Proposed Re-evaluation Decision PRVD2014-04

Isoxaben

(publié aussi en français)

20 June 2014

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. 6604-E2
Ottawa, Ontario K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

ISSN: 1925-0878 (print)
1925-0886 (online)

Catalogue number: H113-97/2014-04E (print)
H113-97/2014-04E-PDF (PDF version)

Table of Contents

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide isoxaben, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing isoxaben for sale and use in Canada.

An evaluation of available scientific information found that products containing isoxaben do not present unacceptable risks to human health or the environment when used according to the proposed label directions. As a condition of the continued registration of isoxaben uses, new risk reduction measures are proposed for the end-use product registered in Canada. No additional data are being requested at this time.

This proposal affects the end-use product containing isoxaben registered in Canada. Once the final re-evaluation decision is made, the registrant will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for isoxaben and presents the reasons for the proposed re-evaluation decision. It also proposes new risk reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of isoxaben.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, presents the details of the cyclical re-evaluation approach, which is in line with the requirements of the *Pest Control Products Act*.

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

What Is Isoxaben

Isoxaben is a selective pre-emergent herbicide that belongs to the benzamide group of pesticides. Isoxaben acts by disrupting root and stem development in germinating seeds. In Canada, it is registered for control of certain broadleaf weeds in conifer bareroot and container nursery stock

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

for listed trees, shrubs and groundcovers grown for silviculture purposes, and containerized ornamentals grown in nurseries. It is registered for outdoor use only and is not for use on cut flowers. Isoxaben is applied by growers or commercial applicators using a low pressure field sprayer.

Health Considerations

Can Approved Uses of Isoxaben Affect Human Health?

Isoxaben is unlikely to affect your health when used according to the proposed label directions.

Potential exposure to isoxaben may occur when applying the product, by entering treated sites or handling treated plants, or through drinking water. Isoxaben is not registered for food use in Canada. The PMRA considers two key factors when assessing health risks: 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 established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Occupational mixer/loader/applicator exposure and postapplication exposure are not of concern under the current conditions of use.

Residential postapplication dermal exposure could occur through contact with treated ornamentals. Residential exposure and risk was qualitatively assessed and is not expected to be of concern. No mitigation measures are proposed with regards to residential exposure to isoxaben.

Exposure to isoxaben through drinking water is not expected to be of concern in Canada. No mitigation is proposed with regards to dietary exposure to isoxaben.

Environmental Considerations

What Happens When Isoxaben Is Introduced Into the Environment?

Isoxaben is unlikely to affect non-target organisms when used according to the proposed label directions.

Non-target terrestrial and aquatic organisms could be exposed to isoxaben in the environment. The use of isoxaben as per current conditions of use is not expected to present a hazard to earthworms or pollinators, or to present an acute hazard to wild birds or mammals through oral ingestion of their food sources. Furthermore, no toxicity to adult birds or effects on reproduction or hatchling survival is expected.

Environmental risk to aquatic organisms and terrestrial plants from spray drift was assessed by the risk quotient method — the ratio of the estimated environmental concentration to the relevant effects endpoint of concern. In this screening level assessment, the resulting risk quotients were compared to corresponding levels of concern. A risk quotient less than the level of concern is considered a negligible risk to non-target organisms, whereas a risk quotient greater than the level of concern indicates some potential risks of concern. Based on this screening-level assessment, the PMRA is proposing the requirement of aquatic and terrestrial buffer zones for isoxaben to protect aquatic organisms and terrestrial plants from spray drift. Additional environmental label statements are also required to further protect the environment.

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. As a result of the re-evaluation of isoxaben, the PMRA is proposing further risk-reduction measures for product labels:

Human Health

- Additional standard statements to reduce potential for contamination of food and feed.
- Clarification of Personal Protective Equipment requirements.

Environment

- Additional advisory label statements to reduce potential surface water contamination.
- Buffer zones to protect non-target, sensitive aquatic and terrestrial habitats.

A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision.

Next Steps

Before making a final re-evaluation decision on isoxaben, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision, and the PMRA's response to these comments.

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

Science Evaluation

1.0 Introduction

Isoxaben is a selective pre-emergent herbicide that acts by disrupting root and stem development in germinating seeds. This active ingredient belongs to the benzamide group of pesticides.

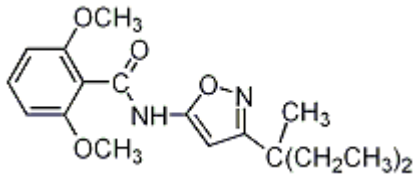
Following the re-evaluation announcement for isoxaben, the registrant of the technical grade active ingredient in Canada indicated continued support for all uses included on the label of the commercial class end-use product currently registered in Canada.

Currently registered products containing isoxaben are listed in Appendix I. All current uses are being supported by the registrant and were, therefore, considered in the re-evaluation of isoxaben.

The purpose of this re-evaluation is to review existing information on the active ingredient, isoxaben, and the currently registered isoxaben technical and commercial class end-use products, to ensure that previous risk assessments meet the standards of modern science and current policy.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Isoxaben
Function	Herbicide
Chemical family	Benzamide
Chemical name	
1 International Union of Pure and Applied Chemistry (IUPAC)	(*N*-[3-(1-ethyl-1-methylpropyl)isoxazol-5-yl]-2,6-dimethoxybenzamide
2 Chemical Abstracts Service (CAS)	*N*-[3-(1-ethyl-1-methylpropyl)-5-isoxazolyl]-2,6-dimethoxybenzamide
CAS Registry Number	82558-50-7
Molecular formula	$C_{18}H_{24}N_2O_4$
Structural formula	

Molecular weight	332.40 amu
Registration Number	24204
Purity of the technical grade active ingredient	93.5%

