and holly Half-life ($t_{1/2}$) estimated at 2 h in semi-qualitative study.	PMRA# 2720625 ((S)-kinoprene and (S)-methoprene)

Parameter	(S)-kinoprene	(S)-methoprene	Reference
Photolysis on soil	Not available	Not available	Not available
Photolysis on inert surfaces	Not available	Half-life ($t_{1/2}$) of 6 h on inert (glass) surfaces (3% remaining after 27-h exposure to sunlight)	PMRA# 1384851 PMRA# 2720626
Aerobic soil	Not available	Half-life ($t_{1/2}$) approximately 10 d (sandy loam)	PMRA# 1384851
Anaerobic soil	Not available	Half-life ($t_{1/2}$) 10-14 d	PMRA# 1384851
Aerobic water sediment	Not available	Half-life ($t_{1/2}$) 30-40 h (pond water, not corrected for abiotic degradation)	PMRA# 1384851
Bioaccumulation	Not available	BCF[2] (fish) 457–950	PMRA# 1384851

1 Enstar II is the product name that preceded Enstar EW.
2 Bioconcentration factor.

Table 2 Toxicity of (S)-kinoprene and (S)-methoprene to non-target organisms

Organism	Study	Toxicity value	Reference
Daphnia magna	Acute, flow-through ((S)-kinoprene; SAN 847, 89.61% purity)	48-h LC_{50}, 113 µg a.i./L	PMRA# 2720628
Rainbow trout	Acute ((S)-methoprene)	96-h LC_{50}, 760 µg a.i./L	PMRA# 1384851
Honey bee	Acute contact ((S)-kinoprene)	48-h LD_{50}, 35 µg a.i./bee; NOEL, < 13 µg a.i./bee (lowest does tested)	PMRA# 2720627

Table 3 Toxic substances management policy considerations-comparison to TSMP track 1 criteria

TSMP track 1 criteria	TSMP track 1 criterion value	(S)-kinoprene are criteria met?
CEPA-toxic or CEPA-toxic equivalent[1]	Yes	Yes
Predominantly anthropogenic[2]	Yes	Yes

TSMP track 1 criteria	TSMP track 1 criterion value		(S)-kinoprene are criteria met?
Persistence[3]:	Soil	Half-life ≥ 182 days	No (aerobic soil, 10 d; anaerobic soil, 10–14 d)[5]
	Water	Half-life ≥ 182 days	No (aerobic water, 30–40 h)[5]
	Whole system (Water + Sediment)	Half-life ≥ 365 days	No[5]
	Air	Half-life ≥ 2 days or evidence of long range transport	Not available
Bioaccumulation[4]	Log K_{ow} ≥ 5		Yes = 5.38
	BCF ≥ 5000		No (BCF, 457–950)[5]
	BAF ≥ 5000		Not available
Is the chemical a TSMP track 1 substance (all four criteria must be met)?			**No, does not meet all TSMP track 1 criteria.**

[1]All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (in other words, all other TSMP criteria are met).

[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgment, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) then the criterion for persistence is considered to be met.

[4]Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, log K_{ow}).

[5]Based on available data for (S)-methoprene.

References

Information considered in the chemistry assessment

A. List of studies/information submitted by registrant

PMRA document number	Reference
1667378	1996, Analysis of (S)-Kinoprene Samples, DACO: 2.13.1,2.13.2
1667380	1997, (S)-Kinoprene Technical Active Ingredient Part 2.14: Chemical and Physical Properties (summary), DACO: 2.14.1,2.14.10,2.14.11,2.14.13,2.14.2,2.14.3,2.14.5,2.14.6,2.14.7,2.14.8, 2.14.9,2.16
1667381	1989, Color of Technical s-Kinoprene, DACO: 2.14.1
1667382	1989, Physical State (Appearance) of Technical s-Kinoprene, DACO: 2.14.2
1667383	1989, Odor of Technical s-Kinoprene, DACO: 2.14.3
1667384	1990, Boiling Point of Technical s-Kinoprene, DACO: 2.14.5
1667386	1989, Density of Technical s-Kinoprene, DACO: 2.14.6
1667388	1991, S-Kinoprene - Determination of n-Octanol/Water Partition Coefficient, DACO: 2.14.11
1667389	1989, pH of Technical s-Kinoprene in Aqueous Dispersion, DACO: 2.16
1667392	1991, Manufacturing Process Description and Discussion of the Formation of Unintentional Ingredients for s-Kinoprene/ENSTAR II, DACO: 2.11.1,2.11.2,2.11.3,2.11.4
1667397	1989, Odor of Technical s-Kinoprene, DACO: 2.14.3
1667401	1993, Vapour Pressure of s-Kinoprene, DACO: 2.14.9
1667402	1991, s-Kinoprene: Solubility in Well Water in the Presence of Cosolvents, DACO: 2.14.7,2.14.8
1667403	1991, s-Kinoprene: Determination of Water Solubility, DACO: 2.14.7
3029065	2019, Preliminary Analysis of Technical (S)-Kinoprene, DACO: 2.13.3 CBI
3043456	2019, Description of Materials and Manufacturing Process for Technical (S)-Kinoprene, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,2.12.1 CBI

