BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Tea Tree Oil
PC Code : 028853

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

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BIOPESTICIDES REGISTRATION ACTION DOCUMENT (BRAD) TEAM

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I. EXECUTIVE SUMMARY:

Tea tree oil is a new biochemical pesticide active ingredient intended for non-food use treatment as a fungicide/bactericide on the following food commodities: leafy vegetables (group 4), fruiting vegetables (group 8), cucurbit vegetables (group 9), berries (group 13), tree nuts (group 14), cereal grains (group 15), avocado, banana, mango, papaya, passion fruit, plantain, and peanuts. The active ingredient is extracted from the leaves and terminal branches of the tea tree (*Melaleuca alternifolia*), which is a member of the plant family Myrtaceae and is indigenous to Australia, New Zealand, and Southeast Asia. Tea tree oil is composed of approximately 100 different compounds which consist of terpene hydrocarbons, primarily monoterpenes, sesquiterpenes, and their associated alcohols. The active ingredient has antifungal properties and is effective against a broad spectrum of plant-pathogenic fungi. Tea tree oil has been shown to affect cell respiration and alter cell membrane structure in yeast. Based on this information, the Agency considers the mode of action to be nontoxic.

The Biopesticides and Pollution Prevention Division (BPPD) has reviewed all of the data and other information submitted in support of the registration of tea tree oil as a fungicide/bactericide under Section 3(c)(5) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), and has determined that the current data requirements (40 CFR part 158.2010 through 158.2070) for registration of a biochemical pesticide have been satisfied. Given that tea tree oil is of low toxicity and presents little, if any, risks to humans, including infants and children, and the environment, the U.S. Environmental Protection Agency (EPA or the Agency) has concluded that it is in the best interest of the public to issue registrations for the manufacturing-use product (MP), Tea Tree Oil Technical (EPA File Symbol No. 86182-E), and the end-use product (EP), Timorex Gold (EPA File Symbol No. 86182-R), which contain this new active ingredient, tea tree oil. The basis for this decision is described in more detail in section IV of this Biopesticide Registration Action Document (BRAD).

On October 1, 2009, EPA announced a policy to provide a more meaningful opportunity for the public to participate on major registration decisions before they occur. According to this policy, EPA provides a public comment period prior to making a registration decision for the following types of applications: new active ingredients, first food use, first outdoor use, first residential use; and any registration decisions for which the Agency believes there may be substantial public interest.

Consistent with the policy of making registration actions more transparent, tea tree oil is subject to a 15-day comment period as a "new active ingredient." EPA has established a comment period of 15 days on the basis of tea tree oil's low toxicity, the determination that tea tree oil presents low risk of any adverse effects to human health and the environment, and need for this active ingredient. The notice for this comment period includes the draft BRAD and draft product labels for the MP, Tea Tree Oil Technical, and EP, Timorex Gold, which contain this new active ingredient, tea tree oil. The docket identification (ID) number is EPA-HQ-OPP-2009-0440. The Agency believes that based on the risk assessment and information submitted in support of the registration of the MP and EP containing tea tree oil, it is in the best interests of the public to issue the registration for Tea Tree Oil Technical and Timorex Gold. The basis for this decision can be found in the risk assessment for tea tree oil, which is characterized in this BRAD.

For definitions of scientific terms, please refer to *http://www.epa.gov/pesticides/glossary/*.

II. ACTIVE INGREDIENT OVERVIEW

Common Name: Tea Tree Oil

Chemical Names: Tea Tree Oil; Oils, tea-tree

Trade & Other Names: Tea Tree Oil Technical

CAS Registry Number: 68647-73-4

OPP Chemical Code: 028853

Type of Pesticide: Fungicide/Bactericide

III. REGULATORY BACKGROUND

On April 10, 2009, EPA received an application filed by Technology Sciences Group, Inc. (TSG), 1150 18th Street, NW, Suite 1000, Washington, DC 20036, on behalf of Biomor Israel, Ltd. (Biomor), P.O. Box 81, Qatzrin, 12900 Israel, to register the products, Timorex Gold (EPA File Symbol No. 86182-R) and Tea Tree Oil Technical (EPA File Symbol No. 86182-E), containing the new biochemical active ingredient, tea tree oil. A notice of receipt (NOR) of this application, allowing for a 30-day comment period, was published in the *Federal Register* on July 22, 2009 (74 FR 36215). No comments were received following this publication.

A. Classification

On October 28, 2004, EPA's Biochemical Classification Committee determined that tea tree oil is a biochemical pesticide. The biochemical classification committee indicated that tea tree oil is a fungicide/bactericide. The active ingredient has been shown to disrupt membranes of fungal/bacterial species. Tea tree oil is the essential oil of the Melaleuca tree (tea tree) and is rich in terpene alcohols (such as terpinen-4-ol and eucalpyptol). The oil is manufactured to contain at least 30% terpinen-4-ol (germicidal) and no more than 15% eucalpyptol (anti-fungal). The terpinen-4-ol is generally accepted to be the active component of tea tree oil. There is a long history of use of tea tree oil as an antiseptic and antifungal agent and it is formulated into creams, soaps, mouthwashes, toothpaste, and other cosmetic products.

B. Food Clearances/Tolerances

The consultant, TSG on behalf of Biomor, filed a petition (PP 9F7558) proposing to establish an exemption from the requirement of a tolerance for residues of tea tree oil in or on all food commodities. A notice of filing (NOF), allowing for a 30-day comment period, was published in

the *Federal Register* on July 22, 2009 (74 FR 36200). No comments were received following this publication.

EPA determined during the review of the petition that the data and information submitted was insufficient to support an exemption from the requirement of a tolerance for residues of tea tree oil in or on all food commodities. However, as noted in the Risk Assessment section of this BRAD (Section IV), EPA has made a non-food use determination, with limitations, for the following food commodities: leafy vegetables (group 4), fruiting vegetables (group 8), cucurbit vegetables (group 9), berries (group 13), tree nuts (group 14), cereal grains (group 15), avocado, banana, mango, papaya, passion fruit, plantain, and peanuts. The limitations for the non-food use determination are a pre-harvest interval (PHI) of 48 hours and a maximum application rate of 1.54 lbs a.i./acre (EPA, 2014b).

IV. RISK ASSESSMENT

A. Active Ingredient Characterization

Tea tree oil is a new biochemical pesticide active ingredient intended for use to prevent and control diseases such as powdery mildew, Botrytis, and black sigatoka in horticultural and agricultural crops. The active ingredient has antifungal properties and is effective against a broad spectrum of plant-pathogenic fungi, but the mode of action is not clearly understood. It has been shown to affect cell respiration and alter cell membrane structure in yeast. Based on this information, the Agency considers the mode of action to be nontoxic.