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the *Canada Gazette*, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including Toxic Substances Management Policy (TSMP) Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 20ºC	5.5×10^{-4} mPa
Ultraviolet (UV) / visible spectrum	λ_{max} = 202 nm Not expected to absorb at λ >300 nm
Solubility in water at 20ºC	1.42 mg/L
n-Octanol/water partition coefficient	Log K_{ow} = 3.94
Dissociation constant	Not applicable

2.3 Description of Registered Isoxaben Uses

Isoxaben is used on conifer bareroot and container nursery stock for listed trees, shrubs and groundcovers grown for silviculture purposes, and containerized ornamentals grown in nurseries. Isoxaben can be applied in early spring, in late summer to early fall, or any time prior to germination of target weeds or immediately after cultivation. Isoxaben may only be applied once per season with an application rate of 0.75 kg a.i./ha. The end-use product is formulated as a dry flowable and is applied using a low pressure field sprayer (for example, groundboom application). The product is not to be applied by air or by using handheld sprayers, and is for outdoor use only.

3.0 Impact on Human and Animal Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

When assessing health risks, the PMRA considers two key factors: 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 established to protect the most sensitive human population (for example, children and nursing mothers).

3.1 Toxicology Summary

In toxicokinetic studies, the absorption of isoxaben was dose-limiting, and absorbed isoxaben was extensively metabolised and rapidly excreted. In acute toxicity studies, technical isoxaben was of low toxicity via the oral, dermal and inhalation route. Technical isoxaben is not a dermal sensitizer, and is a mild and reversible dermal and eye irritant. In subchronic and chronic studies in several species, the liver was identified as the target organ. In rats, two-year treatment with isoxaben resulted in decreased body weight gains and food efficiency, and increased liver and kidney weights. In a three-generation reproduction study, developmental toxicity was observed in the high-dose group (decreased pup weights, increased incidence of microphthalmia and hydrocephaly in pups). Increased resorptions and reduced numbers of corpora lutea, implantations and live fetuses were also observed in dams. Teratogenicity studies in rats and rabbits did not reveal any evidence of teratogenicity. The majority of mutagenicity studies did not demonstrate genotoxic potential. A weak positive result was obtained in micronucleus assays conducted with male Swiss mice. The unscheduled DNA synthesis and the dominant lethal assays were considered inconclusive. A two-year chronic toxicity/oncogenicity study in mice found a significant increase of hepatocellular adenoma in the high-dose animals. Since there was no decrease in latency or progression to carcinomas, and the liver is a target organ, the effect was considered a threshold response.

Appendix II provides an overview of isoxaben toxicology endpoints used in human health risk assessments by the PMRA. Non-cancer endpoints are considered protective of potential cancer effects; no endpoint for cancer risk assessments (that is, cancer potency factor., Q1*) is required.

3.2 Pest Control Products Act Hazard Consideration

The *Pest Control Products Act* factor was not established as part of this assessment and is therefore not incorporated into the quantitative risk assessment.

The database for isoxaben contains developmental (teratogenicity) toxicity studies in rats and rabbits and a three-generation reproductive toxicity study in rats. No data gaps were identified in the original toxicology review for technical isoxaben. No evidence of increased susceptibility was observed in offspring in the available studies.

No evidence of developmental effects was observed in the rat and rabbit teratogenicity studies. However, developmental effects were observed in the three-generation rat reproductive study. The developmental no observed effect level (NOEL) was set at 200 mg/kg bw/day based on decreased pup weights (through lactation), increased incidence of microphthalmia and hydrocephaly in pups. The NOEL for parental toxicity was established at 40 mg/kg bw/day based on reduced body weights of dams and increased liver weights in parents of the top two dose groups.

Based on the information above, a qualitative assessment of the toxicity database suggest that the potential risks to sensitive populations and the reliability of the scientific data are accounted for by the current assessment.

3.3 Dermal Absorption

The dermal absorption factor for use in isoxaben risk assessments was determined to be 25%, based on a dermal study conducted in rhesus monkeys.

3.4 Occupational Exposure

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used 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.

Workers can be exposed to isoxaben through mixing, loading or applying the herbicide or when entering a treated site to conduct activities such as scouting and/or handling treated crops.

3.4.1 Mixer/Loader/Applicator Exposure and Risk

Workers can be exposed to isoxaben through mixing and loading the dry flowable formulation and during application using ground spray equipment. Aerial application and application via handheld sprayers are prohibited on the current label. Based on the isoxaben use pattern, there is potential for short-term (<30 days) exposure to isoxaben for mixers, loaders and applicators.

A quantitative mixer/loader/applicator risk assessment was previously conducted by the PMRA using the Pesticide Handlers Exposure Database (PHED). The assessment was based on the following assumptions:

- Mixing, loading and application of a dry flowable (open mixing) using a groundboom open-cab tractor
- Application to 8 ha/day
- Long-sleeved shirt and long pants, or coveralls, in addition to gloves during mixing/loading (no gloves during application)
- Maximum application rate of 1.14 kg a.i./ha
- 25% dermal absorption, 100% inhalation absorption (default)

A risk estimate was generated using a NOEL of 14 mg/kg bw/day from a 13-week dietary study in mice. The calculated combined dermal and inhalation margin of safety of 600 was not of concern. On this basis, mixer/loader/applicator exposure and risk is not expected to be of concern under current conditions of use.

The current end-use product label requires workers to wear coveralls during all activities, and chemical-resistant gloves during mixing, loading, clean-up and repair activities. For clarity and consistency with current labelling practices, it is proposed that PRECAUTIONS statements be revised to require workers to wear "a long-sleeved shirt and long pants" during all activities instead of "coveralls." No further mitigation is proposed with regards to mixer/loader/application exposure to isoxaben.

3.4.2 Postapplication Exposure and Risk

Postapplication occupational risk assessments consider dermal exposure to workers entering treated agricultural sites to conduct agronomic activities involving foliar contact (for example, scouting). Based on the isoxaben use pattern, there is potential for short-term (<30 days) postapplication exposure for workers.

