BIOPESTICIDES REGISTRATION ACTION DOCUMENT

SAPONINS OF QUILLAJA SAPONARIA

(PC Code **097095**)

U.S. Environmental Protection Agency Office of Pesticide Programs Biopesticides and Pollution Prevention Division Biochemical Pesticides Branch

TABLE OF CONTENTS

I.	EXECUTIVE SUMMARY:	6
II.	OVERVIEW	7
A.	ACTIVE INGREDIENT OVERVIEW	7
B.	USE PROFILE	7
C.	ESTIMATED USAGE	8
D.	DATA REQUIREMENTS	8
E.	REGULATORY HISTORY	9
F.	CLASSIFICATION	9
G.	FOOD CLEARANCES/TOLERANCES	9
III.	SCIENCE ASSESSMENT	9
A. 1. 2.	 PHYSICAL/CHEMICAL PROPERTIES ASSESSMENT. Product Identity and Mode of Action. a. Product Identity. b. Mode of Action b. Mode of Action Physical and Chemical Properties Assessment 	10 10 10
B. 1.	 a. Acute Toxicity b. Mutagenicity, Developmental Toxicity, and Immunotoxicity c. Subchronic Toxicity d. Chronic Exposure and Oncogenicity Assessment e. Effects on the Endocrine System 	11 14 14 14 15 16
3	 Dietary Exposure and Risk Characterization	17 17 17 17
6	. Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and hildren	
8. 9.	. Cumulative Effects	18

C. ENVIRONMENTAL ASSESSMENT	
1. Ecological Effects Hazard Assessment	
2. Environmental Fate and Ground Water Data	
3. Ecological Exposure and Risk Characterization	
D. EFFICACY DATA	
IV. RISK MANAGEMENT DECISION	
A. DETERMINATION OF ELIGIBILITY FOR REGISTRATION	
B. REGULATORY POSITION	
1. Unconditional Registration	
2. CODEX Harmonization	
3. Nonfood Registrations	
4. Risk Mitigation	
5. Endangered Species Statement	
C. LABELING RATIONALE	
1. Human Health Hazard	
a. Worker Protection Standard	
b. Non-Worker Protection Standard	
c. Precautionary Labeling	
d. Spray Drift Advisory	
2. Environmental Hazards Labeling	
3. Application Rate	
D. LABELING	
V. ACTIONS REQUIRED BY REGISTRANTS	
A. REPORTING OF ADVERSE EFFECTS	
B. REPORTING OF HYPERSENSITIVITY INCIDENTS	
VI. APPENDIX A	
VII. APPENDIX B	
VIII. APPENDIX C	

LIST OF TABLES

TABLE 1. PRODUCT CHEMISTRY DATA REQUIREMENTS FOR QUILLAJA EXTRACT	10
TABLE 2. PHYSICAL AND CHEMICAL PROPERTIES FOR QUILLAJA EXTRACT	11
TABLE 3. MAMMALIAN TOXICITY REQUIREMENTS FOR SAPONINS OF QUILLAJA	
SAPONARIA	13
TABLE 4. NON-TARGET ORGANISM TOXICITY REQUIREMENTS FOR SAPONINS OF	
QUILLAJA SAPONARIA	21
TABLE 5. INPUTS USED FOR GENEEC MODELING	22
TABLE 6. GENERIC ESTIMATED ENVIRONMENTAL CONCENTRATIONS (GEECS)	
FROM THE	
GENEEC MODEL USED FOR CHRONIC EXPOSURE RISK QUOTIENTS	23
TABLE 7. RISK QUOTIENTS BASED ON ESTIMATED QUILLAJA SAPNONINS	
CONCENTRATIONS IN WATER	23
TABLE 8. USE SITES	31

BIOPESTICIDES REGISTRATION ACTION DOCUMENT TEAM

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Biopesticides and Pollution Prevention Division

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I. EXECUTIVE SUMMARY:

Saponins of *Quillaja saponaria* is a new active ingredient that comprises 8.60% of the end use product Quillaja Extract. The saponins are derived by extraction from the logs and bark of the soapbark tree (*Quillaja saponaria*). Quillaja Extract is intended to control fungi and nematodes on ornamentals, food crops and turfgrass.

Product chemistry data requirements were satisfied (product identity, product analysis, manufacturing process, and physical/chemical properties).

Adequate mammalian toxicology data/information was submitted in support of registration of saponins of *Quillaja saponaria*. Acceptable acute toxicity guideline studies were submitted, and data waivers were granted by the Agency to fulfill the remaining toxicity requirements based on the lack of toxicity of the active ingredient, its natural occurrence in plants, and the existing use of Quillaja saponins as food additives.

Ecological effects data requirements for saponins of *Quillaja saponaria* were fulfilled by acceptable guideline studies and additional data/information from the scientific literature sufficient to support data waivers for the remaining Tier I and Tier II requirements.

There are no significant issues identified for dietary risk, residential risk, or ground and surface water contamination from the use of saponins of *Quillaja saponaria* as an active ingredient. Mitigation measures for occupational routes of exposure are addressed in that applicators and other handlers are required to wear appropriate personal protective equipment (PPE).

The Agency has considered saponins of *Quillaja saponaria* in light of the relevant safety factors in the Food Quality Protection Act (FQPA) of 1996 and under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and has not identified any dietary or non-dietary exposure issues that may affect the U.S. population in general, including infants and children. The Agency has thereby determined that there is reasonable certainty that no harm will result from aggregate exposure to saponins of *Quillaja saponaria* residues, including dietary exposures and all other exposures for which there is reliable information.

II. OVERVIEW

A. ACTIVE INGREDIENT OVERVIEW

Common Name:	Saponins of Quillaja saponaria
Chemical Names:	Saponins of <i>Quillaja saponaria</i> (bidesmosidic derivatives of quillaic acid with a trisaccharide at C-3 and an oligosaccharide in C-28)
Trade & Other Names:	Quillaja Extract
CAS Registry Number:	68990-67-0
OPP Chemical Code:	097095
Basic Manufacturer:	Desert King Chile Ltd. 77 Antonio Bellet, Suite 401 Providencia, Santiago, Chile

B. USE PROFILE

Pesticide uses and application methods include the following:

Type of Pesticide: Biochemical pesticide; nematicide; fungicide.

Use Sites: Vineyards, orchards, field crops, ornamentals.

Target Pests: Nematodes, pathogenic fungi.

Formulation Type: Liquid.

Method and Rates of Application:

Quillaja Extract may be applied using ground equipment with a band sprayer, soil fertilizer shanks, drip irrigation, or aboveground sprinkler systems. For ground application, apply with a band or broadcast type sprayer such as a flat-fan or hollow cone nozzle tip system. In orchards or around trees, begin application next to the tree trunk and spray at least 50% of the soil area or the area under the canopy of the tree, whichever is greater. In areas where roots are present, apply by shank injection. In chemigation applications, apply through low pressure irrigation equipment (including drip, mini-sprinklers, micro-jet sprinklers, and strip tubing) only.

