



BIOPESTICIDES REGISTRATION ACTION DOCUMENT

l-Carvone

**U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division**

(Last updated *August 31, 2009*)

This document is for informational purposes only and is representative of the Agency's justification in registering products containing this active ingredient. This is not a legal document.

TABLE OF CONTENTS

I.	EXECUTIVE SUMMARY	5
II.	ACTIVE INGREDIENT OVERVIEW	6
III.	REGULATORY BACKGROUND	6
A.	Food Clearances/Tolerances	6
IV.	RISK ASSESSMENT	6
A.	Active Ingredient Characterization	6
B.	Human Health Assessment	7
1.	Toxicology	7
a.	Acute Toxicity	8
b.	Subchronic Toxicity	8
c.	Developmental Toxicity and Mutagenicity	9
d.	Effects on the Endocrine System	9
2.	Dose Response Assessment	10
3.	Drinking Water Exposure and Risk Characterization	10
4.	Occupational, Residential, School and Day Care Exposure and Risk Characterization ..	10
a.	Occupational Exposure and Risk Characterization	10
b.	Residential, School and Day Care Exposure and Risk Characterization	10
5.	Risk Characterization	10
C.	ENVIRONMENTAL ASSESSMENT	10
1.	Ecological Hazards	10
2.	Environmental Fate and Ground Water Data	11
3.	Ecological Exposure and Risk Characterization	11
4.	Endangered Species Assessment	11
V.	Risk Management Decision	11
A.	Determination of Eligibility for Registration	11
B.	Regulatory Decision	11
1.	Conditional/Unconditional Registration	12
C.	Environmental Justice	12
VI.	ACTIONS REQUIRED BY REGISTRANTS	12
A.	Reporting of Adverse Effects	12
B.	Reporting of Hypersensitivity Incidents	12

VII. Appendix A. Data Requirements (40 C.F.R. Part 158-Subpart U)..... 12

VIII. Appendix B. Product Specific Information. 15

IX. Appendix C. References 16

BIOPESTICIDES REGISTRATION ACTION DOCUMENT TEAM

Office of Pesticide Programs:

Biopesticides and Pollution Prevention Division

Biochemical Pesticides Branch (BPB)

Linda A. Hollis

Colin Walsh

Mike Rexrode

Jacob Moore

Chief

Regulatory Action Leader

Biologist, Acute Toxicology

Chemist

I. EXECUTIVE SUMMARY

l-Carvone, which is the fragrance of mint, comprises 50-65% of the essential oil from the spearmint plant (*Mentha spicata*). It can also be made synthetically from d-limonene. *l*-Carvone has a long history of use as a flavoring in a variety of foods and beverages, as well as in toothpaste and mouth wash. It is also used as a fragrance in personal care products, and in consumer products such as air fresheners. The technical grade active ingredient (TGAI) is identified as Bedoukian L-Carvone and is intended for use in the manufacture of an area repellent for mosquitoes and biting flies.

The Tier I toxicology data suggest that *l*-Carvone is acutely non toxic (Toxicology Category IV) and has very low acute dermal and inhalation concerns (Toxicology Category III). This compound is a mild-slight dermal sensitizer, and a negative mutagen. L-Carvone has been used as a fragrance for personal care products and flavoring in various foods (safe exposure limits have already been established). There is no evidence of inhalation toxicity (Toxicology Category IV) and primary eye irritation cleared in seven days (Toxicology Category III). Therefore, the information submitted is sufficient to justify the requested waivers for Acute Oral Toxicity, Acute Inhalation, Acute Dermal Toxicity, Primary Eye Irritation, Primary Dermal Irritation, Dermal Sensitization, Hypersensitivity, Prenatal Development, Bacterial Reverse Mutation Testing, *In vitro* Mammalian Cell Assay and the 90-Day Inhalation Toxicity. Since this is a manufacturing use registration, all Tier I Ecotoxicity data requirements per 40 C.F.R. 158.2060 have also been waived at this time. The registrant, however, should be reminded that this requirement will be reexamined upon application of an end use product. The Agency has determined that use of the technical grade of *l*-Carvone will have **No Adverse Effects (NAE)** on threatened and/or endangered species.