A postapplication dermal exposure and risk assessment was previously conducted by the PMRA. The assessment was based on re-entry to nurseries to conduct any re-entry tasks associated with container grown ornamentals. Default dislodgeable foliar residues of 20% of the application rate on the day of application were assumed and a transfer co-efficient (TC) of 400 cm^2/hour was used for all activities. The NOEL chosen for the risk assessment was 14 mg/kg bw/day from a 90-day dietary mouse study, and the dermal absorption factor was 25%. The resulting dermal MOE was greater than 800 and therefore was not of concern (target MOE=100). The following statements were required on the product label: "*Do not re-enter treated areas within 12 hours of application*", "*For outdoor use only*" and "*Not for use on cut flowers*".

The postapplication exposure scenarios assessed by the PMRA encompass the registered use pattern for isoxaben. No further mitigation is proposed with regards to occupational postapplication exposure to isoxaben.

3.5 Non-occupational Exposure

3.5.1 Residential Exposure and Risk

Residential exposure is estimated using the MOE approach described in Section 3.4.

The isoxaben commercial class end-use product does not include a statement prohibiting residential application. However, based on the label use instructions, the product is for use on conifer bareroot and container nursery stock grown for silviculture purposes, and on ornamentals grown in nurseries. Furthermore, handheld application of the product is prohibited. On this basis, use in residential areas is not expected to occur.

Homeowners could be exposed to isoxaben when handling treated ornamentals. Risk from residential exposure has been qualitatively assessed by the PMRA for the re-evaluation of isoxaben.

Risk to workers entering treated sites on the day of the application was quantitatively assessed by PMRA, and was not of concern (see Section 3.4.2). Although the transfer coefficient (TC) used in the assessment for worker re-entry activities (400 cm^2/hr) is lower than TCs assumed for residential re-entry activities (TC of 4000 cm^2/hr for all activities for flowers, shrubs), residential postapplication exposure is not expected to be of concern based on the following:

- the duration of the exposure (dermal contact with treated plants) of eight hours per day assumed in the worker assessment is expected to be conservative with respect to residential exposure; and
- MOEs generated for occupational postapplication exposure are well above the target MOE of 100.

On this basis, no mitigation is proposed with regards to residential exposure to isoxaben.

3.5.2 Residue Limits in Food Commodities

Isoxaben is not registered for food use in Canada. Canadian maximum residue limits (MRLs) for imported commodities have not been established for isoxaben.

American tolerances for isoxaben for grapes and several tree nuts range from 0.01 to 0.40 ppm. Codex MRLs have not been established for isoxaben.

3.5.3 Dietary Exposure and Risk

No dietary (food) risk assessment is required for isoxaben. Exposure and risk from drinking water has been assessed using a 2010 United States Environmental Protection Agency assessment.

Isoxaben Tier I estimated drinking water concentrations (EDWCs) in surface (FIRST) and ground water (SCI-GROW) were calculated. EDWCs were based on annual American application rates for use on ornamentals. The application rate used in the assessment was 3.36 kg a.i./ha/yr with a 60-day re-treatment interval. The maximum 1-in-10-year peak and annual mean EDWCs in surface water were 284 and 120 µg/L, respectively. The maximum estimated acute concentration in groundwater was 43.6 µg/L. The maximum annual mean EDWC in surface water (120 µg/L) was used to estimate exposure to isoxaben from drinking water.

Chronic risk from food plus drinking water occupied 5.1% of the chronic population adjusted dose (cPAD) for the general American population. The most highly exposed population subgroup was infants (<1 year old) where exposure accounted for 17% of the cPAD.

The 2010 United States Environmental Protection Agency dietary exposure and risk assessment is expected to be conservative compared to the Canadian situation since the assessment includes food uses, and the application rate used to estimate residues in drinking water was higher than the Canadian maximum application rate (0.75 kg a.i./ha/yr). The cPAD selected by the United States Environmental Protection Agency for assessment of dietary exposure and risk is equivalent to the PMRA Acceptable Daily Intake . On this basis, exposure to isoxaben through drinking water is not expected to be of concern in Canada. No mitigation is proposed with regards to dietary exposure to isoxaben.

3.5.4 Aggregate Exposure and Risk

Aggregate risk combines the different routes of exposure to isoxaben. Short- and intermediate-term aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

Isoxaben is not registered for food uses in Canada. Thus, only drinking water and residential exposures are expected to contribute to aggregate exposure for this active ingredient. As noted in section 3.5.1 and 3.5.3, drinking water and residential exposures to isoxaben is not expected to be of concern. Based on the Canadian use pattern (for example, one application per season on ornamentals grown in nurseries), aggregate exposure to isoxaben is expected to be limited. On this basis, no mitigation is proposed with regards to aggregate exposure to isoxaben.

3.6 Cumulative Exposure and Risk

A common mechanism of action has not been found for isoxaben and other pesticide products, nor is this active ingredient considered to produce a metabolite common to other pesticide active ingredients.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

An environmental evaluation of isoxaben was conducted by the PMRA for the original registration. Isoxaben was determined to have low solubility in water. Based on its vapour pressure, isoxaben was considered relatively non-volatile under field conditions. Henry's law constant for isoxaben indicated that it would be non-volatile to slightly volatile from soil and water. Based on isoxaben's log K_{ow} value and bioconcentration factors in edible tissue, nonedible tissue and whole fish, isoxaben has a low potential for bioaccumulation in biota. Isoxaben and its transformation products were determined to have a low potential for accumulation in fish.