For control/suppression of plant parasitic nematodes in grape, citrus, pome fruit, stone fruit, nut, horseradish, potato, radish, turnip, yam, or strawberry crops: 1.5 to 4 gallons/acre applied to the full irrigated zone one to six times per season.

For control/suppression of plant parasitic nematodes in fruiting vegetables, cucurbit vegetables, leafy vegetables, cole crops, bulb vegetables, root and tuber vegetables, and ornamental bulbs: 2.5 to 4 gallons/acre applied to the planting zone prior to planting.

For control/suppression of pathogenic fungi in grape or strawberry crops: 1 to 4 pints in 50 to 100 gallons of water/acre applied as a foliar spray every 7 to 10 days.

For control/suppression of pathogenic fungi in avocado crops: 2 to 4 quarts/acre applied to the full irrigated zone one to six times per season.

For control/suppression of *Anguina pacifica* nematode in turfgrasses: 9.0 fluid ounces per 1000 square feet or 3.0 gallons/acre, applied in a minimum of 5-7 gallons of water/100 square feet (approximately 220-300 gallons/acre) every 5 to 10 days.

Timing: For control/suppression of plant parasitic nematodes in grape, citrus, pome fruit, stone fruit, nut, horseradish, potato, radish, turnip, yam, or strawberry crops: apply just prior to or during root flushes. For fruiting vegetables, cucurbit vegetables, leafy vegetables, and cole crops: apply 1 to 7 days prior to planting. For bulb vegetables, root and tuber vegetables, and ornamental bulbs: apply prior to planting. For control/suppression of root rot in avocado: apply in early Spring when soil temperatures are optimum for root infection.

Use Practice Limitations: For control of pathogenic fungi in grape or strawberry crops: Do not tank mix with sulfur products. Do not apply within 7 days of a sulfur application. For control of *Anguina pacifica* nematode in turfgrasse: Do not water turf or sod for at least 12 hours following application. Do not exceed a concentration of 1.5% solution of Quillaja Extract in any application.

C. ESTIMATED USAGE

None used yet since this is the first registered product.

D. DATA REQUIREMENTS

The Biopesticides and Pollution Prevention Division (BPPD) reviewed data requirements for granting this registration under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). The product analysis and manufacturing process data requirements are adequately satisfied by the data submitted by the registrant for an end use product (see Table 1). Physical and chemical properties requirements are adequately satisfied by the data/information submitted as listed in Table 2. The mammalian toxicology requirements were satisfied by the data/information submitted for acute toxicity and primary irritation (see Table 3). Ecological effects data requirements were satisfied by the data/information submitted for non-target organism toxicity (Table 4) and by data/information submitted for Tier II non-target organism, fate, and expression studies. The Agency reviewed all the data/information submitted and determined that they adequately satisfy current guideline requirements. The Agency issued a product registration for Quillaja Extract, EPA Registration Number 82572-1, on July 14, 2007. In granting this product registration, the Agency does not foresee any unreasonable adverse effects to humans and the environment from the use of saponins of *Quillaja saponaria* when used as directed by the product labeling.

E. REGULATORY HISTORY

Desert King Chile, Ltd. submitted an application for the registration of the end use product (EP) Quillaja Extract, EPA Registration Number 82572-1, containing the active ingredient saponins of *Quillaja saponaria*, on August 26, 2005. A notice of receipt of an application for registration of Quillaja extract, containing saponins of *Quillaja saponaria* as an active ingredient, was published in the Federal Register on April 5, 2006 (71 FR 17095) with a 30-day comment period. No comments were received following this publication.

Saponins of *Quillaja saponaria* is a new active ingredient for a pesticide formulation. The EP is intended to be used to control of nematodes and pathogenic fungi in turfgrasse and ornamental and food crops. A conditional registration for this active ingredient was issued on July 14, 2007.

F. CLASSIFICATION

On September 7, 2000, the Biochemical Classification Committee determined that saponins of *Quillaja saponaria* can be classified as a biochemical pesticide due to its apparent non-toxic mode of action.

G. FOOD CLEARANCES/TOLERANCES

The registrant has filed a petition (PP 5F6982) proposing to establish an exemption from the requirement of a tolerance for residues of Quillaja Extract in or on all food commodities (71 FR 13388).

On August 1, 2007, residues of the biochemical pesticide *Quillaja saponaria* extract (saponins), were exempt from a tolerance in or on all food commodities (72 FR 41931).

III.SCIENCE ASSESSMENT

A. PHYSICAL/CHEMICAL PROPERTIES ASSESSMENT

All product chemistry data requirements for the registration of saponins of *Quillaja saponaria*, when formulated into the end use product Quillaja Extract, have been satisfied.

1. Product Identity and Mode of Action

a. Product Identity

The active ingredient saponins of *Quillaja saponaria* represents 8.60% by weight of the EP Quillaja Extract, which is a dark brown liquid with a sweet, pungent odor. The saponins are derived by extraction from logs and bark of the soapbark tree (*Quillaja saponaria*).

The descriptions of the product formulation and production process, as well as the formation of impurities, were examined by the Agency and found to be acceptable in meeting current guideline standards. A preliminary analysis was conducted to determine the saponins of *Quillaja saponaria* content in five batches of Quillaja Extract, and the results were determined to be acceptable by the Agency. The analytical method is high pressure liquid chromatography.

b. Mode of Action

Quillaja Extract inhibits the growth of pathogenic fungi and nematodes.

2. Physical and Chemical Properties Assessment

The physical and chemical characteristics of Quillaja Extract were submitted to support the registration. The product chemistry requirements are summarized in Table 1. The physical and chemical properties of Quillaja Extract are summarized in Table 2.

TABLE 1. Product Chemistry Data Requirements for Quillaja Extract				
OPPTS GUIDELINE NO.	STUDY	RESULTS	MRID NO.	
830.1550 to 830.1670	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	Submitted data satisfy the data requirements for product identity, manufacturing process, and discussion of formation of impurities.	46568401	
830.1700	Analysis of samples	Submitted data satisfy the data requirements for analysis of samples.	46568401	
830.1750	Certification of limits	Limits listed in the CSF are adequate / acceptable.	46568401	
830.1800	Analytical method	Acceptable.	46568401	