The registrant has noted that *l*-Carvone is to be used in an end use product in order to repel mosquitoes and other biting insects. Since this is a public health issue, the registrant must submit an appropriate efficacy study for Agency review upon registration request for the end use product.

To mitigate any risk for handlers of the TGAI, the Agency will require the appropriate signal word and precautionary statements on the product label. Residential, school, or day care exposure to *l*-Carvone is unlikely due to the expected use pattern. Should an exposure occur, the health risk is expected to be minimal, based on the low acute toxicity and the history of safe use of *l*-Carvone in foods, beverages, and consumer products. No significant exposure via drinking water is expected when *l*-Carvone is used according to the product label directions. In the unlikely event that exposure via drinking water does occur, the health risk is expected to be minimal, based on the low acute toxicity of *l*-Carvone and its long history of safe use as a flavoring ingredient in foods and beverages. BPPD has determined that no unreasonable adverse effects to the U.S. population will result from the use of *l*-Carvone when label directions are followed.

The Biopesticides and Pollution Prevention Division (BPPD) has reviewed data requirements for granting registration under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), and has determined that the data/information submitted for Tier I Acute Toxicity and Product Chemistry adequately satisfy current guideline requirements (refer to 40 C.F.R. Subpart U § 158.2000).

II. ACTIVE INGREDIENT OVERVIEW

Common Name: *l*-Carvone

Chemical Names: 2-Cyclohexen-1-one, 2-methyl-5-(1-methylethenyl)-, (5R)-
2-Cyclohexen-1-one, 2-methyl-5-(1-methylethenyl)-, (R)- (9CI)
2-Cyclohexen-1-one, 2-methyl-5-(1-methylethenyl)-, (theta)-
(-)-Carvone
(R)-Carvone
L(-)-Carvone
p-Mentha-6,8-dien-2-one, (-)-
p-Mentha-6,8-dien-2-one, (R)-(-)-
l-p-Mentha-1(6),8-dien-2-one
l-1-Methyl-4-isopropenyl-6-cyclohexen-2-one

Trade & Other Names: Bedoukian L-Carvone

CAS Registry Number: 6485-40-1

OPP Chemical Code: 079500

Type of Pesticide: Biochemical pesticide (Insect Repellent)

Application rates and methods vary depending on the product. For specific information regarding the product(s) refer to Appendix B.

III. REGULATORY BACKGROUND

On July 15, 2008, the Agency received an application filed by Bedoukian Research, Inc. 21 Finance Dr., Danbury, CT 06810 (submitted by Keller and Heckman LLP, 1001 G Street, N.W., Suite 500 West, Washington, DC 20001) to register the product Bedoukian *l*-Carvone containing the new biochemical active ingredient *l*-Carvone at 99.5%. A notice of receipt of this application was published in the Federal Register March 4, 2009 (74 FR Number 41 Page 9396).

A. Food Clearances/Tolerances

Currently, this active ingredient is not registered for use on food or feed commodities. A tolerance or exemption from the requirement of a tolerance is not relevant.

IV. RISK ASSESSMENT

A. Active Ingredient Characterization

The active ingredient *l*-Carvone is the fragrance of mint, and comprises 50-65% of the essential oil from the spearmint plant (*Mentha spicata*). It can also be made synthetically from d-*limonene*. Both the natural and synthetic forms of *l*-Carvone are used as flavorings in a variety of foods, including candies, chewing gum, beverages, and baked goods, and are also used to flavor toothpaste and mouthwash. Additionally, *l*-Carvone is used as a fragrance in personal care products such as soaps, cosmetics, and perfumes, and in consumer products such as air fresheners.