Isoxaben was found to be stable to hydrolysis. It was determined that phototransformation may be a significant route of transformation of isoxaben in water but not on soil. Half-lives in clay loam, loam and sandy loam soils indicated a potential for persistence in aerobic soil. Isoxaben biotransformed in loam soil with a half-life of > 120 days under anaerobic conditions. No data was available regarding aquatic anaerobic and aerobic biotransformation. In laboratory studies, isoxaben was found to have low to medium mobility in soil; however, the major transformation

product[3] was expected to be mobile. In American field studies, isoxaben was found to be moderately persistent in soil, but not mobile. Based on these studies, and in the absence of Canadian field dissipation data, it was concluded that isoxaben would be persistent with the possibility of residues being carried over the following season. Based on these studies, isoxaben was not expected to be mobile; however, the major transformation product was expected to be mobile following operational nursery applications in Canada.

4.2 Environmental Exposure and Risk Assessment

In the PMRA environmental assessment, earthworms exposed to soil-incorporated isoxaben at concentrations up to 100 mg/kg showed no significant differences in growth compared to control animals. Isoxaben was found to be practically non-toxic to honey bees. In acute studies, technical isoxaben was found to be practically non-toxic to birds and slightly toxic to mammals. NOELs for freshwater fish and freshwater invertebrates were found to be $\geq$ 1.1 mg/L and $\geq$ 1.3 mg/L, respectively.

Expected environmental concentrations (EECs) were estimated assuming that residues were obtained immediately following application at a rate of 1.125 kg a.i./ha. At this application rate, isoxaben was not expected to present a hazard to earthworms or pollinators, and was not expected to be acutely toxic to wild birds or mammals through oral ingestion of their food sources. No toxicity to adult birds or effects on reproduction or hatchling survival was expected. Isoxaben was not expected to be toxic to algae or other primary producers, or acutely toxic to aquatic invertebrates and fish even if a waterbody was directly oversprayed at a rate of 0.75 kg a.i./ha. A potential for chronic effects on some species of aquatic invertebrates, however, was indicated.

In consideration of current policy, terrestrial and aquatic buffer zones have been calculated by the PMRA to minimize spray drift to non-target species during ground application. In addition to toxicological data from the PMRA assessment, information published by the United States Environmental Protection Agency was also considered in the buffer zone calculations. Appendix III shows the buffer zone calculations and Appendix IV the proposed label statements.

5.0 Value

Isoxaben is one of a few herbicides registered for use specifically on ornamental nursery stock. Isoxaben is the only alternative soil-applied broadleaf herbicide to flumioxazin for use on nursery stock (both field and container grown). It may play a role in delaying herbicide resistance development in weeds when used in rotation with active ingredients from other herbicide mode of action groups.

[3] (*N*-[3-(2-hydroxybut-2-yl)isoxazol-5-yl]-2,6-dimethoxybenzamide)

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

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 [those that meet all four criteria outlined in the policy: in other words, persistent (in air, soil, water and/or sediment), bioaccumulative, primarily a result of human activity, and toxic as defined by the *Canadian Environmental Protection Act*].

During the re-evaluation process, isoxaben was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy,* and evaluated against the Track 1 criteria. In order for isoxaben to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met. The PMRA has reached the following conclusion:

- Persistence. Isoxaben was found to be moderately persistent in soil (half-life in aerobic soils ranging from 4.3 to 10.6 months). Given that TSMP Track 1 criterion is a half-life in soil or water ≥182 days or in sediment >365 days it is concluded that isoxaben does meet the criteria for persistence.
- Bioaccumulation. Bioconcentration factors (BCFs) for isoxaben of up to 122-fold were found for isoxaben, which is below the TSMP Track 1 criterion (BCF ≥ 5,000). Furthermore, the log K_{ow} of 2.64 for isoxaben is below the TSMP Track 1 criterion (log $K_{ow} \geq 5$). On this basis, it is concluded that isoxaben does not meet the criteria for bioaccumulation.
- Isoxaben does not meet all Track 1 criteria and therefore is not considered a Track 1 substance.

6.2 Contaminants and Formulants of Health or Environmental Concern

During the re-evaluation of isoxaben, contaminants in the technical 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 PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including DIR99-03 and DIR2006-02, and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusion:

[4] *Canada Gazette*, Part II, Volume 139, Number 24, 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, 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."

- Technical grade isoxaben does not contain any contaminants of health or environmental concern identified in the *Canada Gazette.*

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

During the review process, the potential presence of impurities known to have, or suspected to have, health and/or environmental implications are assessed in accordance with DIR98-04.[5]

7.0 Incident Reports

Since 26 April, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA. As of 9 December 2013, one human incident involving the active ingredient isoxaben has been reported to the PMRA. This incident occurred in the United States and was assigned a severity classification of Major.

According to the report, the individual was exposed, in an occupational setting and over the course of 22 years, to several active ingredients including isoxaben as well as aromatic solvents present in pesticide products. No details surrounding the use of the products containing the various active ingredients were provided in the report. Causality could not be established for isoxaben.

This incident report was considered in this re-evaluation.

8.0 Organization for Economic Co-operation and Development Status of Isoxaben

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 34 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

Isoxaben is currently registered for use in several OECD countries, including the United States, Australia and certain European Union countries. No decision by an OECD member country to prohibit all uses of isoxaben for health or environmental reasons has been identified.

[5] DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product.*

9.0 Proposed Re-evaluation Decision

The PMRA is proposing that products containing isoxaben for sale and use in Canada are acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment.

- Additional standard statement to reduce potential for contamination of food and feed.
- Clarification of personal protective equipment requirements.
- Additional advisory label statements to reduce potential surface water contamination.
- Buffer zones to protect non-target, sensitive aquatic and terrestrial habitats.

The proposed mitigation measures are presented in Appendix IV. No additional data are being requested at this time.

10.0 Supporting Documentation

PMRA documents, such as DIR2012-02 and DACO tables can be found on the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca

The federal Toxic Substances Management Policy (TSMP) is available through Environment Canada's website at www.ec.gc.ca/toxiques-toxics/default.asp.