TABLE 2. Physical and Chemical Properties for Quillaja Extract ^a			
OPPTS O	Guideline Reference No./Property	Description of Result	
830.6302	Color	Dark brown ^b	
830.6303	Physical State	Liquid at room temperature	
830.6304	Odor	Sweet, pungent ^b	
830.6313	Stability	Stable for at least 2.2 years when stored in the original containers at ambient temperature. Quillaja Extract is stored and shipped in HDPE containers. There will be no contact with metals or metal ions during storage or shipment. ^b	
830.6314	Oxidation/Reduction:	The product contains nominally 67% water and none of the	
Ch	emical incompatibility	ingredients is a strong oxidant or reductant.	
830.6315	Flammability	The product is not flammable and contains nominally 67% water and no volatile or flammable components.	
830.6316	Explodability	The product contains 67% water and no explosive ingredients.	
830.6317	Storage Stability	Stable for at least two years when stored in the original container.	
830.6319	Miscibility	Not applicable, the product will not be used with non-aqueous solvents.	
830.6320	Corrosion Characteristics	The product contains nominally 67% water and none of the ingredients is a strong oxidant or reductant.	
830.6321	Dielectric Breakdown Voltage	Not applicable, the product is not intended for use around electrical equipment.	
830.7000	pН	4.9 under ambient conditions.	
830.7050	UV/Visible	Not applicable.	
830.7100	Viscosity	29-37 mPa (kinematic viscosity)	
830.7200	Melting Range	Not applicable; the product is liquid at room temperature	
830.7220	Boiling Range	105-107°C ^b	
830.7300	Bulk Density	1.1435-1.1438	
830.7370	Dissociation Constant in Water	Not applicable; does not dissociate.	
830.7550	Partition Coefficient	Not applicable.	
830.7840	Water Solubility	The product is aqueous.	
830.7950	Vapor Pressure	The product does not vaporize at room temperature and does not have a measurable vapor pressure.	

^aData from MRID 46568402 unless otherwise noted.

bData from MRID 46972502

B. HUMAN HEALTH ASSESSMENT

The mammalian toxicity studies and other data/information submitted to support the registration application for saponins of *Quillaja saponaria* satisfy the requirements to register a new biochemical pesticide intended for food and non-food uses.

1. Toxicology Assessment

Adequate mammalian toxicology data/information are available to support registration of the EP Quillaja Extract. No additional toxicological data are needed.

a. Acute Toxicity

The submitted acute toxicity guideline studies are summarized in Table 3. This product is in Toxicity Category III for acute oral and acute dermal toxicity, Toxicity Category I for primary eye irritation, and Toxicity Category IV for acute inhalation toxicity and primary dermal irritation. The product is not a dermal sensitizer. Based on the review and analysis

of the guideline studies, no additional toxicity data are required to support food or nonfood uses of this biochemical.

TABLE 3. Mammalian toxicity requirements for saponins of Quillaja saponaria ¹			
Study/OPPTS Guideline No.	Results	Toxicity category	MRID No.
Acute oral toxicity (870.1100)	LD ₅₀ >3000 mg product/kg Acceptable	III	46608101
Acute dermal toxicity (870.1200)	LD ₅₀ >4000 mg product/kg Acceptable	III	46608102
Acute inhalation toxicity (870.1300)	LC ₅₀ >2 mg product/L Acceptable	IV	46774901
Primary eye irritation (870.2400)	Corneal opacity was noted on 3/3 rabbits at 24 hrs post-instillation with symptoms clearing on one rabbit by 48 hrs, on another rabbit by 72 hrs, and persistence on the third rabbit through 72 hrs.	I ²	46608103
Primary dermal irritation(870.2500)	Acceptable Very slight erythema was noted on 3/3 rabbits one hour after patch removal, with clearance on one rabbit by 24 hrs and on two rabbits by 48 hrs; not an irritant. Acceptable	IV	46608104
Dermal sensitization (870.2600)	Test and naive control animals showed no positive signs of reactivity 24 and 48 hrs after challenge. Acceptable	Not a sensitizer	46608105
Hypersensitivity incidents (885.3400)	Must be reported		
Genotoxicity, immune response, and teratogenicity (870.5000, 880.3550, 870.3700	No studies submitted; waivers requested on long history of oral acute and chronic exposure to humans in food. The a.i. is also an EPA List 4A inert and is an FDA-approved flavoring agent and food additive (21 CFR 172.510). Acceptable	Not genotoxic or a mutagen	
90-Day feeding (870.3100)	NOAEL (rat, male) = 2470 mg/kg/day NOAEL (rat, female) = 3030 mg/kg/day Acceptable	No subchronic oral toxicity is expected ³	46608106
90-Day dermal toxicity (870.3250)	No studies submitted; waiver request based on lack of prolonged human dermal exposure and no intentional application to human skin. No toxicity in oral acute and chronic studies; dermal metabolism not expected to differ from oral metabolism. The a.i. is also an EPA List 4A inert. Acceptable	No subchronic dermal toxicity is expected	46608110
90-Day inhalation toxicity (870.3465)	Waived		46608110
Combined chronic toxicity/carcinogenicity Non-guideline studies	84-wk NOAEL (mouse) >700 mg a.i./kg/day 84-wk LOAEL (mouse) = 2200 mg a.i./kg/day ⁴ 2-yr NOAEL (rat) >1500 mg/kg/day Acceptable	Not a chronic toxicant; not a carcinogen	Phillips, et al. (1979) Drake, et al. (1982

¹Test substance was TGAI/EP containing 8.60% Quillaja extract

²The test substance is conservatively considered to be at least a moderate irritant, although it is not corrosive. Since it is not known when corneal opacity would have cleared, the primary eye irritation study is classified in Toxicity Category I.

³Based on a lack of toxicity in long term chronic studies.

⁴Based on reduced body weight that was due to reduced food intake; reduced food intake likely due to taste aversion to saponins.

b. Mutagenicity, Developmental Toxicity, and Immunotoxicity

The registrant requested waivers for the mutagenicity (OPPTS 870.5100), developmental toxicity (OPPTS 870.3700), and immunotoxicity (OPPTS 870.7800) testing requirements based on the following information: Humans are regularly exposed to Quillaja saponins via their use as an FDA-approved flavoring agent and food additive (21 CFR 172.510). Undiluted Quillaja saponaria extracts are used in soft drinks at levels of 100-500 mg/kg (WHO, 2002). The Joint WHO/FAO Expert Committee on Food Additives (WHO, 2002) established an acceptable daily intake (ADI) of Quillaja saponins of up to 5 mg/kg/day. The mean intake of Quillaja extracts in the US from soft drinks (the major food use) is as much as 0.54 mg/kg/day, or 11% of the ADI (WHO, 2006). Quillaja extracts are also used as emulsifiers in baked goods, candies, frozen dairy products, gelatins, and puddings. The active ingredient is not a mutagen nor is it related to any known classes of mutagens. Chronic feeding studies have demonstrated that Quillaja saponins are not carcinogenic in mice or rats fed up to 2200 mg/kg in the diet (Phillips et al., 1979; Drake et al., 1982). Saponins have been demonstrated to have anticarcinogenic properties (Li et al., 2002; Rao and Sung, 1995) and to stimulate the immune system (Kenarova et al., 1990; Wu et al., 1990). Dietary levels of Quillaja saponin (up to 700 ppm in feed) stimulated the immune systems of piglets fed for 20 days post-weaning (Ilsey et al., 2005). Based on the information provided, the request for waivers of mutagenicity, developmental toxicity, and immunotoxicity testing requirements was granted by the Agency.