The active ingredient is extracted from the leaves and terminal branches of the tea tree (*Melaleuca alternifolia*) which is a member of the plant family Myrtaceae and is indigenous to Australia, New Zealand, and Southeast Asia. Tea tree oil is composed of approximately 100 different compounds which consist of terpene hydrocarbons: primarily monoterpenes, sesquiterpenes, and their associated alcohols. These biogenic chemicals are aromatic hydrocarbons which are found in the essential oils of a multitude of plants and are characterized by their high volatility and low aqueous solubility (EPA, 2010). The composition of tea tree oil used in commerce is regulated by an international standard (ISO 4730, International Organization for Standardisation), which sets maximum and minimum limits for 14 of its components. Of the several varieties or chemotypes of tea tree oil, only the terpinen-4-ol chemotype, which contains 30-48% terpinen-4-ol, will be used as the TGAI in the proposed MP, Tea Tree Oil Technical (EPA File Symbol No. 86182-E). ISO 4730 defines the main ingredients as α-terpinine (5-13%); 1,8-cineole (traces to 15%); γ-terpinine (10-28%); p-cymene (0.5-12%); and terpinen-4-ol (30-48%). The specifications for all 14 ingredients are listed in Table 1 below.

TABLE 1. Specifications of Tea Tree Oil Components per ISO Standard 4730[1]

Name	CAS No.	Minimum %	Maximum %
Terpinen-4-ol	562-74-3	30	48
γ-Terpinine	99-85-4	10	28
α-Terpinine	99-86-5	5	13
α-Terpineol	98-55-5	1.5	8
α-Terpinolene	586-62-9	1.5	5

α-Pinene	80-56-8	1	6
p-Cymene	99-87-6	0.5	8
1,8-Cineole	470-82-6	Trace	15
Limonene	138-86-3	0.5	1.5
Aromadendrene	489-39-4	0.5	3
δ-Cadinene	483-76-1	Trace	3
Sabinene	3387-41-5	Trace	3.5
Globulol	489-41-8	Trace	1
Viridiflorol	552-02-3	Trace	1
Ledene		Trace	3

[1]from MRID 47730409

Humans are already naturally exposed to the major constituents of tea tree oil (terpinen-4-ol, γ-terpinene, 1,8-cineole, and α-terpinene) in the diet as they are found in herbs, spices, fruits, and some vegetables (EPA, 2014b). Humans are also exposed to the major constituents of tea tree oil as food additives in the diet, as they have been approved as substances that may directly be added to food by the U.S. Food and Drug Administration (FDA) under 21 CFR § 172.515(b). Tea tree oil is comprised of primarily terpenes and their associated alcohols which are found in the environment as they are emitted by and present in a variety of plant species and water sources. Additionally, tea tree oil has a long history of use as a remedy for acne, eczema, skin infections, cold sores, blisters, and warts; and is used in cosmetic and personal care products such as shampoo, toothpaste, mouthwash, deodorants, lotions, and bath oils, as well as in animal care products (EPA, 2010).

Descriptions of the product formulation and production process, formation of impurities, and physical and chemical characteristics of tea tree oil were examined by BPPD and found to be acceptable in meeting current guideline standards.

All product chemistry data requirements for registration of tea tree oil have been **satisfied.**

For more information regarding product chemistry data requirements, refer to Tables 4 and 5 in Appendix A.

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 indicates the highest toxicity and Toxicity Category IV indicates the lowest toxicity.

Adequate mammalian toxicology data/information is available to support registration of tea tree oil. All toxicology data requirements for tea tree oil 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).

A Tier I primary dermal irritation study in rabbits submitted and reviewed showed that tea tree oil is corrosive to the skin at undiluted concentrations (toxicity category I). Based on the results in the primary dermal irritation study, the primary eye irritation and dermal sensitization data requirements were waived; therefore, tea tree oil is classified as corrosive to the eye (toxicity category I). Tea tree oil is a toxicity category III (slightly toxic) compound via the acute oral and dermal toxicity routes of exposure based on a median lethal dose (LD_{50}) of 1,752 mg/kg body weight in rats and a LD_{50} of greater than 2,000 mg/kg in rabbits, respectively. Tea tree oil is a toxicity category IV (not toxic) compound for acute inhalation toxicity based on a medial lethal concentration (LC_{50}) of 3.64 mg/L.

For more information regarding acute toxicity data requirements, refer to Table 6 in Appendix A.

b. Subchronic Toxicity

Subchronic data are required to determine a no-observed-effect-level (NOEL) and any toxic effects associated with repeated or continuous exposure to a test substance for a period of 90 days via the oral, dermal, and inhalation routes of exposure.

A 90-day oral toxicity study (OCSPP 870.3100) was conducted on tea tree oil and submitted in MRID 48598702. Adequate supportive information regarding homogeneity testing of the test substance was submitted in MRID 48878202. Tea tree oil was administered to Wistar rats by gavage at dosages of 0 (peanut oil), 30, 60 or 120 mg/kg/day. An additional 20 rats were included in the high dose group, and an additional 10 rats were included in the control group. To determine the reversibility of any effects observed, 10 rats from the high dose group and 5 rats from the control group were sacrificed 14 days and 28 days after completion of the 90-day dosing period. No mortality was observed in male rats. Two moribund females in the high dose group were sacrificed during the treatment period. At all dose levels salivation was observed which persisted for about 30 minutes after dosing. Salivation incidences were dose-related. No treatment-related effects on body weight and body weight gain were observed. Toxicologically relevant hematological, clinical chemistry, or urinalysis findings were not noted at any dose level. In the high dose group, some motor activity measurements were statistically ($p \leq 0.05$) affected in both sexes; however, the toxicological significance of these observations is unclear as there was no correlation with abnormal functional observations. Statistically significant increases in liver to body weight ratios at the mid- and high-dose levels (+11% and +9%, respectively) were noted in females, and a significant increase in ovary to body weight ratio was noted in the 28-day high dose recovery group (+31%). There was no microscopic correlation for the organ weight findings in females. Flaccid testes, some with a small appearance, were observed in high-dose males (4/10 at the end of treatment; 2/10 after the 14-day recovery period; 8/10 after the 28-day recovery period). Absolute organ weight and organ-to-body-weight ratios were significantly reduced in the testes and epididymides of males in the high-dose 28-day recovery group. These