The 2010 United States Environmental Protection Agency human health risk assessment document for the first food uses of isoxaben is available at www.regulations.gov (Document ID: EPA-HQ-OPP-2007-0504-0005).

List of Abbreviations

µg	microgram
ADI	acceptable daily intake
a.i.	active ingredient
ARfD	acute reference dose
atm	atmosphere(s)
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetre(s)
cPAD	chronic population adjusted dose
DACO	data code
EDWC	estimated drinking water concentration
EEC	expected environmental concentration [also estimated environmental concentration]
FIRST	FQPA Index Reservoir Screening Tool
FQPA	*Food Quality Protection Act*
g	gram(s)
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
m^3	metre(s) cubed
mg	milligram(s)
mm Hg	millimetre mercury
MOE	margin of exposure
MRL	maximum residue limit
nm	nanometre
NOEC	no observed effect concentration
NOEL	no observed effect level
PCPA	*Pest Control Products Act*
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
SCI-GROW	Screening Concentration in Ground Water
TC	transfer coefficient
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Registered Products Containing Isoxaben as of 9 December 2013

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
24110	Commercial	Dow AgroSciences Canada Inc.	Gallery 75 DF Herbicide	Dry Flowable	75
24204	Technical	Dow AgroSciences Canada Inc.	Isoxaben Technical Herbicide	Solid	93.5

Appendix II Toxicological Endpoints for Isoxaben Health Risk Assessments

Summary of Isoxaben Toxicology Endpoints Established for use in Human Health Risk Assessments

Exposure Scenario	Dose (mg/kg bw/day)	Study	Safety Factor or Target MOE
Chronic dietary	NOEL = 5	Two-year rat feeding study. Based on the dose-related progressive glomerulo-nephrosis seen in the next two higher dose groups (that is, 51 and 527 mg/kg bw/day in males).	100
	ADI[1] = 0.05 mg/kg bw/day		
Short and intermediate-term dermal	NOEL[1] = 14	13-week mouse dietary study. Based on liver hypertrophy and reduced weight gain in animals of the next dose group (that is, 200 mg/kg bw/day)	100
	Dermal absorption factor is 25%, based on a dermal study conducted in rhesus monkeys.		
Short- and intermediate-term inhalation	NOEL = 14	13-week mouse dietary study. Based on liver hypertrophy and reduced weight gain in animals of the next dose group (that is, 200 mg/kg bw/day)	100
Cancer (oral, dermal, inhalation)	Non-cancer endpoints are considered protective of potential carcinogenic effects (threshold effect).		

[1] ADI = Acceptable Daily Intake ; NOEL = No Observed Effect Level ; MOE = Margin of Exposure ; n/s = not specified.

Appendix III Inputs to the Buffer Zone Models

Ground Use Data (from Canadian label)

Crop	Formulation Type	Method of Application	Number of Applications	Maximum Application Rate (g a.i./ha)
Conifer bareroot and container grown nursery stock for listed trees, shrubs and groundcovers grown for silviculture purposes	Dry flowable	Groundboom (low pressure herbicide sprayer)	1	750 g a.i./ha
Containerized ornamentals grown in nurseries (outdoor use only)	Dry flowable	Groundboom (low pressure herbicide sprayer)	1	750 g a.i./ha

Model Input Data for Aquatic Buffer Zones[6]

Input	Value	Species
Half life for aquatic buffer zones	n/a	n/a
Toxicity endpoint for amphibian	1/10 LC_{50} = 0.1 mg/L	Rainbow trout
Most sensitive freshwater species	NOEC = 0.005 mg/L	*Lemna gibba* (7 day)
Most sensitive estuarine/marine species	NOEC = 0.005 mg/L	*Lemna gibba* (7 day)

Model Input Data for Terrestrial Buffer Zones[6]

Input	Value	Species
Half life for terrestrial buffer zones	n/a	n/a
Most sensitive terrestrial plant species	EC_{25} = 10.7 g/ha	lettuce (vegetative vigour)

[6] From United States Environmental Protection Agency (2010). *Environmental Fate and Ecological Risk Assessment for the Section 3 New Uses of Isoxaben on Bearing Nut Trees and Vineyards.*

Appendix IV Label Amendments for End-Use Products Containing Isoxaben

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

I) Under **PRECAUTIONS**, the following statement must be removed:

> Wear coveralls during all activities and chemical-resistant gloves during mixing, loading, clean-up and repair activities.

and replaced by:

> Wear a long-sleeved shirt and long pants during all activities and chemical-resistant gloves during mixing, loading, clean-up and repair activities.

II) The following statements must be included in a section entitled **DIRECTIONS FOR USE**.

> As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests.
>
> DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
>
> Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) fine/medium/coarse classification. Boom height must be 60 cm or less above the crop or ground.
>
> **DO NOT** apply by air.
>
> **Buffer zones:**
>
> The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, wood lots, hedgerows, riparian areas and shrublands), sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of application	Crop	Buffer Zones (metres) Required for the Protection of:		
		Freshwater Habitat	Estuarine/Marine Habitat	Terrestrial habitat
Field sprayer	Conifer bareroot and container grown nursery stock, containerized ornamentals	1	1	3

III) The following statements must be included in a section entitled **ENVIRONMENTAL HAZARDS**.

TOXIC to aquatic organisms and non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE.

To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.

Avoid application when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

IV) The following statements must be included in a section entitled **STORAGE**.

To prevent contamination store this product away from food or feed.