c. Subchronic Toxicity

The requirement for a 90-day feeding study (OPPTS 870.3100) was satisfied by submission of a study in which Quillaja extract was administered to 15 CFE rats at dietary concentrations equivalent to 0, 360, 1180, or 2470 mg/kg bw/day for males and 0, 440, 1370, or 3030 mg/kg bw/day for females for 13 weeks. Additional groups of 5 rats were administered 0, 2.0, or 4.0% test material for 2 weeks or 6 weeks for interim evaluations. There were no treatment-related effects on morality, clinical signs, hematology and erythrocyte osmotic fragility, clinical chemistry, urinalysis, or gross and histologic pathology. High-dose males had a mean weight loss during the first 24 hours followed by statistically significant decreases in absolute body weight (at least 4-8% less than controls) until day 78, and the cumulative body weight gain of this group was 89% of controls. High-dose females had statistically significant decreases in absolute body weight during the first two weeks of treatment, and mid- and high-dose females had marginally decreased body weight gain over the 0-29 day interval (both 92% of controls). Markedly decreased food consumption was seen on day 1 at the mid- and high-dose

treatment levels in both sexes (males: 76% and 48%; females: 85% and 41% of controls, at the mid- and high-dose concentrations, respectively; n.s.). Mid- and high-dose males also had decreased mean overall water consumption (90% and 82% of controls; p<0.05 and p<0.001, respectively). Decreased absolute and relative liver weight were seen in males at the 2.0% and 4.0% dietary concentrations at weeks 2, 6, and 13, but it is unlikely that these resulted from direct toxicity of the test material on the organs themselves as there were no correlated clinical chemistry changes at any of the time points, and no histopathological changes were noted at week 13. The NOAEL for the study was the highest dose tested of 2470 mg/kg bw/day for males and 3030 mg/kg bw/day for females.

Data waivers were granted for the 90-day dermal (OPPTS 870.3250) and 90-day inhalation (OPPTS 870.3465) testing. Dermal metabolism of the product is not expected to differ from its oral metabolism. In the acute guideline studies, the product was demonstrated to have no acute dermal toxicity ($LD_{50} > 4000 \text{ mg/kg}$), was not a dermal irritant, and was not a dermal sensitizer (MRIDs 46608102, 46608104, 46608105). Prolonged human dermal exposure is unlikely. The product label statement for personal protective equipment (PPE) requires applicators and handlers to wear long-sleeved shirts and long pants, chemical resistant gloves made of waterproof material, and shoes plus socks, which will mitigate dermal exposure.

Based on the lack of toxicity (Toxicity Category IV) demonstrated in the acute inhalation toxicity study (MRID 46774901) and the anticipated lack of repeated inhalation exposure under the conditions of product use at a concentration that is likely to be toxic, the requirement for a 90-day inhalation study was waived by the Agency.

d. Chronic Exposure and Oncogenicity Assessment

Repeated dose studies are conditionally required if the potential for adverse chronic effects is indicated based on: 1) the subchronic effect levels established in Tier I subchronic oral, inhalation, or dermal studies, 2) the pesticide use pattern, or 3) the frequency and the level of repeated human exposure that is expected. Oncogenicity studies are required only if the active ingredient or any of its metabolites, degradation products, or impurities produced in Tier I studies any morphologic effects in any organ that potentially could lead to neoplastic changes. None of the results of the submitted studies triggered the need for chronic exposure or oncogenicity testing.

Although not required, the registrant submitted two acceptable nonguideline studies. In the first study (Drake et al., 1982), groups of 48 male and 48 female Wistar rats were administered Quillaja extract at concentrations of 0, 0.3, 1.0, and 3.0% for 2 years. The equivalent doses in mg/kg bw/day were 120, 390, and 1175 for males, and 147, 497, and 1500 for females. No treatment-related toxic effects or mortality were observed. Although not statistically significant, high-dose males and females weighed 8% and 7% less than controls, respectively, by the end of the 106 week study period. The average daily food consumption by all treated males and females was generally 1-10% less than controls, although there were measurement intervals when both sexes consumed more than controls by as much as 12-16% in a manner that was not dose-related. No treatment-

related effects were observed on hematologic, clinical chemistry, or urinalysis parameters. Necropsies were negative. The incidence of benign tumors and carcinomas of the thyroid, pituitary, and peritoneal cavity were either not statistically different from controls, or fell within the spontaneous incidence rate for the Wistar rat. A lowestobserved-adverse-effect level (LOAEL) of Quillaja extract in rats was not identified for either sex. The no-observed-adverse-effect level (NOAEL) was 3.0% in the diet (1175 mg/kg/day for males and 1500 nig/kg/day for females). Quillaja extract was not a chronic toxicant nor was it a carcinogen in the rat under the conditions of this study.

An earlier non-guideline study that gave similar results (Phillips et al., 1979) was also submitted. Groups of 48 male and 48 female TO-strain mice were administered Quillaja extract at concentrations of 0, 0.1, 0.5, and 1.5% for 84 weeks. There were no treatment-related effects on death rate or any histopathological factors, including tumors, although there was reduced body weight gain at the highest dose (equivalent to 2200 mg/kg/day). Reduced body weight was associated with reduced food intake, which may have been caused by aversion of food treated with high levels of saponins. The NOAEL was 700 mg Quillaja extract/mg/day. Quillaja extract was not a chronic toxicant nor was it a carcinogen in the rat under the conditions of this study.

e. 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 the active ingredient saponins of *Quillaja saponaria* 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. Dietary Exposure and Risk Characterization

The Agency is not concerned about dietary exposure *Quillaja* Saponins because of the long history of human consumption as a food additive and flavoring agent without any reports of adverse effects. Quillaja Extract is in Toxicity Category III for acute oral toxicity. Dietary exposure is likely to occur only via the crops (grapes and strawberries) for which foliar applications of product are intended to control pathogenic fungi. The product label use directions indicate both commodities can be treated with a maximum of four pints of product at seven-day intervals, with no limit on the number of applications. Using the Agency's Terrestrial Exposure Model (T-Rex v. 1.2.3) and a worst-case scenario of one spray application every seven days for 52 weeks, the maximum potential residues of quillaja saponins (upper bound Kenaga value) would never exceed 1.26 mg a.i./kg of strawberries or grapes. Based on annual consumption values, the average daily intake of Quillaja saponins from treated strawberries, grapes, and raisins (processed from treated grapes) together is estimated to be 0.18 mg/kg body wt. This is well below the established ADI of 5 mg/kg body wt (WHO, 2002). Due to the expected low exposure to humans and the low toxicity to laboratory animals, no risk to human health is expected.

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

a. Occupational Exposure and Risk Characterization

The potential for dermal, eye, and inhalation exposure to saponins of *Quillaja saponaria* for handlers and applicators is mitigated as long as the Quillaja Extract EP is used according to label directions. The Agency will require the label to include the appropriate signal word and precautionary statements, including the requirement for personal protective equipment, to mitigate any risk of exposure.

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

No indoor residential, school, or day care uses currently appear on the product label. The product is not intended for homeowner (residential) use, and residential exposure is not expected. Should accidental exposure occur, the health risk is expected to be minimal due to the low concentration of saponins in the product and the results of the mammalian acute toxicity studies.

