Re-evaluation Decision RVD2021-06

(S)-kinoprene and Its Associated End-use Products

Final Decision

(publié aussi en français)

16 June 2021

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6607 D
Ottawa, Ontario K1A 0K9

Internet: canada.ca/pesticides
hc.pmra.publications-arla.sc@canada.ca
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
hc.pmra.info-arla.sc@canada.ca

Canada

ISSN: 1925-1017 (print)
1925-1025 (online)

Catalogue number: H113-28/2021-6E (print version)
H113-28/2021-6E-PDF (PDF version)

Re-evaluation decision for (S)-kinoprene and its associated end-use products

Under the authority of the *Pest Control Products Act*, all registered pesticides must be re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they continue to meet current health and environmental standards and continue to have value. The re-evaluation considers data and information from pesticide manufacturers, published scientific reports and other regulatory agencies, as well as comments received during public consultations. 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 the Pesticide Label Search and in Appendix I.

The Proposed Re-evaluation Decision PRVD2020-11, (S)-kinoprene and its Associated End-use Products[1] containing the evaluation of (S)-kinoprene and proposed decision, underwent a 90 day consultation period ending on 4 November 2020. In PRVD2020-11, (S)-kinoprene was found to present potential risks to certain terrestrial and aquatic organisms, however risks were shown to be acceptable with additional standard precautionary label statements to protect aquatic organisms and beneficial arthropods and with updated use directions. 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 measure were considered. Therefore, cancellation of the registration of (S)-kinoprene and all associated end-use products for sale and use in Canada was proposed.

Health Canada received comments relating to the health and value assessments. Commenters are listed in Appendix II. These comments are summarized in Appendix III along with the responses by Health Canada. These comments did not result in revisions to the toxicology/occupational/ or value assessments (see Science evaluation update), and did not result in changes to the proposed re-evaluation decision as described in PRVD2020-11.

A reference list of information used as the basis for the proposed re-evaluation decision is included in PRVD2020-11, and no further information was used in the final re-evaluation decision. Therefore, the complete reference list of all information used is set out in PRVD2020-11.

This document presents the final re-evaluation decision[2] for the re-evaluation of (S)-kinoprene. All products containing (S)-kinoprene that are registered in Canada are subject to this re-evaluation decision.

[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*.

Re-evaluation decision for (S)-kinoprene

Health Canada has completed the re-evaluation of (S)-kinoprene. Under the authority of the *Pest Control Products Act*, Health Canada is cancelling the registration of (S)-kinoprene and all associated end-use products. An evaluation of available scientific information found that risks to human health were not shown to be acceptable when (S)-kinoprene is used according to the current conditions of registration, or when additional mitigation is considered.

Next steps

To comply with this decision, all (S)-kinoprene products are to be phased-out following the implementation timeline outlined below. Appendix I lists the products containing (S)-kinoprene that are registered under the authority of the *Pest Control Products Act*.

- One (1) year of sale by registrant from the publication date of this decision document, followed by;
- One (1) year of sale by retailer from the last date of sale by registrant, followed by;
- One (1) year of permitted use from the last date of sale by retailer.

Other information

Any person may file a notice of objection[3] regarding this decision on (S)-kinoprene and its associated end-use products within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides section of the Canada.ca website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service.

The relevant confidential test data on which the decision is based on, is referenced in PRVD2020-11 and are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (hc.pmra-info-arla.sc@canada.ca).

[3] As per subsection 35(1) of the *Pest Control Products Act*

Science evaluation update

1.0 Revised health risk assessment

Comments relating to the toxicology and occupational risk assessments were received during the public consultation period for PRVD2020-11 (refer to Appendix III). The review of these comments did not result in any change in the toxicology reference values as presented in PRVD2020-11. In addition, the occupational assessment for (S)-kinoprene was not updated as neither the registrant nor industry stakeholder provided sufficient supporting information to support changes to this assessment. Therefore, occupational risks were not shown to be acceptable for (S)-kinoprene and all uses are to be cancelled.

2.0 Environmental risk assessment

No comments relating to the environment risk assessment were received during the public consultation period for PRVD2020-11.

3.0 Value assessment

(S)-Kinoprene is an insect growth regulator and the only Insecticide Resistance Action Committee Mode of Action group 7A insecticide registered in Canada. (S)-Kinoprene works by contact action or ingestion, interfering with pupation, and causing sterile adults and eggs. The (S)-kinoprene product is of value since its unique mode of action lends itself to rotation with other insecticides to delay the development of resistance in susceptible pests.