References

A. Studies considered for the Chemistry Assessment

LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1292259	2006, Applicants and Manufacturers Name and Address, DACO: 2.1,2.2 CBI
1292264	2005, Characterization of Five Batches of Isoxaben Herbicide, DACO: 2.13.2,2.13.3 CBI
1292265	2004, Characterization of Five Batches of Isoxaben HerbicideN-(3-(1-thyl-1-methylpropyl)-5-isoxazolyl)-2,6-dimethoxybenzamide, Manufactured at [Privacy Removed]., DACO: 2.13.2,2.13.3 CBI
1304450	1986, Product Identity & Composition of Technical Isoxaben, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,2.3,2.3.1,2.4,2.5,2.6,2.7,2.8,2.9 CBI
1374791	1991, Determination of Spectral Data of Isoxaben (Technical), RMM 1611, DACO: 2.14.12 CBI

B. Studies considered for the Toxicological Risk Assessment

LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1136589	Acute oral toxicity of compound 121607 (EL-107) in ICR mice (M-0-49-81;M-0-50-81)(Gallery 75DF), DACO: 4.2.1
1136590	Acute oral toxicity of compound 121607 (EL-107) in Fischer 344 rats (R-0-48-81;R-0-49-81)(Gallery 75DF), DACO: 4.2.1
1136588	Acute oral & inhalation toxicity of technical isoxaben (R-0-256-86;R-0-257-86;M-0-171-86;M-0-172-86;R-H-146-86)(Gallery 75DF), DACO: 4.2.1,4.2.3
1136587	The acute dermal toxicity of technical EL-107 in the New Zealand white rabbit (B-D-124-84)(Gallery 75DF), DACO: 4.2.2
1136586	The acute dermal, ocular & inhalation toxicity testing of compound 121607 (B-D-58-81;B-E-61-81;R-H-37-81)(Gallery 75DF), DACO: 4.2.2,4.2.4

1136591 Acute intraperitoneal toxicity of compound 121607 (EL-107) in ICR mice (M-P-18-81;M-P-19-81)(Gallery 75DF), DACO: 4.2.9

1136599 Acute intraperitoneal toxicity of compound 121607 (EL-107) in Fischer 344 rats (R-P-4-81;R-P-5-81)(Gallery 75DF), DACO: 4.2.9

1136535 A subchronic toxicity study in Fischer 344 rats maintained for three months on diets containing EL-107 (Lilly compound 121607)(R00182)(Gallery 75DF), DACO: 4.3.1

1136537 An interim report on a subchronic toxicity study of EL-107 administered in the diet to Fischer 344 rats for three months with a one month reversibility phase (R12582)(Gallery 75DF), DACO: 4.3.1

1136538 A subchronic liver toxicity study of EL-107 administered in the diet to B6C3F1 mice for three months (M01083)(Gallery 75DF), DACO: 4.3.1

1136547 A subchronic toxicity study of EL-107 (Compound 121607 & 135520) administered orally to beagle dogs for three months (D00783)(Gallery 75DF), DACO: 4.3.1

1136553 A subchronic toxicity study of EL-107 administered in the diet to B6C3F1 mice for 3 mths with a 1 mth reversibility phase (M02782)(Gallery 75DF), DACO: 4.3.1

1136554 A subchronic toxicity study of EL-107 administered in the diet to Fischer 344 rats for 3 mths with a 1 mth reversibility phase (R12582) (Compound 121607 & 135520) (Gallery 75DF), DACO: 4.3.1

1136539 Interim report on a chronic toxicity study of EL-107 administered in the diet to Fischer 344 rats for up to one year (R01483)(Gallery 75DF), DACO: 4.4.1

1136540 One year toxicity study of EL-107 administered orally to beagle dogs final report (D04783;T00131)(Gallery 75DF), DACO: 4.4.1

1136548 Continued from roll#1166 interim report on a chronic toxicity study of EL-107 administered in the diet to Fischer 344 rats for up to one year (RO1483)(Gallery 75DF), DACO: 4.4.1

1136559 Final report on a chronic toxicity study of EL-107 administered in the diet to Fischer 344 rats for up to one year (R01483)(Gallery 75DF), DACO: 4.4.1

1137745 An interim report on a chronic toxicity study of EL-107 administered in the diet to Fischer 344 rats for up to one year (R01483)(Gallery 75DF), DACO: 4.4.1

1136555 2 yr toxicity/oncogenicity study of EL 107 administered in the diet to Fischer 344 rats final report (R01583;R01683)(Gallery 75DF), DACO: 4.4.1,4.4.2

1136556 2 yr toxicity/oncogenicity study of EL-107 administered in the diet to Fischer 344 rats. Final report (R01583;R01683)(Gallery 75DF), DACO: 4.4.1,4.4.2

1136570 A two year chronic oncogenic toxicity study of EL-107 administered in the diet to B6C3f1 mice (M00833;M00983) (Gallery 75DF), DACO: 4.4.1,4.4.2

1136557 3 generation reproduction study with EL-107 in the Wistar rat (R15382;R03783;R14183) (Gallery 75DF), DACO: 4.5.1

1136558 A male effect & dominant lethal study of EL-107 in the Wistar rat (R01984)(Gallery 75DF), DACO: 4.5.1

1136562 A teratology study of EL-107 administered orally to Dutch belted rabbits (B03383)(Gallery 75DF), DACO: 4.5.2

1136541 The effect of EL-107 (compound 121607) on the induction of bacterial mutation using a modification of the Ames test (821115GPA1378)(Gallery 75DF), DACO: 4.5.4

1136542 The effect of EL-107 (compound 121607) on the induction of DNA repair synthesis in primary cultures of adult rat hepatocytes (890921UDS1378;821026UDS1378)(Gallery 75DF), DACO: 4.5.4

1136543 The effect of EL-107 on the induction of reverse mutations in Salmonella typhimurium using the Ames test (841001AMS1378)(Gallery 75df), DACO: 4.5.4

1136544 The effect of EL-107 on the in vivo induction of sister chromatid exchange in bone marrow of Chinese hamsters (820921SCE1378)(Gallery 75DF), DACO: 4.5.4

1136545 The effect of EL-107 on the induction of forward mutation at the thymidine kinase locus of l5178y mouse lymphoma cells (820928MLA1378)(Gallery 75DF), DACO: 4.5.4