5. Drinking Water Exposure and Risk Characterization

No significant drinking water exposure is expected from accumulation of saponins of *Quillaja saponaria* in the aquatic environment when the Quillaja Extract EP is used

according to label directions. Mono- and bidesmosidic saponins degrade readily in the environment (3-5 days; Molgaard et al., 2000).

6. Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children

FFDCA section 408 provides that the Agency shall apply an additional tenfold margin of exposure (safety) for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the database unless the Agency determines that a different margin of exposure (safety) will be safe for infants and children. Margins of exposure (safety) are often referred to as uncertainty (safety) factors. In this instance, based on all the available information, the Agency has concluded that there is reasonable certainty that no harm to infants and children or adults will result from the use of saponins of *Quillaja saponaria* as registered.

7. Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation

There is reasonable certainty that no harm to the US population will result from aggregate exposure to residues of saponins of *Quillaja saponaria*. This includes all exposures for which there is reliable information. The Agency arrived at this conclusion based on the low level of toxicity of Quillaja Extract and the already widespread exposure to Quillaja saponins without any reported adverse effects on human health. The risks from aggregate exposure via oral, dermal and inhalation exposure are a compilation of three low-risk exposure scenarios and are negligible. Since there are no threshold effects of concern, the provision requiring an additional margin of safety does not apply. Therefore, the Agency has not used a margin of exposure (safety) approach to assess the safety of saponins of *Quillaja saponaria*.

8. Cumulative Effects

When used as proposed, residues of saponins of *Quillaja saponaria* will not reach levels that are of toxicological concern. Because of its low toxicity, no cumulative effect with other toxins is anticipated.

9. Risk Characterization

The Agency considered human exposure to saponins of *Quillaja saponaria* in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that no unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, will result from the use of saponins of *Quillaja saponaria* when label instructions are followed.

C. ENVIRONMENTAL ASSESSMENT

1. Ecological Effects Hazard Assessment

Non-target organism toxicity study data are summarized in Table 4. An acceptable guideline avian acute oral toxicity study (OPPTS 850.2100) was submitted, in which groups of northern bobwhite (*Colinus virginianus*) were administered a single nominal oral dose of 0, 292, 486, 810, 1350, or 2250 mg of Quillaja Extract/kg body weight and observed for 14 days. The acute oral LD₅₀ was >2250 mg Quillaja Extract/kg body wt (practically non-toxic), the highest dose tested. The no-mortality level was 1350 mg/kg (the single mortality was likely not treatment-related), and the no-observed-effect level (NOEL) was 292 mg/kg based on food aversion, erect posture, and/or ruffled appearance.

No avian dietary study (OPPTS 850.2100) was submitted. In lieu of a study, the registrant submitted a waiver request supported by a study obtained from the technical literature (Jenkins and Atwal, 1994). In this study, 200 one-day old, unsexed chicks, Meat Strain 31, were fed Quillaja saponins at 0.1, 0.3, or 0.9% [equivalent to 1000, 3000, and 9000 ppm (mg Quillaja saponins/kg feed)] in the diet for 28 days. All chicks survived and gained weight throughout the study. Weight gain was significantly reduced only at the highest dose (9000 ppm) which was associated with reduced food intake. Other effects at the high dose included reduced lipid digestibility and increased cholesterol excretion, but there were no effects on blood concentration of total cholesterol or high density lipoprotein cholesterol. There was equivocal evidence that absorption of vitamins A and F was reduced. Otherwise, no clinical signs of toxicity were reported for chicks at any dose level. Based on reduced food intake and subsequent weight gain, the LOAEL was 9000 ppm and the NOAEL was 3000 ppm Quillaja saponins in the diet.

In an acceptable freshwater fish LC_{50} study (OPPTS 850.1075) (96-hour static-renewal bioassay), common carp (*Cyprinus carpio*) were exposed to a nominal concentration of 100 mg/L QL Agri 35°B (Quillaja Extract) in dechlorinated tap water. Control fish were exposed to dechlorinated tap water only. There was no mortality in the treatment or control groups, and all fish appeared normal during the test. The 96-hour LC_{50} for common carp in this test was >100 mg/L.

In two non-guideline studies obtained by the Agency, Nile tilapia (*Oreochromis miloticus*) administered diets containing up to 300-700 ppm Quillaja saponin had higher growth rates than untreated controls (Francis et al., 2001; Francis et al., 2002c). However, at dietary levels of 150 ppm Quillaja saponin for 14 weeks, one of two female fish failed to produce eggs, and at the 300 ppm dietary level, both treated females failed to produce eggs. Control females and one female at the 150 ppm dose produced eggs once every 14 days (Francis et al., 2001). In the second study, dietary levels of 700 ppm Quillaja saponin for 6 months induced a change in the normal 1:1 male:female sex ratio towards a significantly higher number of males (Francis et al., 2002c). These data would indicate that chronic exposure to dietary saponins may be fish reproductive toxicants at 300 ppm and endocrine disruptors at 700 ppm. It is noted that these studies were conducted under laboratory conditions by the same investigators, and no other studies are available that

demonstrate similar reproductive or endocrine-related effects in fish. While these studies suggest that there may be potential teratogenic and/or endocrine effects in fish at extremely high concentrations of Quillaja saponins (i.e. >150 ppm) for periods of at least 14 weeks, modeled concentrations of Quillaja saponins in surface water following application according to label use directions indicate that the expected environmental concentrations would be well below the above values (see Environmental Fate and Groundwater Data section below).

In a non-guideline study submitted by the registrant (Chen et al., 1996), Kuruma shrimp (*Penaeus japonicus*) were exposed to seven levels of purified Quillaja saponin (15 to 30 ppm) in a flow-through system for up to 96 hours. The 24-, 48-, 72-, and 96-hr EC₅₀s were 27.08, 20.83, 18.91, and 18.14 ppm, respectively. In the same study, the investigators also evaluated the effects of Quillaja saponins on growth. After 36-60 days exposure, significant reductions in growth, feeding, and molting frequency were observed with a lowest observed effect concentration (LOEC) of 0.5 ppm and a no observed effect concentration (NOEC) of 0.1 ppm. The studies indicate potential adverse effects on aquatic invertebrates with a chronic exposure of at least 36 days at \geq 0.5 ppm.

No non-target plant studies (OPPTS 850.4100) were submitted, but none is required. No plant toxicity was observed in any of the product efficacy trials conducted by the registrant (MRIDs 46608111 to 46608124 and 46631001) using a test substance that contained 35% active ingredient. Furthermore, saponins are widespread in plants and triterpenoid saponins (such as those present in the active ingredient) are common in many cultivated crops (Oakenfull, 1981). The product is not intended for use on forests or grasslands. There are no concerns for non-target plants, and no additional data are required.