findings were microscopically associated with degenerative changes in the seminiferous tubules (loss of germ cells, formation of multinucleated germ cells, presence of cell debris in tubular lumen, atrophic appearance, and sertoli cell vacuolation). The testicular effects occurred at the same or higher rate of incidence with an overall greater degree of severity in the high dose animals in the 14-day and 28-day recovery groups. Sperm granulomas and cellular debris in the lumen (inflammation involving epididymal lumen and interstitium with the presence of large zones of spermatozoa surrounded by a zone of macrophages, giant cells and fibroblasts) were observed in the epididymides of high dose males at the end of the 90-day treatment period. The incidence of sperm granulomas peaked in the 14-day recovery group, but the incidence and severity of cellular debris in the epididymal lumen increased in the 14- and 28-day recovery groups. Minimal cell debris was observed in the lumen of the epididymides in 1/10 male rats dosed at 60 mg/kg/day. No treatment-related histological changes were observed in males dosed at 30 mg/kg/day. Statistically significant treatment-related effects on sperm motility, sperm morphology, and epididymal sperm counts were observed at the high dose level at the end of the treatment period and in the 14- and 28-day recovery groups. Sperm counts were significantly lower relative to controls in the mid-dose group, and there was a significant decrease in sperm motility and an insignificant increase in abnormal sperm at this dose level. Based on these data, the lowest-observed-adverse-effect level (LOAEL) of tea tree oil in rats was 60 mg/kg/day based on testicular toxicity in males and increased liver to body weight ratios in females. The no-observed-adverse-effect level (NOAEL) is 30 mg/kg/day for males and females (EPA, 2013).

A 90-day dermal toxicity study was not submitted and is not required. Exposure via the dermal route is not anticipated due to the following: 1) prolonged dermal exposure is not expected because the product is not purposely applied to the skin and handlers/applicators are required to wear appropriate personal protective equipment (PPE); 2) a 4-hour restricted-entry interval (REI) requirement has been included on the proposed EP label which will further mitigate exposure; and 3) tea tree oil has a long history of use in a variety of dermally-applied products, including shampoo, deodorants, lotions, and antifungal treatments. In a non-guideline 30-day dermal irritation study on rabbits (MRID 47730404), undiluted tea tree oil caused severe irritation to the skin on the first day of the study. For the remainder of the study, a 25% solution in paraffin oil was applied to the skin which did not result in visible irritation; however, non-specific microscopic dermatitis consistent with irritation was observed (EPA, 2013).

A 90-day inhalation toxicity study was not submitted for tea tree oil. In lieu of a study, the applicant cited the data from the 90-day oral toxicity study (MRID 48598702). Due to the use pattern of the active ingredient as a spray and the volatility of the constituents of tea tree oil, exposure to handlers/applicators is possible. There are no PPE requirements regarding mitigation of inhalation exposure on the proposed EP label. A route to route extrapolation using the default assumption that 100% of the tea tree oil is absorbed into the body has been employed. The Agency is confident that this approach is protective of potential repeat exposure inhalation toxicity for the following reasons: 1) tea tree oil is classified into Toxicity Category IV for acute inhalation toxicity and Toxicity Category III for acute oral toxicity; and 2) humans are already exposed to the constituents of tea tree oil as the oil is used in a variety of dermally-applied cosmetic and pharmaceutical products. Moreover, five of the main components of tea tree oil (terpinen-4-ol, γ-terpinine, α-terpinine, p-cymene, and 1,8-cineole) are all approved for use by the FDA as direct food additives under 21 CFR 172.515. Further, in an occupational risk

assessment conducted for applicators and handlers (who may be exposed via inhalation to tea tree oil), margins of exposure (MOEs) were derived and were significantly higher than the Agency's level of concern (LOC) of 100 (MOEs ranged from 4,900 to 150,000). Because the MOEs were significantly higher than the LOC, the Agency believes that an adequate margin of safety has been achieved to account for any potential difference in toxicity from oral versus inhalation exposure (EPA, 2013).

For more information regarding the subchronic toxicity data requirements, refer to Table 7 in Appendix A.

c. Developmental Toxicity and Mutagenicity

A developmental toxicity study conducted on tea tree oil was submitted in MRID 49166401. In the study, Wistar rats were administered doses of tea tree oil by gavage at 0, 30, 60, or 120 mg/kg/day from day 5 to day 19 of gestation. Each treatment group consisted of 24 female rats; the control group which received peanut oil, the test substance vehicle, also consisted of 24 female rats. Initially, rats were dosed at 75, 150, and 300 mg/kg/day; however, there was a mortality on day two of treatment in the high dose group and treatment related clinical signs in the mid- and high-dose groups. Consequently, doses were reduced to 30, 60 and 120 mg/kg/day. At the start of treatment, animals were approximately 13-15 weeks old, within a weight range of approximate 224g ± 15g and healthy in appearance. Animal acclimatization, housing, diet, and water supply were reported adequately. Test substance characterization and preparation was also reported adequately. Animals were dosed once a day at approximately the same time each day. Physical examinations occurred on day 0 of gestation and at weekly intervals during the gestation period. Clinical observations occurred at least twice a day on treatment days (pre- and post-dosing) and once a day on other days. Body weights were measured on days 0, 3 and 5, 8, 11, 14, 17, and 20 after mating and food consumption was measured throughout the study. Animals were sacrificed on day 20 after mating under isoflurane anesthesia. Gross necropsy was performed on all rats, which consisted of external observation and examination of thoracic and abdomen viscera and examination of uterine contents. Gravid uterine weights, the number of corpora lutea in each ovary, the number of implantation sites, the number of early and late resorptions sites, the number of live and dead fetuses, individual fetal body weights, fetal sex, and the fetal sex ratio were recorded. Fetuses were also examined for external abnormalities, visceral organ abnormalities and skeletal development and abnormalities. Statistical analyses of the data were provided in the study. Significant reductions in maternal body weight gain and food intake were observed during the treatment period in the mid- and high-dose groups and throughout gestation in the high dose group. These observations were considered treatment related. No gross pathological findings were observed in the dams in any group. At all dose levels, mean gravid uterine weights, the number of corpora lutea, the number of implantations, and pre and post-implantation losses were all statistically comparable to the control group. Significant resorption was observed in dams in the high dose group when compared to the control group. At all dose levels, the total number of fetuses, mean litter size, number of live fetuses, and the sex ration were all statistically comparable to the control group. Mean fetal body weights of males, females, and total fetuses were significantly reduced at the mid and high dose level; however, the weights of the fetuses in the mid dose group were comparable to historical control data. Any fetal anomalies and abnormalities that were observed were routinely observed

in rat fetuses, were comparable to the control group or were comparable to historical control data; none were considered treatment related. Based on the results of the study, the maternal NOAEL is 30 mg/kg/day and the LOAEL is 60 mg/kg/day based on reduced body weight gain and food consumption. The developmental NOAEL is 60 mg/kg/day and the LOAEL is 120 mg/kg/day based on reduced fetal body weight (EPA, 2014a).