The technical grade active ingredient (TGAI) is identified on the proposed product label as Bedoukian L-Carvone. The description of the production process, including the formation of impurities, was examined by the Agency and found to be acceptable in meeting current guideline standards. The analytical method used to determine the content of the active ingredient is also acceptable. Physical and chemical properties were submitted for the TGAI and are adequate. Refer to Table 1 in Appendix A for a summary of product chemistry data requirements. Refer to Table 2 in Appendix A for the summary of physical and chemical characteristics for *l*-Carvone.

All product chemistry data requirements for registration of *l*-Carvone have been **satisfied**.

B. Human Health Assessment

1. Toxicology

For acute toxicity data requirements, toxicity categories are assigned based on the hazard(s) identified from studies and/or information on file with the Agency. The active ingredient is classified into Toxicity Category I, II, III or IV where Toxicity Category I represents the highest toxicity and Toxicity Category IV indicates the lowest toxicity. For more information, refer to <http://www.epa.gov/pesticides/pestlabels/>.

The registrant requested waivers for the Tier I mammalian toxicity studies (Table 3) based on the historically safe use of *l*-Carvone as a flavoring and fragrance agent, and the availability of previously-generated toxicity data for *l*-Carvone or surrogate compounds in the open literature. The Agency has reviewed the information submitted to support the mammalian toxicity data waivers and found it to be adequate to support registration of *l*-Carvone.

Adequate mammalian toxicology data/information is available to support registration of *l*-Carvone. All toxicology data requirements for *l*-Carvone have been **satisfied**.

a. Acute Toxicity

Acute toxicity testing is required to 1) determine systemic toxicity from acute exposure via the dermal, inhalation and oral routes, 2) determine irritant effects from exposure to the eyes and 3) determine the potential for skin sensitization (allergic contact dermatitis). The registrant requested waivers for conducting acute toxicity testing, based on the history of safe use in food, fragrances, and other consumer products, and the availability of sufficient acute toxicity data for *l*-Carvone or surrogate compounds in the public literature.

In an acute oral toxicity study with rats, the LD₅₀ (the dose required to kill half the members of the tested population) for *l*-Carvone administered orally by gavage was 5.4 grams/kilogram of body weight (mg/kg bw) (Quest International, 1986a).

In an acute dermal toxicity study with the surrogate chemical d-Carvone, the acute dermal LD₅₀ in rabbits was 3,860 mg/kg bw (Opdyke, 1978).

Carvone has been used extensively as a fragrance in consumer and personal care products, resulting in much higher exposures than those that would likely result from the use of products containing *l*-Carvone as an area insect repellent, with no evidence of inhalation toxicity.

In studies to determine irritant/corrosive effects on the eyes of mammals (Quest International, 1986b, 1986c), *l*-Carvone was instilled into the eye of New Zealand white rabbits. Three rabbits treated with 10% test material in Tween 80 had a slight transient conjunctivitis, with unaffected corneas, resolving within 24 hours. One rabbit treated with 50% test material in Tween 80 showed loss of an extensive area of corneal epithelium, with moderate corneal swelling and iritis. Conjunctivitis was slight, but lasted eight days. A persistent pannus developed. One rabbit treated with undiluted test material showed superficial corneal effects with slight conjunctivitis, healing by day four.

l-Carvone was not found to be a dermal irritant in guinea pigs treated with 10%, 20%, or 50% *l*-Carvone in acetone/polyethylene glycol for 24 hours (Quest International, 1983). In humans, *l*-Carvone was not an irritant when applied at a concentration of 2.25% in 1:3 ethanol:diethyl phthalate for 24 hours, which was repeated nine times at 24-hour intervals (Harrison and Spey, 2000).

In a dermal sensitization test with guinea pigs, *l*-Carvone produced sensitization at a challenge concentration of 1% following an intradermal induction using 10% *l*-Carvone (Kozuka, 1996). In a patch test, human subjects were induced with 0.3 mL of *l*-Carvone nine times over three weeks (Harrison and Spey, 2007). A challenge with 2.25% (2657 µg/cm²) Carvone did not produce sensitization in any of the 99 subjects.