Currently, there are alternatives registered for all site and pest combinations.

4.0 Conclusion of science evaluation

Environmental risks would be acceptable when used according to revised label directions, however, occupational health risks were not shown to be acceptable when current label directions, or additional mitigation measures were considered, therefore all uses of (S)-kinoprene and associated end-use products will be cancelled. There are several registered alternatives available representing different modes of action groups that may help to delay the development of resistance.

Appendix I Registered products containing (S)-kinoprene in Canada[1]

Table 1 Products Containing (S)-kinoprene Cancelled as a Result of Re-evaluation

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Active ingredient (%, g/L)
25575	Technical	Wellmark International	(S)-kinoprene Technical	Solution	95.8%
29661	Commercial		Enstar® EW	Emulsifiable Concentrate	18.42%

[1]as of 10 February 2021, excluding discontinued products or products with a submission for discontinuation

Appendix II List of commenters to PRVD2020-11

List of commenters' affiliations for comments submitted in response to PRVD2020-11

Category	Commenter
Registrant	Wellmark International
Agriculture association	Flowers Canada Growers Inc.

Appendix III Comments and responses

Health Canada received two written comments during the public consultation for the (S)-kinoprene proposed re-evaluation decision. Commenters' affiliations are listed in Appendix II. These comments were considered during the final decision phase of this re-evaluation. Summarized comments and Health Canada's responses to them are provided below.

1.0 Comments related to the health risk assessment

1.1 Comments related to the toxicological assessment

1.1.1 Point of departure

The registrant requested that the point of departure (POD) selected for the dermal and inhalation risk assessment, the LOAEL from the 1974 90-day dietary study in dogs, be reconsidered in favour of the NOAEL determined from the 90-day dietary study in rats. The registrant noted that the effects on testes and prostate in the dietary dog study were not replicated in the subsequent oral capsule dog study, and suggested that these effects were related to the general health status of the dogs in the dietary study.

Health Canada response

The 1974 dog study was conducted prior to the establishment of Good Laboratory Practice (GLP) standards as well as the OECD Test Guidelines for 90-day repeat-dose toxicity studies, and therefore contained deficiencies when measuring to current standards. However, there was sufficient information to characterize the effects of dietary kinoprene administration to dogs for 90 days and thus, Health Canada continues to consider this study to be acceptable for risk assessment purposes. Effects on the male reproductive system were observed down to the lowest dose tested, where there was no mortality or clinical signs of toxicity, and where body weight and food consumption were not greatly impacted. The original study authors also concluded that the findings in testes and prostate were related to treatment.

The registrant claims that palatability of the test substance played a role in these effects; however, the magnitude of reduction in food consumption for males was greatest during weeks 3, 5, and 12, whereas it would be expected to be reduced to the greatest extent at the beginning of the study if palatability was a major factor. In addition, food consumption and palatability were not issues for females in this study. Therefore, the potential role of palatability of test substance for males in this study is not clear.

Health Canada notes that effects on the male reproductive system were not seen in the 1979 90-day oral capsule study in male dogs. Like the dietary dog study, this study also predates the adoption of the OECD TG 409 for a Repeated Dose 90-Day Oral Toxicity Study in Non-Rodents, though it was conducted in compliance with GLP standards. However, this study contained several deficiencies such as including only four animals per dose group, limited methods of analysis of stability of the test compound, issues with semen collection, and not conducting individual clinical observations, gross pathological examination, or histopathological evaluation of any tissues other than testes or prostate. In turn, it is Health Canada's position that this study continues to not adequately serve as a replacement study for the 1974 dog study, nor as definitive invalidation of the effects on the male reproductive system seen in the 1974 dog study.

Furthermore, the scarcity of data in the kinoprene database, particularly the lack of reproductive studies, confounds the interpretation of the findings in the male reproductive system.

Similarly, the 1973 90-day dietary study conducted in rats predates the appropriate OECD TG, and was not conducted in compliance with GLP regulations. Numerous deficiencies were also identified in this study, beginning with lack of information on diet preparation, analysis of stability, and concentration and storage conditions of the test compound in the prepared diet. Significant food waste by the animals was only estimated visually and therefore had an unknown effect on the actual doses received by the animals. A significant issue with this study was that the submitted raw data was hand-written and in many instances was difficult to decipher. Calculation errors were identified by the reviewer, presumably due to study authors calculating values by hand. Given these numerous study deficiencies, and the indication that the dog may be more sensitive to the effects of kinoprene than the rat, Health Canada does not deem it prudent to select the NOAEL from the 90-day rat study for the POD.