In a study published in the New England Journal of Medicine (Henley, 2007), study authors reported that repeated topical exposure to lavender and tea tree oils may cause prepubertal gynecomastia in boys. Three prepubertal boys who were otherwise healthy and had normal serum concentrations of endogenous steroids exhibited gynecomastia that coincided with the topical application of products that contained lavender and tea tree oils. The effect resolved in each boy shortly after the use of the products was discontinued. The authors also reported that studies in human cell lines indicated that lavender and tea tree oils had estrogenic and antiandrogenic activities. Although the study suggests that exposure to topical applications of products containing lavender and tea tree oils may result in gynecomastia in boys, the Agency has concluded that the uses of tea tree oil as a pesticide will not result in unreasonable adverse effects to this population subgroup. This conclusion is based upon the following: 1) tea tree oil will not be applied topically to the skin. The active ingredient will be applied to crops as an agricultural use; thus, exposure is mainly anticipated to be via the oral route, 2) dietary exposure to tea tree oil as a pesticide is anticipated to be minimal as it degrades rapidly in the environment, 3) dermal exposure is not anticipated to result in risk as occupational exposure assessments (see subchronic toxicity section above) indicate MOEs that do not exceed the Agency's level of concern, and 4) humans are already exposed to the constituents of tea tree oil as they are found naturally in the diet, are used as food additives, and are found in a variety of cosmetic and pharmaceutical products.

A Tier I mutagenicity study [*in vitro* reverse gene mutation assay (Ames) using *Salmonella typhimurium* strains TA98, TA100, and TA102 (MRID 47730404)] showed that tea tree oil did not increase the number of revertants at doses of <50 µg in the presence or absence of S9 metabolic activation. A Tier II mutagenicity study [*in vivo* mammalian erythrocyte micronucleus assay (MRID 47730407)] showed that tea tree oil did not produce a statistically significant increase in the frequency of micronucleated polychromatic erythrocytes in bone marrow of mice given oral doses of 1000-1750 mg/kg body weight. Therefore, under the conditions of both assays, tea tree oil is considered to be non-mutagenic.

For more information regarding prenatal developmental and mutagenicity data requirements, refer to Table 7 in Appendix A.

d. Tier II/Tier III

Tiers II and III data were not required due to the nature of the active ingredient and its intended uses in potential new EP products (fungicides/bactericides).

e. Effects on the Endocrine System

As required under Federal Food, Drug, and Cosmetic Act (FFDCA) section 408(p), EPA has

developed the Endocrine Disruptor Screening Program (EDSP) to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and nine inert ingredients. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

Tea tree oil is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA section 408(p) the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP test orders/data call-ins for all pesticide active ingredients.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier 1 screening battery, please visit our website: http://www.epa.gov/endo/.

2. Dose Response Assessment

The NOAEL of 30 mg/kg bw/day has been selected as the point of departure (POD) for the hazard and risk assessment. The NOAEL is based on toxic endpoints observed in the 90-day oral toxicity study. The POD is protective of developmental toxicity because the NOAEL in the 90-day oral toxicity study is lower than the developmental (fetal) toxicity NOAEL of 60 mg/kg bw/day.

3. Food Quality Protection Act (FQPA) Considerations

a. Dietary Exposure and Risk Characterization

EPA has made a non-food use determination, with limitations, for the following food commodities: leafy vegetables (group 4), fruiting vegetables (group 8), cucurbit vegetables (group 9), berries (group 13), tree nuts (group 14), cereal grains (group 15), avocado, banana, mango, papaya, passion fruit, plantain, and peanuts. The limitations for the non-food use determination are a PHI of 48 hours and a maximum application rate of 1.54 lbs a.i./acre (EPA,

2014b). The Agency's reasoning for the non-food use determination, with limitations, for tea tree oil is provided below.

As stated earlier in the document, the major components of tea tree oil are moderately to highly volatile substances. A substance with a high vapor pressure at normal temperatures is often referred to as volatile. The vapor pressure is an indication of a substance's evaporation rate and relates to the tendency of particles to escape from the substance. Up to 90% of tea tree oil has been shown to volatilize within 24 hours after application (Chadwick, 2008; Gatenio, 2007). Based on these studies, substantial volatilization is expected within the first 24 hours of application from plant, soil, and water surfaces. Tea tree oil constituents are quickly broken down in air through atmospheric reactions (PMRA, 2014; EFSA, 2012). Further, residue data reviewed by EPA in support of this non-food use determination indicate the absence of quantifiable residues on tomatoes, peppers, and bananas immediately after application when tea tree oil was applied at a proposed application rate of 1.54 pounds of active ingredient per acre. These data demonstrate that tea tree oil, when applied at that application rate, volatilizes even faster than what is reported in the Chadwick & Gatenio reports referenced above in this paragraph, and volatilizes completely. Volatilization from plant surfaces and soil can be a major dissipation pathway for pesticides applied to crops. Generally, pesticides volatilize from plant surfaces faster and to a greater extent than from soil (Bedos, 2002). Pesticide volatilization from plant surfaces often occurs rapidly after application (Bedos, 2002). For example, 30 to 50% of lindane (vapor pressure estimated at 5 x 10-4 mmHg) was reported to volatilize from plant surfaces within one hour application regardless of the crop species, canopy structure or plant age (Bedos et al., 2002). More than 90% of the lindane application volatilized from the plant surfaces over a period of 3 days. The data suggest that over longer periods after application, leaf characteristics do not interfere with volatilization (Bedos, 2002). Most of the pesticides evaluated by Bedos for volatilization after application have low vapor pressures, such as diazinon, with a vapor pressure of 5.43 x 10-5 mmHg, or dieldrin with a vapor pressure of 1.77x 10-5 mmHg (as estimated by EpiSuite™). These data suggest that tea tree oil, which has a much higher vapor pressure than the example pesticides presented by Bedos (2002), would readily volatilize from plant surfaces soon after application, regardless of the surface area of the plant. Table 2 provides information on the vapor pressures of the constituents of tea tree oil all of which were measured at or near room temperature. As indicated in the table, the vapor pressure of tea tree oil is significantly higher than (by a magnitude of ~ 10,000) diazinon, a pesticide that has a low vapor pressure and therefore is not considered to be a volatile substance.