No non-target insect studies or waiver requests were submitted. Little data are available regarding the effects of Quillaja saponins on insects. An Agency ECOTOX search of the literature revealed two studies regarding the effects of Quillaja saponins on larval mosquitoes. In the first study (Weisman and Chapagain, 2003), it was demonstrated that after a two day exposure to 500 and 1000 ppm Quillaja saponins, larval survival was reduced by approximately 60% and 98%, respectively. The second study reported a 24-hr LC₅₀ of 58 ppm for larval *Culex fatigans* (Tabassum et al., 1993). These levels are considered slightly toxic for aquatic invertebrates. However, it is unlikely that terrestrially-applied Quillaja saponins will cause adverse effects in aquatic insects due to their rapid degradation in the environment (see Environmental Fate and Groundwater Data section below). It also is unlikely that non-target adult insects will be adversely affected, as the *Quillaja saponaria* tree is known to host a large number of beneficial insects.

Study/OPPTS	Non-target organism toxicity requirements for sapo Results	Toxicity category	MRID No.
Guideline No.	Results	Toxicity category	
Avian acute oral	LD ₅₀ >2250 mg product/kg	Practically non-	46568412
toxicity		toxic	10500112
(850.2100)	Acceptable		
Avian dietary toxicity	28-day LD ₅₀ >9000 ppm	Practically non-	Jenkins and
(850.4100)	28-day LOAEL = 9000 ppm	toxic	Atwal (1994)
Non-guideline study	28-day NOAEL >3000 ppm		46608110
	Acceptable		
Freshwater fish LC ₅₀	LD ₅₀ >100 ppm product ²	Practically non-	46608109
Cyprinus carpio (carp) (850.1075)	Acceptable	toxic	
Fish feeding studies	8-wk 150-300 ppm Quillaja saponins in feed	No toxic effects	Francis et al.,
Cyprinus carpio (carp)	increased growth and metabolic rate	observed	2002a, 2002b
Non-guideline	Acceptable		
Two fish feeding	17-day old fry fed dietary Quillaja saponins up to	No toxic effects	
studies Oreochromis niloticus	700 ppm in feed for 8 wks; increased growth rate; shift in 1:1 male:female ratio towards males was	observed, but	
(Nile tilapia)	observed at all dose levels, was statistically	possible endocrine effects	
Non-guideline	significant at highest dose.	enects	
Non-guidenne	Supplemental		
	Adult tilapia fed dietary Quillaja saponins at 150-	No toxic effects	
	300 ppm in feed for 14 wks.	observed, but	
	At 150 ppm: 1 of 2 females produced no eggs	potential	
	At 300 ppm: 2 of 2 females produced no eggs	teratogenic effects	
	Supplemental		
Aquatic penaeid acute	48-hr $EC_{50} = 20.83$ ppm (mortality)	Slightly toxic	Chen et al.,
toxicity	Acceptable		1996
(Aquatic invertebrate)	36-day LOEC = 1 ppm		46608110
OPPTS 850.1045 Non-guideline	60-day LOEC = 0.5 ppm		
Non-guidenne	60-day NOEC = 0.1 ppm		
	(based on reduced growth, feeding, molting frequency)		
	Supplemental		
Non-target plant toxicity	No toxic effects reported in any efficacy studies	No toxic effects observed	
Non-target insect	No studies or waivers submitted	No known toxic	Tabassum et
testing (880.4350)	Culex fatigans 24-hr $LC_{50} = 58 \text{ ppm}^3$	effects on terrestrial insects; slightly toxic to aquatic larvae	al., 1993

¹Test substance was the TGAI/EP containing 8.60% Quillaja extract (determined by 5-batch analysis) ²Test substance was QL-35B containing 34.4% Quillaja extract (determined by brixometer) ³Data obtained via ECOTOX literature search

2. Environmental Fate and Ground Water Data

In response to an Agency request for Tier II non-target organism and environmental fate studies, the registrant submitted a request for waive the testing guidelines for Tier II non-target organism, fate, and expression studies.

No study was submitted for the partition coefficient, K_{ow} requirement (OPPTS 830.7560), but none is required. The K_{ow} is highly correlated with water solubility, soil/sediment

sorption coefficient, and bioaccumulation (US EPA, 1996). It is possible to estimate whether the K_{ow} will be relatively low or high based on a compound's known characteristics. The water solubility of Quillaja Extract is very high (90,000 ppm). As a result, Quillaja Extract is expected to desorb fairly rapidly from soil and not bioconcentrate. Surrogate data for saponins show that they have a short half-life in soil and are readily degraded by microorganisms. The high solubility, short half-life in soil, and ready degradation by microorganisms indicate that Quillaja Extract will have a very low K_{ow} . Thus, the low default K_{ow} in the screening level environmental fate model used below should be adequate to estimate potential environmental concentrations of Quillaja saponins. The submitted information is acceptable to support the requested waiver.

No studies were submitted for UV Absorption (OPPTS 830.750), Volatility (OPPTS 830.7950), Soil Thin Layer Chromatography (OPPTS 835.1210), Sediment and Soil Absorption/Desorption (OPPTS 835.1220), Hydrolysis as a Function of pH (OPPTS 835.2110), Direct Photolysis Rate in Water by Sunlight (OPPTS 835.2210), and Fish Life Cycle Toxicity (OPPTS 850.1400) requirements, but none is required. Sufficient data are available from the technical literature to show that Quillaja saponins readily biodegrade in soil and water, and these data were used by the registrant to run a screening level model to estimate environmental concentrations of Quillaja saponins resulting from its agricultural use. Estimates of Quillaja saponins in surface water were derived using version 2 of EPA's Generic Estimated Environmental Concentration (GENEEC) model. GENEEC estimates concentrations of pesticides in surface water following their application to agricultural fields. Data input into the model are given in Table 5.

TABLE 5. Inputs used for GENEEC modeling ¹		
GENEEC Parameter	Input	
Soil aerobic metabolism half life	7.73 days ²	
Aquatic half life	0.66 days^3	
K _{oc}	0 (no data default) ⁴	
Solubility	90,000 ppm	
Application method	High boom ground spray ⁶	
Droplet size	Fine ⁶	
Incorporation depth	0 inches ⁶	
Photolysis time	0 (no default data) ⁶	
Application rate	2.15 lbs/A ⁵	
Maximum applications/year	106	
Reapplication interval	7 days ⁶	

¹Table from p. 7, MRID 46972503

² The soil aerobic metabolism half-life was taken from Chen et al. (1996). The mean time for 50% degradation of the saponins was 5.8 ± 2.28 days. The upper 90% confidence limit on the mean value was calculated to be 7.73 days and was used as the input.

³The aerobic aquatic half-life in water was taken from Molgaard et al. (2000) using saponins extracted from berries of the Endod plant.

⁴The K_{oc} was input into the model as 0, based on the characteristics of Quillaja Extract. The 0 input caused the model to default to the low conservative K_{oc} of 0.09.

⁵The application rate of 2.15 lbs/acre was calculated using the maximum label rate of 2.5 gal/acre, the product density, and the upper certified limit for saponins given on the CSF. Since GENEEC allows only a single input for application rate, the 2.15 lbs acre rate was assumed for all 10 applications, even though

the label rate for the second through tenth applications corresponds to only 0.36 lbs/acre/application. As a result, the potential concentration of Quillaja saponins in surface water is overestimated.
⁶All other inputs were from the proposed product label or were the EFED-recommended defaults.