For more information regarding the acute toxicity data requirements, refer to Table 3 in Appendix A.

b. Subchronic Toxicity

Subchronic data is required to determine a no-observed-effect-level (NOEL) and toxic effects (if any) associated with repeated or continuous exposure to a test substance for a period of 90 days.

The registrant requested waivers for conducting a 90-Day Inhalation Toxicity study, based on the history of safe use. Carvone has been used extensively as a fragrance in consumer and personal care products, resulting in much higher exposures than those anticipated to result from the use of *l*-Carvone as an area insect repellent, with no evidence of inhalation toxicity.

For more information regarding the subchronic data requirements, refer to Table 3 in Appendix A.

c. Developmental Toxicity and Mutagenicity

The registrant requested waivers for Developmental Toxicity and Mutagenicity testing, based on the history of safe use in food, fragrances, and other consumer products, and the availability of sufficient mutagenicity data for *l*-Carvone or surrogate compounds in the public literature.

Carvone has a long history of use as a flavoring in foods. Based on current levels of per capita intake in the US (9900 µg/day), the World Health Organization (WHO) has concluded that there is no safety concern for Carvone (WHO, 1999). Furthermore, the level of exposure to pregnant women based on the proposed use pattern as an area insect repellent would be negligible.

Carvone and surrogate compounds have tested negative in a variety of gene mutation studies (Florin et al., 1980; Mortelmans et al., 1986; National Toxicology Program (NTP), 1990; Rockwell, 1979; Matsui et al., 1989). Equivocal results were found in a sister chromatid exchange study and a chromosomal aberration study with Chinese hamster ovary cells (NTP, 1990), but WHO did not consider this to be an issue in its assessment of *l*-Carvone as a safe food additive (WHO, 1999).

For more information regarding these data requirements, refer to Table 3 in Appendix A.

d. Effects on the Endocrine System

EPA is required under the Federal Food, Drug, and Cosmetics Act (FFDCA), as amended by the Food Quality Protection Act (FQPA), to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC’s recommendation that the program include evaluations of potential effects in wildlife. For pesticide chemicals, the Agency will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

The Agency is not requiring information on the endocrine effects of *l*-Carvone at this time. The Agency has considered, among other relevant factors, available information concerning whether the active ingredient may have an effect on humans similar to an effect produced by naturally occurring estrogen or other endocrine effects. There is no known metabolite that acts as an endocrine disrupter produced by this active ingredient. Based on the low potential exposure level

associated with the proposed use, the Agency expects no incremental adverse effects to the endocrine or immune systems.

2. Dose Response Assessment

No toxicological endpoints were identified; therefore, a dose response assessment was not required.

3. Drinking Water Exposure and Risk Characterization

No significant exposure via drinking water is expected when *l*-Carvone is used according to the product label directions. The TGAI is intended for use in the manufacture of an area repellent for mosquitoes and other biting flies. End use products using the TGAI will be placed in stations that release small amounts of *l*-Carvone over the area, and it is unlikely to accumulate in drinking water. In the unlikely event that exposure via drinking water did occur, the health risk would be expected to be minimal, based on the low acute and dermal toxicity of *l*-Carvone and its long history of safe use as a flavoring ingredient in foods and beverages.

4. Occupational, Residential, School and Day Care Exposure and Risk Characterization

a. Occupational Exposure and Risk Characterization

The potential for oral, dermal, eye and inhalation exposure to *l*-Carvone exists for handlers. The Agency will require the appropriate signal word and precautionary statements on the product label to mitigate any risk from exposure via these routes. Due to the low acute oral and acute dermal toxicity and history of safe use in foods, beverages, and consumer products, worker exposure data are not required.

b. Residential, School and Day Care Exposure and Risk Characterization

Residential, school, or day care exposure to *l*-Carvone is expected to be minimal since products containing *l*-Carvone will release the TGAI in low amounts. The health risks are expected to be minimal based on the low acute oral and acute dermal toxicity and the history of safe uses in foods, beverages and other consumer products.