Table 2. Vapor Pressures of Tea Tree Oil Constituents

Component	Temperature (°C)	Vapor Pressure (mmHg)
Terpinen-4-ol	20	0.40
ɤ-terpinene	20	0.70
ɤ-terpinene	23.5	0.77
α-terpinene	20	0.80
p-cymene	25	1.50
1,8-cineole	25	1.90

Residue studies were submitted in which products containing varying amounts of tea tree oil (one to seven times the proposed application rate) were applied to tomatoes, peppers, and bananas. Analyses for residues of the three major components in the oil (terpinen-4-ol, γ-

terpinene, and 1,8-cineole) were performed in the studies. No detectable residues (below the limit of quantification [LOQ] which was 0.05 ppm for the residue studies) were found in any of the commodities at the proposed application rate. The LOQ is the lowest amount of a substance that can be distinguished from the absence of that substance for any particular analytical method. Residue studies were submitted in which a product was tested at approximately seven times (7X) the proposed application rate on tomatoes and peppers. No detectable residues were found in tomatoes. Detectable residues of terpinen-4-ol only were found for up to 48-hours on peppers at the 7X application rate. No detectable residues were found at 48-hours post-application. Acceptable residue data have not been submitted for any other crop. The available data indicate that residues of tea tree oil are not likely to be present on edible commodities when tea tree oil is applied at the proposed application rate with a PHI of 48 hours. As stated above, the major constituents of tea tree oil are found naturally in most of the crops and crop groups listed in this document. Tea tree oil is primarily comprised of terpenes and their associated alcohols, all of which are found in a multitude of plants, as they are ubiquitous in the environment. Therefore, based on the rapid volatilization from the plant surfaces, it is likely that even if there are any tea tree oil constituent residues, the residues of these substances will not be distinguishable from background levels when tea tree oil is applied at the proposed application rate and at the PHI of 48 hours.

Rationale behind the non-food use determination for each crop group

Fruiting vegetables (group 8): tomatoes and peppers are representative commodities in this crop group. Residue studies on these crops indicate that 1) residues are not likely to be present on treated commodities in this crop group when tea tree oil is applied at an application rate of 1.54 lbs a.i./acre and 2) residues are not likely to be present on treated commodities after 48 hours when tea tree oil is applied at an application rate approximately seven times the proposed rate. The limitation in the non-food use determination for tea tree oil would be that the active ingredient cannot be applied at more than 1.54 lbs a.i./acre; therefore, residues are not likely to be present on these commodities when consumed.

Leafy vegetables (group 4): even though residue data have not been submitted for leafy vegetables, the residue data on fruiting vegetables (tomatoes and peppers) can be bridged to this crop group and a non-food use determination can be made based on the following: 1) as stated above, the data from Bedos (2002) suggest that leaf characteristics do not interfere with volatilization; thus, the difference in surface texture between fruiting and leafy vegetables is not likely to affect residue profiles; 2) a 48-hour PHI would give ample time for volatilization of the constituents of tea tree oil from plant surfaces. Further, the PHI of 48 hours is further supported because residues of terpinen-4-ol were below the LOQ by 48 hours in the residue study where tea tree oil was applied at the 7X application rate; and 3) the limitation in the non-food use determination for tea tree oil would be that the active ingredient cannot be applied at more than 1.54 lbs a.i./acre, the level at which no detectable residues of tea tree oil were found. This information indicates that residues of tea tree oil are not likely to be present when these commodities are consumed.

Cucurbit vegetables (group 9): even though residue data have not been submitted for cucurbits, the residue data on fruiting vegetables (tomatoes and peppers) can be bridged to this crop group

and a non-food use determination can be made based on the following: 1) residue profiles are anticipated to be similar between cucurbits and fruiting vegetables because they have similar surfaces (smooth, non-textured); 2) a 48-hour PHI would give ample time for volatilization of the constituents of tea tree oil from plant surfaces. Further, the PHI of 48 hours is further supported because residues of terpinen-4-ol were below the LOQ by 48 hours in the residue study where tea tree oil was applied at the 7X application rate and 3) the limitation in the non-food use determination for tea tree oil would be that the active ingredient cannot be applied at more than 1.54 lbs a.i./acre, the level at which no detectable residues of tea tree oil were found. This information indicates that residues of tea tree oil are not likely to be present when these commodities are consumed.

Berries (group 13): even though residue data have not been submitted for berries, the residue data on fruiting vegetables (tomatoes and peppers) can be bridged to this crop group and a non-food use determination can be made based on the following: 1) as stated above, the data from Bedos (2002) suggest that leaf characteristics do not interfere with volatilization; thus, the difference in surface texture between fruiting vegetables and berries is not likely to affect residue profiles; 2) a 48-hour PHI would give ample time for volatilization of the constituents of tea tree oil from plant surfaces. Further, the PHI of 48 hours is further supported because residues of terpinen-4-ol were below the LOQ by 48 hours in the residue study where tea tree oil was applied at the 7X application rate; and 3) the limitation in the non-food use determination for tea tree oil would be that the active ingredient cannot be applied at more than 1.54 lbs a.i./acre, the level at which no detectable residues of tea tree oil were found. This information indicates that residues of tea tree oil are not likely to be present when these commodities are consumed.

Tree nuts (group 14): even though residue data have not been submitted for tree nuts, the residue data on fruiting vegetables (tomatoes and peppers) can be bridged to this crop group and a non-food use determination can be made based on the following: 1) as stated above, the data from Bedos (2002) suggest that leaf characteristics do not interfere with volatilization; thus, the difference in surface texture between fruiting vegetables and tree nuts is not likely to affect residue profiles; 2) a 48-hour PHI would give ample time for volatilization of the constituents of tea tree oil from plant surfaces. Further, the PHI of 48 hours is further supported because residues of terpinen-4-ol were below the LOQ by 48 hours in the residue study where tea tree oil was applied at the 7X application rate; and 3) the limitation in the non-food use determination for tea tree oil would be that the active ingredient cannot be applied at more than 1.54 lbs a.i./acre, the level at which no detectable residues of tea tree oil were found. This information indicates that residues of tea tree oil are not likely to be present when these commodities are consumed. Additionally, although not anticipated, if residues were available, they would be found on the shells of the nuts, which are not consumed.