3043457	2019, Description of Materials For Manufacturing Technical (S)-Kinoprene, DACO: 2.11.2 CBI
3050875	2019, Response to the deficiencies in the 5-batch analysis of technical S-kinoprene., DACO: 2.13.1,2.13.3 CBI
3029062	2019, Re-evaluation of S-Kinoprene Reference Number 2015-3161 - Product Chemistry, DACO: 0.8

Information considered in the toxicological assessment

A. List of studies/information submitted by registrant

PMRA document number	Reference
1660862	2008, Acute Oral Toxicity Up and Down Procedure in Rats, DACO: 4.6.1
1660863	2008, Acute Dermal Toxicity in Rats - Limit Test, DACO: 4.6.2
1660864	2008, Acute Inhalation Toxicity in Rats - Limit Test, DACO: 4.6.3
1660865	2008, Primary Eye Irritation Study in Rabbits, DACO: 4.6.4
1660866	2008, Primary Skin Irritation Study in Rabbits, DACO: 4.6.5
1660868	2008, Dermal Sensitization Study in Guinea Pigs - (Buehler Method), DACO: 4.6.6
1132384	Acute Oral Toxicity To Rats Of S-Kinoprene Technical (SAN 847) (90129D/SNC 78/AC)(ENSTAR II). Authors: Sheena R.Kynoch; Stuart M. Denton; Guy Healing Of Huntingdon Research Centre Ltd. Addressee: M.S. Root, Sandoz Crop Protection Corporation, Des Plaines, Illinois. Study Finalized: January 30, 1990, DACO: 4.2.1
1132385	Acute Dermal Toxicity To Rats Of S-Kinoprene Technical (SAN 847) (891497D/SNC 79/AC)(ENSTAR II). Authors: Sheena R. Kynoch; Stuart M. Denton; Guy Healing Of Huntingdon Research Centre Ltd. Addressee: Ms. M. Root. Study Finalized: November 20, 1989, DACO: 4.2.2
1132386	S-Kinoprene Technical (SAN 847) Acute Inhalation Toxicity Study In Rats 4-Hour Exposure (SNC 83/90438)(ENSTAR II). Authors: Paul A. Smith; Graham C. Jackson; Colin J. Hardy; Fiona Sims; Pamela A.Mullins; Chirukandath Gopinath Of Huntingdon Research Centre Ltd. Addressee: Mildred S. Root, Sandoz Crop Protection Corp. Study Finalized: June 18, 1990, DACO: 4.2.3