Considering that a relationship to treatment with kinoprene could not be ruled out for the male reproductive findings in the 90-day dietary dog study, combined with the limitations in the 90-day rat study, the reference values selected for human health risk assessment outlined in PRVD2020-11 will remain unchanged.

1.2 Comments related to occupational exposure

1.2.1 Area treated per day

The registrant indicated that a hydraulic sprayer is equivalent to the “mechanically pressurized handgun and handheld airblast/mistblower”, for which mixer/loader/applicator risk assessments were completed. The users have confirmed that spraying two hectares with a hydraulic sprayer would be a lot of work for one day and not likely. The larger sprayers hold 900 L of water and the water volume used is 990 to 1480 L of water per hectare. Therefore, the maximum treated area per day would be one hectare. The users of the product will use a backpack sprayer for only spot treatments. The most the tank holds is 20 L, which is 48 mL of product for the high rate, which is equivalent to approximately 8.8 g a.i. handled.

Health Canada response

Based on the available data, up to 3800 L can be applied per day using a mechanically pressurized handgun, which would spray an area much greater than one hectare specified by the applicant. In addition, the use of two hectares per day for handheld airblast/mistblowers is based on Statistics Canada’s 95th percentile value of the total area of greenhouses across Canada.

Although reducing the area treated per day of backpack sprayers could be considered, the occupational exposure assessment was not revised, as the risks to postapplication workers, which were not shown to be acceptable in PRVD2020-11, would not change.

1.2.2 Types of sprayers

The registrant sought clarification on the language used to describe certain application equipment.

Health Canada response

Stationary airblast/mistblower equipment are considered to be low volume misters or hydraulic sprayers.

1.2.3 Use pattern

a) To reduce postapplication worker exposure to acceptable levels, the registrant proposed to limit the application rate and/or the number of applications.

b) Flowers Canada Growers Inc. (FCG) commented that default values, such as transfer coefficients (TCs) and percent dissipation per day in greenhouse environments, used in the postapplication risk assessments by Canadian evaluators differ significantly from those used by other regulatory bodies. FCG indicated that (S)-kinoprene users/applicators would accept use pattern adjustments including multi-day re-entry intervals. However, FCG did not submit specific information/data, to adjust the default values, for consideration by Health Canada.

Health Canada response

a) The registrant did not specify the proposed amendments to the current label use directions for (S)-kinoprene. Therefore, the postapplication exposure scenarios presented in PRVD2020-11 were not revised.

b) The TCs used by Health Canada are derived from the dataset generated by the Agricultural Re-Entry Task Force and they are similar to those used by other international regulatory authorities.

Health Canada also determined that dissipation in indoor environments is not equivalent to that of outdoor field environments. As such, a default value of 2% dissipation per day has been established for all indoor-grown crops, which differs from the default value of 10% dissipation per day for outdoor-grown crops, used by other international regulatory authorities.

This information was communicated to industry stakeholders, including FCG, in December 2019.

In terms of a multi-day entry period after application, it is not possible to establish agronomically feasibly restricted-entry intervals due to the large extent by which the calculated MOEs do not reach the target MOE of 1000.

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

2.0 Comment related to the value assessment

2.1 Impact on greenhouse ornamentals

Flowers Canada Growers Inc. (FCG) commented on the impact the proposed cancellation of (S)-kinoprene would have on greenhouse ornamental production. Consumers of greenhouse ornamentals expect the plants to be faultless in appearance. Growers manage insect pests and diseases to achieve this. (S)-Kinoprene is a critical rotational tool that many farmers rely on for successful production.

Health Canada response

Health Canada recognizes the value of (S)-kinoprene to the production of greenhouse ornamentals. However, health risks of concern remain, and therefore, the use of (S)-kinoprene on greenhouse ornamentals is cancelled. There are several registered alternatives available to users to control aphids and whiteflies, or to suppress mealybugs on greenhouse ornamentals. Since the remaining insecticides represent different modes of action groups, rotation between these groups is possible to help delay the development of resistance.