1136563 Test for genotoxicity of EL-107 using a micronucleus technique in the mouse (871)(Sept 6 1984)(Gallery 75DF), DACO: 4.5.4

1136564 Research for possible mutagenic potentiality of EL-107 using the technique of sister chromatid exchanges in the Chinese hamster final report (886;R1/12/88)(Gallery 75DF), DACO: 4.5.4

1136565 Research for possible genotoxic potentiality of EL-107 using the micronucleus technique in the mouse (894;R1/12/88)(Gallery 75DF), DACO: 4.5.4

1136567 The effect of EL-107 on the induction of reverse mutations in Escherichia coli strain WP2UVRA using the Ames test (840924AMS1378;870615AMS1378B)(Gallery 75DF), DACO: 4.5.4

1136568 The effect of EL-107 on the induction of reverse mutations in Salmonella typhimurium & Escherichia coli using the Ames test (840924AMS1378;870615AMS1378A)(Gallery 75DF), DACO: 4.5.4

1136640 Mutagenicity test on EL-107 in an in vitro cytogenetic assay measuring chromosal aberration frequencies in Chinese hamster ovary (CHO) cells final report (9686-0-437)(Gallery 75DF), DACO: 4.5.4

1137734 A subchronic toxicity study in Fischer 344 rats maintained for three months on diets containing EL-107 (Compound 121607)(R00182)(Gallery 75DF), DACO: 4.7

1136610 Overview of [14C] -EL-107 disposition in mice (M03082;M03182)(Gallery 75DF), DACO: 6.4

1136611 Biliary excretion of radiocarbon in male & female Fischer 344 rats given single oral doses of 14C- EL-107 (R10582;R11482)(Gallery 75DF), DACO: 6.4

1136612 The radiocarbon excretion by Fischer 344 rats given single oral doses of 14C-EL-107 (R07282;R08882)(Gallery 75DF), DACO: 6.4

1136613 Radiocarbon excretion of 14C02 in the expired air from Fischer 344 rats given single oral doses of EL-107 (R02186)(Gallery 75DF), DACO: 6.4

1136614 Tissue distribution of radiocarbon in male & female Fischer 344 rats given a single oral doses of [14C] (R05082;R06182)(Gallery 75DF), DACO: 6.4

1136615 Metabolism of 14C EL-107 in male & female Wistar rats (ABC-1053)(Gallery 75DF), DACO: 6.4

1136618 Percutaneous absorption of 14C-EL-107 in rhesus monkeys (PO3983;P04083)(Gallery 75DF), DACO: 6.4

1136628 Distribution of radioactivity into tissues & organs from Fischer 344 rats given single oral doses of 14C-EL-107 (R11285)(Gallery 75DF), DACO: 6.4

1136630 Distribution of radioactivity into tissues & organs from Fischer 344 rats given oral doses of unlabeled EL-107 daily for two weeks followed by a single dose of 14C EL-107(R13885)(Gallery 75DF), DACO: 6.4

C. Studies considered for the Occupational Risk Assessment

LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1136618	Percutaneous absorption of 14C-EL-107 in rhesus monkeys (PO3983;P04083) (Gallery 75DF), DACO: 6.4

D. Studies considered for the Dietary Risk Assessment

ADDITIONAL INFORMATION CONSIDERED

Published Information

United States Environmental Protection Agency. 2010. *Isoxaben. Human Health Risk Assessment for the First Food Uses of the Herbicide on Grapes, Tree Nuts and Pistachios*. Document ID: EPA-HQ-OPP-2007-0504-0005.

E. Studies considered in the Environmental Risk Assessment

LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1136593	Vapour pressure of the herbicide EL-107 (I-EWD-83-36)(Gallery 75DF), DACO: 8.2.1
1136581	*N*-Octanol-to-water partition coefficient of EL-107 (I-AL-82-07)(Gallery 75DF), DACO: 8.2.1
1824974	ISX-ELA-4 Physical and Chemical Characteristics of Technical Isoxaben, Isoxaben Manufactured Product Characterization, DACO: 2.99
1136577	Potential for injury to nontarget plants from applications of isoxaben (EWD8732;ABC0342;ABC0354;AAC8850)(Gallery 75DF), DACO: 9.8.4

1136579 14C Isoxaben anaerobic soil metabolism study (ABC-0224)(Gallery 75DF), DACO: 8.2.3.1

1189502 Isoxaben soil/turf field dissipation study. Study completed on: 23 February 1988. Supplementary submission in support of isoxaben soil/turf field dissipation study. B.Rutherford and O.Decker. Study no.: AAC8521. MRID NO.40059508. (AAC8521). [isoxaben], DACO: 8.3.2.3

1189525 Isoxaben soil/turf field dissipation study. Study completed on: 1 December 1986. (AAC8521). [Florida-sand/turf fall and spring applications + Indiana-loam, clay loam, spring application + Texas sandy loam, fall application] [isoxaben], DACO: 8.3.2.3

1189536 Isoxaben turf field dissipation study + Illinois site. Study completed on: February 23,1988. (AAC8521). [turf plot on a golf course in Champaign, Illinois] [isoxaben], DACO: 8.3.2.3

1136578 The effect of EL-107 on nitrification in soil (I-RMK-83-03)(Gallery 75DF), DACO: 8.2.3.1

1136575 The toxicity of soil-incorporated EL-107 to earthworms in a 14 day test (W01182)(Gallery 75DF), DACO: 9.2.3.1

1136617 Acute toxicity of EL-107 to adult honeybees (Gallery 75DF)(BY E. Laurence Atkins), DACO: 9.2.4.1

1136623 Toxicity of EL-107 to bobwhite in a 14-day acute oral study (A00682)(Gallery 75DF), DACO: 9.6.2.4

1136571 The toxicity of EL-107 to bobwhite in a five day dietary study (A01082)(Gallery 75DF), DACO: 9.6.2.4

1136598 The toxicity of EL-107 to mallards in a five day dietary study (A00882)(Gallery 75DF), DACO: 9.6.2.4

1136616 Toxicity of EL-107 in a one-generation reproduction study with mallards (A00483)(Gallery 75DF), DACO: 9.6.3.1

1136625 Introduction & summary of one generation studies with EL-107 and bobwhite & mallards (A00184;A02782)(Gallery 75DF), DACO: 9.6.3.1