Cereal grains (group 15): even though residue data have not been submitted for cereal grains, the residue data on fruiting vegetables (tomatoes and peppers) can be bridged to this crop group and a non-food use determination can be made based on the following: 1) as stated above, the data from Bedos (2002) suggest that leaf characteristics do not interfere with volatilization; thus, the difference in surface texture between fruiting vegetables and cereal grains is not likely to affect residue profiles; 2) a 48-hour PHI would give ample time for volatilization of the constituents of tea tree oil from plant surfaces. Further, the PHI of 48 hours is further supported because

residues of terpinen-4-ol were below the LOQ by 48 hours in the residue study where tea tree oil was applied at the 7X application rate; and 3) the limitation in the non-food use determination for tea tree oil would be that the active ingredient cannot be applied at more than 1.54 lbs a.i./acre, the level at which no detectable residues of tea tree oil were found. This information indicates that residues of tea tree oil are not likely to be present when these commodities are consumed. Additionally, cereal grains are not typically consumed straight from the field and are processed and/or cooked prior to consumption which would further mitigate the potential for residues due to the increased time for volatilization and/or removal of tea tree oil's constituents.

Avocado, banana, mango, papaya, passion fruit, peanut, and plantain: residue data have been submitted for bananas which indicated that no residues were found at the proposed application rate. Even though residue data have not been submitted for the other crops, the residue data on fruiting vegetables (tomatoes and peppers) can be bridged to this crop group and a non-food use determination can be made based on the following: 1) as stated above, the data from Bedos (2002) suggest that leaf characteristics do not interfere with volatilization; thus, the difference in surface texture between fruiting vegetables and tree nuts is not likely to affect residue profiles; 2) a 48-hour PHI would give ample time for volatilization of the constituents of tea tree oil from plant surfaces. Further, the PHI of 48 hours is further supported because residues of terpinen-4-ol were below the LOQ by 48 hours in the residue study where tea tree oil was applied at the 7X application rate; and 3) the limitation in the non-food use determination for tea tree oil would be that the active ingredient cannot be applied at more than 1.54 lbs a.i./acre, the level at which no detectable residues of tea tree oil were found. This information indicates that residues of tea tree oil are not likely to be present when these commodities are consumed. Further, for the crops for which the skin is not consumed, (avocado, plantain, and peanuts), the potential for residues available at the time of consumption is further reduced.

There is sufficient justification to support a non-food use determination for tea tree oil with limitations on the crops and crop groups identified previously in this document. The non-food use determination is based on the following: 1) the constituents of tea tree oil are very volatile which indicates that residues are not likely to be present in or on food; 2) no residues of the major constituents of tea tree oil were found on bananas, peppers, and tomatoes in residue studies at the proposed application rate for the rule; 3) a PHI of 48-hours is sufficient to compensate for the lack of residue data on the other listed crops and will provide ample time for dissipation of any residues; 4) the application rate limitation mitigates the potential for residues because no residues were found on bananas, peppers, and tomatoes at this application rate; 5) even if residues of tea tree oil's constituents were found on edible crops they are not likely to be distinguishable from background levels since these substances are naturally found in plants; and 6) washing, rinsing, and processing of commodities and weather events such as rain will further reduce any possibility for residues.

Based on the analysis provided in this BRAD, the Agency concludes that use of tea tree oil in accordance with the limitations specified in the paragraph above will not result in residues on food. For the sake of transparency, the Agency intends to promulgate an amendment to 40 CFR § 180.2020 to document this finding as follows:

Pesticide Chemical	CAS Reg. No.	Limits	Uses
Tea Tree Oil	68647-73-4	Post-harvest interval of 48 hours; maximum application rate of 1.54 lbs a.i./acre	Fruiting vegetables (group 8), leafy vegetables (group 4), cucurbit vegetables (group 9), berries (group 13), tree nuts (group 14), cereal grains (group 15), avocados, bananas, mangoes, papaya, passion fruit, peanuts, and plantains

b. Drinking Water Exposure and Risk Characterization

Residues of the constituents of tea tree oil in drinking water are not expected when pesticide products are used according to label instructions. Tea tree oil and its constituents are expected to volatilize and degrade rapidly in the environment and are not directly applied to water; therefore, residues of tea tree oil in drinking water are unlikely.

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

The Agency has made a non-food use determination, with limitations, for the active ingredient, tea tree oil; therefore, there are no foreseeable dietary risks to sensitive subpopulations, including infants and children, from the use of tea tree oil in the proposed product when label instructions are followed. This conclusion is based on the following: 1) significant dietary exposure is not anticipated when label instructions for the proposed product are followed, 2) dietary risk to infants and children is anticipated to be negligible based on the results of the dietary risk assessments that the Agency has conducted (see Section IV.B.3.a above) and 3) humans are already exposed to tea tree oil in cosmetic and personal care products, and its major constituents are found naturally in the diet, in the environment, and are used as food additives.

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

a. Occupational Exposure and Risk Characterization

Dermal exposure to mixers/loaders and applicators is not anticipated as adequate PPE requirements are on the proposed EP label. Additionally, the active ingredient degrades rapidly in the environment which further mitigates dermal exposure. Due to the potential for inhalation exposure of residues of tea tree oil to mixers/loaders and applicators (the EP is applied as a spray, fog or drench), and the effects observed in the 90-day oral toxicity and prenatal developmental studies, an occupational exposure and risk assessment was conducted. The results of the risk assessment indicate that risk from inhalation exposure to tea tree oil is negligible for mixers/loaders and applicators when the pesticide product (Timorex Gold [EPA File Symbol No. 86182-R]) is used according to label instructions. A summary of the assessment is provided below.

The assessment was conducted using a POD of 30 mg/kg bw/day (the NOAEL from the 90-day oral and developmental toxicity studies) and the occupational handler exposure calculation spreadsheet developed by OPP's Health Effects Division (HED). Because 90-day inhalation toxicity data are not available, the Agency has bridged the data from the 90-day oral toxicity study and assumed 100% absorption via inhalation. The standard body weight for females (69 kg) was used for all exposure scenarios in the assessment due to the incidence of developmental effects. Based on label instructions, exposure scenarios consisted of the following application methods: ground boom, airblast, aerial, and mechanically-pressured handgun. The application rate used for the exposure assessment was the maximum application rate on the label (1.6 lbs a.i./acre on a previously proposed label). Potential daily exposures for occupational handlers (mixer/loaders and applicators) were calculated in the spreadsheet using the following formulas:

Daily exposure to the pesticide:

*Daily Exposure (mg ai /day) = UE (µg ai / lb ai) * AR (lb ai /A) * AT (A /day) * 1E-3 mg/µg*

Daily Exposure = amount of the active ingredient that is available for inhalation absorption,
UE = Unit Exposure (generic values derived using measurements of exposure data in the field)
AR = maximum application rate according to proposed label
AT = daily acres treated.