Based on the estimated environmental concentrations (EECs) from the GENEEC model (Table 6) and results from aquatic studies in the technical literature, risk quotients (RQs) were derived to evaluate the potential risk to aquatic animals (Table 7). RQs are normally calculated by dividing the EEC by the LC_{50} or the EC_{50} ; in this case they were calculated based on target concentrations cited in the literature. The calculated RQs were well below the EPA levels of concern (LOC) for fish and aquatic invertebrates (including endangered species) chronically exposed to a pesticide. Based on the information/data provided by the registrant, there are no concerns for fish or aquatic invertebrates when the product is applied according to label directions. The submitted material is acceptable to support the requested waivers.

TABLE 6. Generic estimated environmental concentrations (GEECs) from the GENEEC model used for chronic exposure risk quotients		
GEEC	Concentration (ppb)	
21-day maximum	28.49	
60-day maximum	9.97	
90-day maximum	6.65	

Table from p. 8, MRID 46972503

TABLE 7. Risk quotients based on estimated Quillaja sapnonins concentrations in water				
Organism	Target concentration ¹	60-day EEC (ppb)	RQ	
Tilapia	150 ppm	9.97	0.00006	
Penaeid shrimp	0.1 ppm NOEC	9.97	0.0997	
21- Day EEC (ppb)				
Penaeid	0.1 ppm NOEC	28.49	0.285	

Table from p. 9, MRID 46972503

¹Lowest chronic endpoint found in literature (Chen et al., 1996 for penaeid shrimp; Francis et al., 2001 and 2002c) for tilapia.

Specific data that characterize the aerobic aquatic biodegradation of Quillaja saponins are not available. The registrant requested a waiver for the aerobic aquatic biodegradation requirement (OPPTS 835.3100) based on a submitted OECD Guideline 301F study from the technical literature (Molgaard, et al., 2000) that characterized the degradation of saponins extracted from the Endod plant (*Phytolacca dodecandra*) in water under aerobic conditions. These results can be used as surrogate data, since the saponins extracted from Endod berries and from Quillaja bark are both triterpenoid saponins (although Endod saponins are monodesmosidic and Quillaja saponins are bidesmosidic). The study showed that the saponins were completely degraded to carbon dioxide and water within five days, with a biodegradation half-life of 15.8 hours. This suggests that the Quillaja saponins are also readily biodegradable in water under aerobic conditions, and an additional study is not necessary. The submitted study was acceptable to support the requested waiver. Specific data that characterize the aerobic soil biodegradation of Quillaja saponins are not available. In support of a waiver request for the soil biodegradation requirement (OPPTS 835.3300), the registrant submitted a study in which ¹⁴C labeled saponins were extracted from alfalfa seedlings and assayed for biodegradation in four non-sterile soils (two silt loams and two clay loams) (Okumura et al., 1999). Biodegradation was determined by measuring ¹⁴CO₂ evolution from the soil. After 14 days, ¹⁴CO₂ release from the four soils ranged from 57.4 to 69.9% of the ¹⁴C- labeled saponins added. The aerobic half-life of the saponins in the soils was approximately six days. These results indicate that saponins are readily biodegraded in soil under aerobic conditions. The submitted study is acceptable to support the requested waiver.

3. Ecological Exposure and Risk Characterization

The potential for exposure to non-target wildlife is minimal. Based on the results/information presented in the Environmental Fate and Groundwater Data section above, it is highly unlikely that non-target organisms, particularly aquatic organisms, would be exposed to potentially toxic levels of saponins via runoff and/or movement through the soil. The saponins undergo rapid biodegradation in soil and water, and no unreasonable adverse effects to the environment are expected from the use of the Quillaja Extract EP when label instructions are followed.

D. EFFICACY DATA

Efficacy data were submitted by the registrant in support of label claims of product performance. Submission of product performance data (OPPTS 810.3000) is listed as a requirement for all pesticide products. Customarily, the Agency requires efficacy data to be submitted for review only in connection with the registration of products directly pertaining to the mitigation of disease bearing human health organisms and certain designated quarantine pests, i.e., ticks, mosquitoes, fleas, Mediterranean fruit flies, gypsy moths, Japanese beetles, etc. In this case, the registrant originally submitted summaries of 14 efficacy studies (MRIDs 46608111 to 46608124 and MRID 46631001) conducted to evaluate the efficacy of a 35% Quillaja Extract formulation mixed with an herbicide as a fungicide, nematicide, plant growth regulator, and herbicide adjuvant. As a group, the efficacy studies were unacceptable for use in supporting most of the proposed label claims. Only three studies were considered acceptable (MRIDs 46608115, 46608116, and 46608117) and only supported label claims for use of the product in controlling powdery mildew on squash. The remainder of the studies did not support label claims for nematicidal activity or plant growth regulator activity. There were no reports of phytotoxicity in any of the treated crops.

In response to a request for additional efficacy studies to support proposed label claims, the registrant submitted more efficacy studies (MRIDs 46972504 to 46972510). Most of these studies demonstrated some nematicidal efficacy. In the first study (MRID 46972504, (classified as supplemental), the data demonstrated that nematode populations are reduced in infested potting soils containing tomato seedlings and treated with the Quillaja saponin product. In the second study, conducted in a Chardonnay grape

vineyard, the data demonstrated that the test material had important nematicidal effects and showed a similar control and fruit yields when compared to synthetic chemical nematicides.

IV. Risk Management Decision

A. DETERMINATION OF ELIGIBILITY FOR REGISTRATION

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

To satisfy criteria "A" above, saponins of *Quillaja saponaria* has fungicidal and nematocidal properties. Criteria "B" is satisfied by the current label and the data presented in this document. It is believed that this pesticidal active ingredient will not cause any unreasonable adverse effects when used according to label directions, satisfying Criteria "C." Criteria "D" is satisfied in that the pesticide is not expected to cause adverse environmental effects. Therefore, saponins of *Quillaja saponaria* is eligible for registration.

B. REGULATORY POSITION

1. Conditional Registration

All of the data requirements are fulfilled and BPPD granted a conditional registration for the active ingredient, saponins of *Quillaja saponaria*.

Tolerance Establishment

The registrant has filed a petition (PP 5F6982) proposing to establish an exemption from the requirement of a tolerance for residues of Quillaja Extract in or on all food commodities (71 FR 13388).

On August 1, 2007, residues of the biochemical pesticide *Quillaja saponaria* extract (saponins), were exempt from a tolerance in or on all food commodities (72 FR 41931).

2. CODEX Harmonization

There are no CODEX maximum residue levels established for saponins of *Quillaja* saponaria.

3. Nonfood Registrations

There are no non-food issues at this time.

4. Risk Mitigation

There are no significant risk issues identified for dietary risk, residential risk, or ground and surface water contamination. Mitigation measures for occupational routes of exposure are required in that applicators and other handlers are required to wear appropriate PPE. Risk to non-target organisms will be mitigated by appropriate label precautions.