5. Risk Characterization

Human exposure to *l*-Carvone in light of the relevant safety factors in FQPA and FIFRA were not considered for this active ingredient since *l*-Carvone is intended for formulation into end use products with non food use patterns.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Hazards

Adequate non-target toxicology information is available to support registration of *l*-Carvone. All non-target toxicology data requirements for *l*-Carvone have been **satisfied**.

Ecological effects data requirements for *l*-Carvone were satisfied by the submitted data waiver requests. Based on the waiver rationales, the Agency concluded that exposure and risk from the manufacturing use product is not expected to pose a threat to non-target organisms.

For more information regarding the non-target toxicity data requirements, refer to Table 4 in Appendix A.

2. Environmental Fate and Ground Water Data

The need for environmental fate and groundwater data was not triggered because results of the acute toxicity studies did not trigger any additional Tier I studies.

3. Ecological Exposure and Risk Characterization

Based on the rationales submitted in the data waiver requests, the proposed use of *l*-Carvone as a manufacturing use product is not expected to result in exposure or risk to non-target organisms.

4. Endangered Species Assessment

Based on the information presented above, the Agency has determined that registered use of *l*-Carvone as an active ingredient will have **No Adverse Effects (NAE)** on threatened and/or endangered species. When the product is used according to label use directions, there are no concerns for any non-target organisms.

V. Risk Management Decision

A. Determination of Eligibility for Registration

Section 3(c)(5) of FIFRA provides for the registration of *l*-Carvone if it is determined that (A) *l*-Carvone's composition is such as to warrant the proposed claims for it; (B) *l*-Carvone's labeling and other materials required to be submitted comply with the requirements of FIFRA; (C) *l*-Carvone will perform its intended function without unreasonable adverse effects on the environment; and (D) when used in accordance with widespread and commonly recognized practice *l*-Carvone will not generally cause unreasonable adverse effects on the environment.

The four criteria of the Eligibility Determination for Pesticidal Active Ingredients are satisfied by the science assessments supporting products containing *l*-Carvone. Such products are not expected to cause unreasonable adverse effects, and are likely to provide protection as claimed when used according to label instructions. Therefore, *l*-Carvone is eligible for registration for the labeled uses.

B. Regulatory Decision

The data submitted fulfill the requirements of registration for use of *l*-Carvone in the manufacture of area insect repellents to repel mosquitoes and other biting flies. Refer to Appendix B for product-specific information.

1. Conditional/Unconditional Registration

All data requirements are fulfilled and EPA has determined that unconditional registration of *l*-Carvone is appropriate.

C. Environmental Justice

EPA seeks to achieve environmental justice - the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income - in the development, implementation, and enforcement of environmental laws, regulations, and policies. At this time EPA does not believe that use of pesticide products containing *l*-Carvone will cause harm or a disproportionate impact on at-risk communities.

For additional information regarding environmental justice issues, please visit EPA's website at: <http://www.epa.gov/compliance/environmentaljustice/index.html>.

VI. ACTIONS REQUIRED BY REGISTRANTS

The Agency evaluated all of the data submitted in connection with the initial registration of *l*-Carvone and determined that these data are sufficient to satisfy current registration data requirements. No additional data are required to be submitted to the Agency at this time. For new uses and/or changes to existing uses, additional data may be required.

Notwithstanding the information stated in the previous paragraph, it should be clearly understood that certain, specific, data are required to be reported to the Agency as a requirement for maintaining the Federal registration for a pesticide product. A brief summary of these types of data are listed below.

A. Reporting of Adverse Effects

Reports of all incidents of adverse effects to the environment must be submitted to the Agency under the provisions stated in FIFRA, Section 6(a)(2).