PMRA document number	Reference
1132387	Irritant Effect On Rabbit Skin Of S-Kinoprene Technical (SAN 847)(9050D/SNC81/SE)(ENSTAR II). Author: Michael P. Liggett Of Huntingdon Research Centre Ltd. Addressee: M.S. Root Of Sandoz Crop Protection Corporation. Report Finalized: March 9, 1990. Report Finalized: March 9, 1990, DACO: 4.2.4
1132388	Irritant Effect On Rabbit Skin Of S-Kinoprene Technical (SAN 847)(9048D/SNC80/SE)(ENSTAR II). Author: Michael P. Liggett Of Huntingdon Research Centre Ltd. Addressee: M.S. Root Of Sandoz Crop Protection Corporation. Study Finalized: March 9, 1990, DACO: 4.2.5
1132391	Mutagenicity Test On S-Kinoprene In The Salmonella/Mammalian Microsome Reverse Mutation Assay (Ames Test) With Confirmatory Assay Revised Final Report (11022-0-401R)(ENSTAR II). Authors: Timothy E. Lawlor; Daren C. Valentine. Study Finalized: December 18, 1989. Published By: Hazleton Laboratories America Inc., DACO: 4.5.4
1132392	Mutagenicity Test On S-Kinoprene Technical In Vivo Mouse Micronucleus Assay Final Report (12227-0-455)(ENSTAR II). Author: James L. Ivett. Study Finalized: August 27, 1990. Published By: Hazleton Laboratories America Inc., DACO: 4.5.4
1132393	Mutagenicity Test On S-Kinoprene Technical In The Vitro Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay Final Report (12227-0-447)(ENSTAR II). Authors: Marie E.Mckeon; M. Phil. Study Finalized: August 24, 1990. Published By: Hazleton Laboratories America Inc., DACO: 4.5.4
2720616	1991, Skin Sensitisation In The Guinea-Pig Of S-Kinoprene Technical, DACO: 4.2.6
2720618	1974, Toxicity Studies of ZR-777 Technical: Ninety-day Subacute in Dogs, DACO: 4.3.1
2720619	1973, Subacute (90 Day) Oral Toxicity of ZR 777 for Rats, DACO: 4.3.1
2720620	1980, Three Month Oral Toxicity Study of Kinoprene Technical (ZR-777) In Dogs, DACO: 4.3.2

Information considered in the occupational and non-occupational assessment

A. List of studies/information submitted by registrant

PMRA document number	Reference
2720614	2017. Attachment 4. Use Description Scenario of Enstar EW (Reg. No. 29661) containing S-Kinoprene. Reference 2015-3161. January 23, 2017. DACO 5.2

B. Studies/information provided by rask forces

PMRA document number	Reference
2115788	Agricultural Re-entry Task Force (ARTF). 2008. Data Submitted by the ARTF to Support Revision of Agricultural Transfer Coefficients.
2572745	AHETF 2015. Agricultural Handler Exposure Scenario Monograph: Open Pour Mixing and Loading of Liquid Formulations. Report Number AGE1003-1. March 31, 2015.
2905452	Testman, R.J. 2015. An Observational Study for the Determination of Air Concentration in the Applicator's Breathing Zone and Deposition of Pyrethrins, Piperonyl Butoxide and MGK 264 from the Use of a ULV Fogger in Various Commercial Applications. Golden Pacific Laboratories. GPL Report No. 110392. Non-Dietary Exposure Task Force (NDETF). Mar.30, 2015. DACO 5.4

C. Additional information considered

i) Unpublished information

PMRA document number	Reference
2873196	Thouvenin, I. 2015. Determination of operator dermal exposure and protective factors provided by personal protective equipment during foliar application using backpack sprayer in vineyards. ANSES. STAPHYT study No. ChR-15-19603, 10 July 2015. Unpublished. DACO 5.6

Information considered in the environmental assessment

PMRA document number	Reference
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1384851	2007, Proposed Acceptability for Continuing Registration: Re-evaluation of S-methoprene, PACR2007-01
2720625	2006, Stability of (S)-Kinoprene (Enstar II) and (S)-Methoprene (Diacon II) When Sprayed on Leaves and Exposed To Sunlight, DACO: 8.2.3.3
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2720627	1990, (S)-Kinoprene Technical (SAN 847): an acute contact toxicity study with the honey bee, DACO: 9.2.4.1
2720628	1993, (S)-Kinoprene: a 48-hour flow-through acute toxicity test with the cladoceran (*Daphnia magna*), DACO: 9.3.2
2824058	2017, Hydrolysis of Technical (S)-Kinoprene, DACO: 8.2.3.2
2824062	2017, Beneficial Insect Toxicity from Use of (S)-Kinoprene on Indoor Ornamentals, DACO: 9.2.5,9.2.6
1255088	1996, U.S. EPA, Science Review: Foreign Review: Date of Document 96.11.00: (S)-Kinoprene: United States EPA Reregistration Eligibility Decision (RED) (S)-Kinoprene:(EPA738-R-96-030;7508W): Subn #95-1186, DACO: 12.5.2