5. Endangered Species Statement

Based on the submitted studies and other information, as well as results of an extensive ECOTOX literature search, the Agency has determined that use of saponins of *Quillaja* saponaria as an active ingredient will have **No Adverse Effects (NAE)** on threatened and/or endangered species when products containing saponins of *Quillaja saponaria* are used according to label directions.

C. LABELING RATIONALE

The Agency's position is that the labeling for the product containing saponins of *Quillaja* saponaria as the active ingredient complies with current pesticide labeling requirements imposed under FIFRA and 40 CFR 156.10.

1. Human Health Hazard

a. Worker Protection Standard

Any product whose labeling reasonably permits use in the production of an agricultural plant on any farm, forest, nursery, or greenhouse, must comply with the labeling requirements of Pesticide Registration (PR) Notice 93-7, "Labeling Revisions Required by the Worker Protection Standard (WPS)," and PR Notice 93-11, "Supplemental Guidance for PR Notice 93-7," which reflect the requirements of EPA's labeling regulations for worker protection statements (40 CFR part 156, subpart K). These labeling revisions are necessary to implement the Worker Protection Standard for Agricultural Pesticides (40 CFR part 170). Unless otherwise specifically directed, all statements required by PR Notices 93-7 and 93-11 are to be on the product label exactly as instructed in those Notices. The labels and labeling of all products must comply with EPA's current regulations and requirements as specified in 40 CFR 156.10 and other applicable notices, such as, and including the WPS labeling.

Uses of the Quillaja Extract EP containing saponins of *Quillaja saponaria* are subject the requirements of the WPS, and as such it has the appropriate language required by the standard. For uses of this product that are covered by the WPS, worker entry into treated areas without protective clothing is not allowed during the restricted entry interval of 12 hours. The PPE requirement for early entry into treated areas that is permitted under the WPS and that involves contact with anything that has been treated, such as plants, soil, or water is coveralls, chemical-resistant gloves made of any waterproof material, and shoes plus socks.

b. Non-Worker Protection Standard

There are no non-worker (non-mixer/loader/applicator) human health hazard issues.

c. Precautionary Labeling

The Agency has examined the toxicological data base for saponins of *Quillaja saponaria* and has concluded that the precautionary labeling (i.e., Signal Word, First Aid statement, and other label statements) listed on the label (See Appendix C - Product Label) adequately mitigates the risks associated with the currently registered uses.

The PPE language and the user safety recommendations box immediately below the precautionary statement read as follows:

Personal Protective Equipment:

Applicators and other handlers must wear: Protective eyewear: Goggles Face Shield, or Safety Glasses Chemical resistant gloves made of any waterproof material Long sleeve shirt and long pants

Shoes and socks

User Safety Recommendations:

Users should:

•Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet. Never apply material so as to contaminate eating or drinking areas.

•Remove clothing immediately if product gets inside. Then wash thoroughly and put on clean clothing.

d. Spray Drift Advisory

An advisory statement is contained in the Directions for Use: "Do not apply this product in a way that will contact workers or other persons, either directly or through drift."

2. Environmental Hazards Labeling

The following language is to appear in this section of the label:

Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water by cleaning of equipment or disposal of equipment wash waters.

3. Application Rate

For control of plant parasitic nematodes in grape, citrus, pome fruit, stone fruit, nut, horseradish, potato, radish, turnip, yam, or strawberry crops: 1.5 to 4 gallons/acre.

For control of plant parasitic nematodes in fruiting vegetables, cucurbit vegetables, leafy vegetables, cole crops, bulb vegetables, root and tuber vegetables, and ornamental bulbs: 2.5 to 4 gallons/acre.

For control of pathogenic fungi in grape or strawberry crops: 1 to 4 pints in 50 to 100 gallons of water/acre.

For control of pathogenic fungi in avocado crops: 2 to 4 quarts/acre.

For control of *Anguina pacifica* nematode in turfgrasse: 9.0 fluid ounces per 1000 square feet or 3.0 gallons/acre, applied in a minimum of 5-7 gallons of water/100 square feet (approximately 220-300 gallons/acre).

D. LABELING

Product name: Quillaja Extract

Active Ingredient:

Saponins of Quillaja saponaria	8.60%
Other Ingredients	91.40%

Total......100.00%

Signal word is "DANGER"

The product shall contain the following information:

- B Product Name
- **B** Ingredient Statement
- **B** Registration Number
- B Signal Word (DANGER)

Label Language Requirements

The following labeling language as listed below is required for Federal registration.

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals: Danger: Causes irreversible eye damage. Harmful if swallowed or absorbed through skin. Do not get on eye or clothing. Wear protective eyewear. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum or using tobacco. Remove and wash contaminated clothing before reuse. Environmental Hazards: Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water by cleaning of equipment or disposal of equipment wash waters.

FIRST AID:

If in eyes:

Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.

Call a poison control center or doctor for treatment advice.

If swallowed:

Call a poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow.

Do not induce vomiting unless told to by a poison control center or doctor. Do not give anything to an unconscious person.

If on skin:

Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.

The following statement must accompany the First Aid text block: "Have the product container or label with you when calling a poison control center or doctor, or going for treatment." The Agency guidance also suggests including a contact telephone number for additional emergency medical treatment information.

V. ACTIONS REQUIRED BY REGISTRANTS

There are no data requirements, label changes or other responses necessary for the reregistration of the end-use product since the product is being registered after November 1984 and is, therefore, not subject to reregistration. There are also no existing stocks provisions at this time.

The Agency evaluated all of the data submitted in connection with the initial registration of saponins of *Quillaja saponaria* and determined that these data are sufficient to satisfy current registration guideline requirements. Therefore, the active ingredient saponins of *Quillaja saponaria* is eligible for registration. No additional data are required to be submitted to the Agency at this time.

Not withstanding 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 CFR Part 158.690(c), guideline reference number 152-16.

VI. APPENDIX A

Table 8 lists the use sites for the product.

TABLE 8. Use Sites	
Quillaja Extract Food Crops: grapes; citrus; pome fruit (apple, loquat, mayhaw, pear, quince); stone fruit (apricot, cherry, nectarine, peach, plum, prune); nuts (almond, cashew, macadamia, pecan, walnut); strawberries, fruiting vegetables (eggplant, peppers, tomatillo, tomato); cucurbit vegetables (cucumber, gherkin, edible gourd, melon, pumpkin, squash, watermelon); leafy vegetables (celery, endive, lettuce, purslane, spinach, swiss chard); cole (broccoli, cabbage, kale, kohlrabi, mustard greens, mustard spinach, rape greens); bulb vegetables (garlic, leek, onion, shallot); root and tuber vegetables (arrowroot, artichoke, beet, burdock, canna, carrot, ginger, ginseng, horseradish; potato; radish; turnip; yam); avocado. Non-food crops: ornamental bulbs. Turfgrasses.	Official date registered: July 14, 2007

VII. APPENDIX B

REFERENCES

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