1136576 Short-term exposure studies with representative wildlife species (bluegill, rainbow trout, daphnia magna, algae, earthworms, bobwhite & mallard) (F07382;F07482;C02182;J00682;W01182;A00682;A00882;A01082) (Gallery 75DF), DACO: 9.2.3.1,9.3.1,9.5.3.1,9.6.2.4,9.8.2

1136577 Potential for injury to nontarget plants from applications of isoxaben (EWD8732;ABC0342;ABC0354;AAC8850)(GALLERY 75DF), DACO: 9.8.4

1136572 The toxicity of EL-107 to algae in a static test system (J00682)(Gallery 75DF), DACO: 9.8.2,9.8.3

1136597 The toxicity of EL-107 to daphnia magna in a static test system (C02182) (Gallery 75DF), DACO: 9.3.1

1136596 The toxicity of EL-107 to daphnia magna in a 21 day-renewal life-cycle test (C03683)(Gallery 75DF), DACO: 9.3.1

1136619 Acute toxicity of EL-107 to rainbow trout in a static test system (F07482) (Gallery 75DF), DACO: 9.5.2.1

1136620 Acute toxicity of EL-107 to bluegill in a static test system (F07382) (Gallery 75DF), DACO: 9.5.2.1

1136624 Toxicity of EL-107 in water to rainbow trout a 66-day early life-stage study (F00383)(Gallery 75DF), DACO: 9.5.5

1136574 Laboratory studies of 14C EL-107 accumulation in fish (ABC-0342;ABC-0354)(Gallery 75DF), DACO: 9.5.5

ADDITIONAL INFORMATION CONSIDERED

Published Information

Atkins, E.L., E.A. Greywood, and R.L. Macdonald. 1975. *Toxicity of pesticides and other agricultural chemicals to honey bees: Laboratory studies.* Univ. of. Calif., Div Agric. Sci., Leaflet 2287. 38 pp.

Banfield, A.W.F. 1974. *The mammals of Canada*. National Museums of Canada, University of Toronto Press.

Chapman, R.F. 1982. *The insects structure and function*. 3rd Edition. Hodder and Stoughton, London.

Dalke, P.D. and P.R. Sime. 1941. *Food habits of the Eastern and New England Cotton tails*. J. Wildl. Manage. 5: 216-228.

Cohen, S.Z., S.M. Creeger, R.F. Carsel and C.G. Enfield. 1984. Potential pesticide contamination of groundwater from agricultural uses. *In:* (Kruegar, R.F. and J.D. Seiber, eds.) *Treatment and disposal of pesticide wastes. American Chemical Society Symposium Series* No. *259.* Pages 297-325. American Chemical Society, Washington, DC.

Harris. 1975. *Guide for estimating toxic residues in animals feeds and diets.* EPA-540/9-75-019. U.S. EPA, Washington, D.C.

Hirt, R.C. R.G. Schmitt, N.D. Searle, and A.P. Sullivan. 1960. *Ultraviolet spectral energy distributors of natural sunlight and accelerated test light sources*. J. Optical Soc. Of Amer. 50: 706-713.

Hoerger, F.D. and E.E. Kenaga. 1972. Pesticide residues on plants: correlation of representative data as a basis for estimation of their magnitude in the environment. *In:* (Coulston, F. and F. Korte, eds.) *EnvironmentalQuality and Safety – Chemistry, Toxicology and Technology. Vol I: Global Aspects of Chemistry, Toxicology and Technology as Applied to the Environment.* Pp. 9-28. Academic Press, New York.

Kennedy, J.M. and R.E. Talbert. 1977. "Comparative persistence of dinitroaniline type herbicides on the soil surface." *Weed Science* 25: 373-381.

McCall, J.P., D.A. Laskowski, R.L. Swann and H.J. Dishburger. 1981. Measurement of sorption coefficients of organic chemicals and their use in environmental fate analysis. *In: Test protocols for environmental fate and movement of toxicants. Proceedings of a symposium.* Pages 89-109. Association of Official Analytical Chemists. 94th Annual Meeting, October 21-22, 1980. Washington, DC.

Pennington, J.A.T. and H.N. Church. 1985. *Food values of portions commonly used.* 14th Edition. Harper and Row, New York.

Peterson, R.L. 1966. *The Mammals of Eastern Canada.* Oxford University Press, Toronto. 465 pp.

Rao, P.S.C. and J.M. Davidson. 1980. Estimation of pesticide retention and transformation parameters required in nonpoint source pollution models. Pages 23-67. *In:* (M.R. Overcash and J.M. Davidson, eds.) *Environmental impact of nonpoint source pollution.* Ann Arbor Sci. Pub. Inc. Ann Arbor, MI.

Sibly, R.M. 1981. Strategies of digestion and defecation. *In:* (C.R. Townsend and P. Colon, eds.) *Physiological Ecology*. Blackwell Publishing.

United States Environmental Protection Agency. 2010. *Environmental Fate and Ecological Risk Assessment for the Section 3 New Uses of Isoxaben on Bearing Nut Trees and Vineyards*. Docket ID: EPA-HQ-OPP-2007-0504-0008.

Urban, D.J. and N.J. Cook. 1986. *Hazard Evaluation Division, Standard Evaluation Procedure, Ecological Risk Assessment.* EPA 540/9-85-001. U.S. EPA, Washington, D.C.