B. Reporting of Hypersensitivity Incidents

Additionally, all incidents of hypersensitivity (including both suspected and confirmed incidents) must be reported to the Agency under the provisions of 40 C.F.R. Part 158.2050(d).

VII. Appendix A. Data Requirements (40 C.F.R. Part 158-Subpart U)

*NOTE: MRID numbers listed in the following tables are representative of supporting data for the original registration of the product containing this active ingredient. Subsequent to this registration, there may be additional MRIDs that support registration of other products containing this active ingredient.

TABLE 1. Product Chemistry Data Requirements for <i>l</i>-Carvone (40 C.F.R. § 158.2030)			
OPPTS Guideline No.	Study	Results (<i>below are example results</i>)	MRID
830.1550 to 830.1670	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	Submitted data satisfy the requirements for product identity, manufacturing process, and discussion of formation of impurities.	47546101
830.1700	Analysis of samples	Submitted data satisfy the requirements for analysis of samples.	47546102
830.1750	Certification of limits	Limits listed in the CSF are adequate / acceptable.	47546102
830.1800	Analytical method	Acceptable.	47515503

TABLE 2. Physical and Chemical Properties of <i>l</i>-Carvone (40 C.F.R. § 158.2030)			
OPPTS Guideline No.	Property	Description of Result	MRID
830.6302	Color	Colorless to light yellow	47515504
830.6303	Physical State	Liquid @ room temperature	47515504
830.6304	Odor	Spearmint	47515504
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Stable	47515504
830.6314	Oxidation/Reduction: Chemical Incompatibility	Not required	
830.6315	Flammability	200°F	47515504
830.6316	Explosibility	Not required	
830.6317	Storage Stability	Store in glass, plastic, plastic- lined or coated containers, not metal. Do not store in iron. Guideline study in progress; initiated 7/21/2008.	47515504 47515506
830.6319	Miscibility	Not applicable, product is only marginally soluble in water.	47515504
830.6320	Corrosion Characteristics	Guideline study in progress; initiated 7/21/2008.	47515504
830.7000	pH	Not applicable, product is only marginally soluble in water.	47515504
830.7100	Viscosity	2.72 Centistokes	47515504
830.7200	Melting Point/Range	<25°C (experimental) 9.86°C (EPA EPISuite, QSAR)	47515504
830.7220	Boiling Point/Range	228.5°C (experimental) 224.23°C (EPA EPISuite, QSAR)	47515504
830.7300	Density	0.960 @ 25°C 7.4 lb/gal @ 25°C	47515504
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not applicable, the product is a liquid	47515504
830.7550 830.7560 830.7570	Partition Coefficient (n- Octanol/Water)	<3.0	47515504
830.7840	Water Solubility	Marginally soluble (367.1 mg/L)	47515504
830.7950	Vapor Pressure	0.1 mm Hg @ 25°C (experimental) 0.13 mm Hg @ 25°C (EPA EPISuite, QSAR)	47515504

Table 3. Human Toxicology Data Requirements for <i>l</i>-Carvone (40 C.F.R. § 158.2050)			
Study/OPPTS Guideline No.	Results	Toxicity Category/Description	MRID
Acute oral toxicity (rat) (870.1100)	LD50 > 5400 mg/kg Data waiver acceptable	IV	Quest International (1986) 47515505
Acute dermal toxicity (rat) (870.1200)	LD₅₀ = 3,860 mg/kg Data waiver acceptable	III	Opdyke, (1978) 47515505
Acute inhalation toxicity (rat) (870.1300)	No evidence of inhalation toxicity Data waiver acceptable	IV	Heuberger, (2001) 47515505
Primary eye irritation (rabbit) (870.2400)	Corneal irritation clearing within 7 days Data waiver acceptable	III	Quest International, (1986) 47515505
Primary dermal irritation (rabbit) (870.2500)	Mild or slight Data waiver acceptable	IV	Quest International (1985) 47515505
Dermal sensitization (guinea pig) (870.2600)	Data waiver acceptable	Produced sensitization effects	47515505
Hypersensitivity incidents (885.3400)	Data waiver acceptable	Potential for sensitization	47515505
90-Day inhalation toxicity (870.3465)	Data waiver acceptable	No safety concern	47515505
Mutagenicity (870.5100, 5300 and 5375)	Data waiver acceptable	Negative	47515505
Developmental toxicity (870.3700)	Data waiver acceptable	No safety concern	47515505