The average daily dose (daily exposure adjusted for absorption and body weight) was calculated using the following formula:

$$\textit{Average Daily Dose (mg ai/kg/day)} = \frac{\textit{[Daily Exposure (mg ai/day) * Absorption (\%)]}}{\textit{Body Weight (kg)}}$$

Average Daily Dose (ADD) = absorbed dose received from exposure to the active ingredient in a given scenario
Daily Exposure = amount of the active ingredient that is available for inhalation absorption
Absorption Factor = a measure of the amount of chemical that crosses a biological boundary such as the skin and lungs (%)
Body Weight = body weight determined to represent the population of interest in a risk assessment

Risk for each application handler scenario was calculated using a MOE, which is a ratio of the toxicological endpoint to the daily dose of concern. The daily inhalation dose received by occupational handlers was compared to the POD (i.e.: NOAEL) to assess the risk to occupational handlers. All MOE values were calculated using the following formula:

$$\textit{MOE} = \frac{\textit{POD (i.e.: NOAEL in mg/kg/day)}}{\textit{ADD (mg/kg/day)}}$$

All MOEs calculated for mixers/loaders and applicators using no inhalation PPE were significantly greater than the Agency's LOC of 100 (10X for intraspecies variation and 10x for

interspecies variation). MOEs greater than 100 do not exceed the Agency's LOC; therefore, risks are not considered to be of concern. Based on the results of the occupational risk assessment, unreasonable adverse effects to handlers are not anticipated when the pesticide product is used according to label instructions. A summary of the exposure scenarios and MOEs is provided in Table 3 below.

TABLE 3. Occupational Risk Assessment Summaries for Tea Tree Oil (Inhalation Route of Exposure)

Worker Activity	Application Equipment/Application Type	Application Type	MOE
Mixer/Loader	Aerial/Broadcast	Orchard	17,000
Mixer/Loader	Aerial/Broadcast	Field crop, typical	17,000
Mixer/Loader	Aerial/Broadcast	Field crop, high-acreage	4,900
Mixer/Loader	Airblast/Broadcast	Orchard	150,000
Mixer/Loader	Groundboom/Broadcast	Field crop, typical	74,000
Mixer/Loader	Groundboom/Broadcast	Field crop, high-acreage	29,000
Applicator	Aerial/Broadcast	Orchard	Exposure not anticipated
Applicator	Aerial/Broadcast	Field crop, typical	Exposure not anticipated
Applicator	Aerial/Broadcast	Field crop, high-acreage	Exposure not anticipated
Applicator	Airblast/Broadcast	Orchard	6,900
Applicator	Groundboom/Broadcast	Field crop, typical	48,000
Applicator	Groundboom/Broadcast	Field crop, high-acreage	19,000
Flagger	Aerial/Broadcast	Orchard	11,000
Flagger	Aerial/Broadcast	Field crop, typical	11,000
Flagger	Aerial/Broadcast	Field crop, high-acreage	11,000

Significant post-application exposure to tea tree oil is not anticipated as there is a 24-hour REI on the EP label and the active ingredient is expected to rapidly degrade in the environment.

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

Significant exposure to tea tree oil is not anticipated in residential, school, and day care areas, as the product containing this active ingredient is intended for use on horticultural and agricultural crops.

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

There is reasonable certainty that no harm to the U.S. population will result from aggregate exposure to tea tree oil. This includes all exposures for which there is reliable information. The Agency arrived at this conclusion based on the following: 1) the non-food use determination, with limitations, for the active ingredient, tea tree oil, 2) residential exposures are not anticipated based on the pesticidal use pattern of tea tree oil, 3) drinking water exposure is not anticipated based on the rapid degradation of the active ingredient in the environment and tea tree oil is not directly applied to water. The risks from aggregate exposure via oral, dermal, and inhalation exposure are a compilation of three low-risk exposure scenarios and are negligible.

6. Cumulative Effects

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative

effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." EPA has not found tea tree oil to share a common mechanism of toxicity with any other substances, and tea tree oil does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that tea tree oil does not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see EPA's website at http://www.epa.gov/pesticides/cumulative.

7. Risk Characterization

The Agency has considered human exposure to tea tree oil 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 tea tree oil as a pesticide when label instructions are followed.

C. Environmental Assessment

1. Ecological Hazards

Adequate nontarget toxicology data/information is available to support registration of tea tree oil with the submission of nontarget toxicology data on the TGAI. All nontarget toxicology data requirements for tea tree oil have been **satisfied.**

Tea tree oil is highly toxic to aquatic invertebrates. Tea tree oil is practically nontoxic to fish and insects. Tea tree oil is not phytotoxic. Significant exposure of tea tree oil to birds is not expected due to volatilization and rapid degradation of the active ingredient in the environment (EPA, 2013).

For more information regarding nontarget organism toxicity data requirements, refer to Table 8 in Appendix A.

2. Environmental Fate and Ground Water Data

Tea tree oil is expected to degrade rapidly in the environment. Up to 90% of tea tree oil has been shown to volatilize within 24 hours after application and residue studies indicate the lack of detectable residues of three of the major constituents of tea tree oil at 48 hours post-application (EPA, 2013). In MRID 48275004, a study was submitted in which the biodegradation of tea tree oil was determined in a 28-day ready biodegradability assay (OECD Guideline 310 and EN ISO 14593) by monitoring the release of carbon dioxide with a non-adapted activated sewage sludge. Based on the results of the assay, biodegradation of tea tree oil was 10% after 2 days, 60% after 5 days, 87% by day 7, and 106% at study termination.

3. Ecological Exposure and Risk Characterization

Significant exposure to birds is not expected because the active ingredient is volatile and degrades rapidly in the environment. Additionally, birds are already exposed to the components of tea tree oil, as they are present in a multitude of plants. Although exposure to fish, insects, and plants is anticipated from use of the product through direct application, accidental application, drift or run-off, results of toxicity testing on pure tea tree oil indicate that tea tree oil is practically nontoxic to these organisms. The proposed EP which contains 23.8% tea tree oil will also be diluted with water prior to application, which will further reduce exposure to these organisms. The aquatic invertebrate toxicity study submitted indicates that tea tree oil is highly toxic to these organisms. Because of the potential for toxicity to freshwater invertebrates, a risk assessment for these organisms was conducted for the EP based on nontarget organism toxicology data on the EP (EPA, 2014a). The results of the risk assessment for the EP indicated that mitigation language for aquatic invertebrates is required on the EP label.