Study/OPPTS Guideline No.	Results	Toxicity Category/Description	MRID
Avian acute oral toxicity <i>Colinus virginianus</i> (850.2100)	Data waiver request submitted.		47515505
Avian oral toxicity <i>Colinus virginianus</i> (850.2200)	Data waiver request submitted.		47515505
Avian dietary toxicity <i>Anas platyrhynchos</i> (850.2200)	Data waiver request submitted.		47515505
Aquatic invertebrate acute toxicity <i>Daphnia magna</i> (850.1010)	Data waiver request submitted.		47515505
Freshwater fish LC ₅₀ <i>Oncorhynchus mykiss</i> (850.1075)	Data waiver request submitted.		47515505
Non-target plant studies (850.4000-4800, as applicable)	Data waiver request submitted.		47515505
Non-target insect testing (880.4350)	Data waiver request submitted.		47515505

VIII. Appendix B.

For product specific information, please refer to <http://www.epa.gov/pesticides/pestlabels>

IX. Appendix C.

REFERENCES

- Florin, I., L. Rutberg, M. Curvall, et al. 1980. Screening of Tobacco Smoke Constituents for Mutagenicity Testing Using the Ames Test. *Toxicology* 15:219-232.
- Harrison, L.B., and D.R. Spey. 2000. Repeated Insult Patch Test with laevo-Carvone. Unpublished Report 52896, Research Institute for Fragrance Materials, Inc.
- Kozuka, T., H. Hayashi, H. Hiroyama et al. 1996. Allergenicity of Fragrance Materials: Collaborative Study of the Second Research Group of the Japanese Society for Cutaneous Health. *Environmental Dermatology* 3(4):326-335.
- Matsui, S., R. Yamamoto, and H. Yamada. 1989. The *Bacillus subtilis*/microsome rec-assay for the Detection of DNA Damaging Substances Which May Occur in Chlorinated and Ozonated Waters. *Water Sci. Technol.* 21:875-887.
- Mortelmans, K. S. Haworth, T. Lawlor, et al. 1986. Salmonella Mutagenicity Tests: II. Results from the Testing of 270 Chemicals. *Environ. Mutag.* 8:1-119.
- National Toxicology Program. 1990. Toxicology and Carcinogenesis Studies of d-Carvone in B6C3F1 Mice (Gavage Studies) (NTP TR 381). Department of Health and Human Services, Research Triangle Park, North Carolina.
- Opdyke, D.L.J. 1978. Fragrance Raw Materials Monographs. d-Carvone. *Food Cosmet. Toxicol.* 16, Suppl. 1:673-674.
- Quest International. 1983. Guinea Pig Skin Sensitization Test with laevo-Carvone. Unpublished Report.
- Quest International. 1986a. Acute Oral Toxicity to Rats of laevo-Carvone. Unpublished Report.
- Quest International. 1986b. Rabbit Eye Irritation Test with laevo-Carvone. Unpublished Report.
- Quest International. 1986c. Rabbit Eye Irritation Test with laevo-Carvone. Unpublished Report.
- Rockwell, P., and I. Raw. 1979. A Mutagenic Screening of Various Herbs, Spices, and Food Additives. *Nutrition and Cancer* 1(4):10-15.
- World Health Organization (WHO). 1999. International Programme on Chemical Safety. Safety Evaluation of Certain Food Additives. WHO Food Additive Series 42.