4. Endangered Species Assessment

The Agency has not conducted a risk assessment that supports a complete endangered species determination. The ecological risk assessment planned during registration review will allow the Agency to determine whether tea tree oil's use has "no effect" or "may effect" federally listed threatened or endangered species (listed species) or their designated critical habitats. When an assessment concludes that a pesticide's use "may affect" a listed species or its designated critical habitat, the Agency will consult with the U.S. Fish and Wildlife Service and/or National Marine Fisheries Services (the Services) as appropriate.

D. Product Performance Data

Product performance data must be developed for all pesticides to ensure that pesticide products will perform as intended and that unnecessary pesticide exposure to the environment will not occur as a result of the use of ineffective products. The Agency reserves the right to require on a case-by-case basis, submission of efficacy data for any pesticide product registered or proposed for registration that are intended to be used to control a pest of significance public health importance and a public health pest as defined in FIFRA section 28(d) and section 2(nn). For further guidance on product performance requirement, refer to Pesticide Registration Notice (PR) Notices 96-7, 2002-1 and Explanation of Statutory Framework for Risk-Benefit Balancing for Public Health Pesticides (http://www.epa.gov/PR_Notices/pr1996-7.pdf) (http://www.ea.gov/PR_Notices/pr2002-1.pdf) and (http://www.epa.gov/pesticides/health/risk-benefit.htm).

The EP submitted with this new active ingredient did not list pests of significant public health importance or a public health pest as defined in FIFRA section 28(d) and section 2(nn). Therefore, product performance (efficacy) was not evaluated.

V. RISK MANAGEMENT DECISION

A. Determination of Eligibility for Registration

Section 3(c)(5) of FIFRA provides for the registration of a new active ingredient if it is determined that: (A) its composition warrants proposed claims; (B) its labeling and other materials 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.

The four criteria of the Eligibility Determination for Pesticidal Active Ingredients are satisfied by the science assessments supporting products containing the TGAI, tea tree oil. Such products are not expected to cause unreasonable adverse effects. Therefore, tea tree oil as a TGAI is eligible for registration for the labeled uses.

B. Regulatory Decision

The data submitted fulfill the registration requirements of tea tree oil for use as a fungicide/bactericide. Refer to Appendix B for product-specific information.

Conditional/Unconditional Registration

All data requirements are fulfilled, and EPA determined that an unconditional registration of tea tree oil 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—with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies. At this time, EPA does not believe that use of tea tree oil pesticide products 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

EPA evaluated all data submitted in connection with the registration of the tea tree oil pesticide products and determined that these data are sufficient to satisfy current registration data requirements. At this time, no additional data must be submitted to EPA for these particular products. For new uses and/or changes to existing uses, EPA may require additional data.

Notwithstanding the information stated in the previous paragraph, it should be clearly understood that certain specific data are required to be reported to EPA 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

Pursuant to FIFRA section 6(a)(2), reports of all incidents of adverse effects to the environment must be submitted to EPA.

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 158.2050(d).

VII. APPENDIX A. DATA REQUIREMENTS (40 CFR PART 158-SUBPART U)

*NOTE: Master Record Identification (MRID) numbers listed in the following tables are representative of supporting data/information 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 4. Product Chemistry Data Requirements for Tea Tree Oil (40 CFR § 158.2030)

OCSPP Guideline Reference No./Study		Description of Result	MRID
880.1100	Product identity and composition	The product identity and composition were adequately addressed. Confidential Business Information (CBI).	47730401
880.1200	Description of starting materials, production, and formulation process	The description of the starting materials, production, and formulation process were adequately addressed. CBI.	47730401
880.1400	Discussion of formation of impurities	The discussion of formation of impurities was adequately addressed. CBI.	47730401
830.1700	Preliminary analysis	The preliminary analysis of the product was acceptable. CBI.	47730402, 47730403
830.1750	Certified limits	The certified limits listed on the CSF are acceptable.	47730401
830.1800	Enforcement analytical method	The enforcement analytical method was adequately addressed. CBI.	47730401

TABLE 5. Physical and Chemical Properties for Tea Tree Oil (40 CFR § 158.2030)			
OCSPP Guideline Reference No./Property		**Description of Result**	**MRID**
830.6302	Color	Colorless to pale yellow	47730401
830.6303	Physical State	Liquid	47730401
830.6304	Odor	Characteristic	47730401
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Decomposition temperature is expected to be >200°C (based on values for the individual components). Generally stable to galvanized steel (packaging material) over 8 months at ambient warehouse storage, 10-35˚C.	47730401 Correspondence between Canada's Pest Management Regulatory Agency (PMRA) and TSG dated May 11, 2009 and PMRA product chemistry review.
830.6315	Flammability	Flashpoint = 55°C 59°C	47918402 47730401
830.6317	Storage Stability	Composition of TGAI may vary considerably during storage, with ρ-cymene levels increasing and α- and γ-terpinene levels decreasing. Light, heat, air exposure and moisture affect oil stability. The MP should be stored in dark, cool, dry conditions in an airtight container. During the 8 month study, of the 5 major components, α-terpinene decreased ~13% and ρ-cymene increased ~15.5%, with the other three not changing significantly.	Correspondence between PMRA and TSG dated May 11, 2009, and PMRA product chemistry review.
830.6319	Miscibility	Not applicable, the product is not to be mixed with petroleum solvents.	47730401
830.6320	Corrosion Characteristics	Generally stable to galvanized steel (packaging material) over 8 months at ambient warehouse storage, 10-35˚C. No visual changes (corrosion, color change) were observed.	Correspondence between PMRA and TSG dated May 11, 2009, and PMRA product chemistry review.
830.7000	pH	Not applicable	47730401
830.7050	UV/Visible light absorption	In propan-2-ol, a single maximum at 265 nm was observed.	47730409 and 47918403
830.7100	Viscosity	2.47 cSt at 25ºC	48275001
830.7200	Melting Range	Not applicable, the product is a liquid.	47730401
830.7220	Boiling Range	Expected to be ca. 200°C (derived from values of the individual components)	47730401
830.7300	Density/Relative Density/Bulk Density	Minimum density = 0.885 g/mL at 20°C Maximum density = 0.906 g/mL at 20°C	47730401
830.7520	Particle size, fiber length, and diameter distribution	Not known for TGAI. Relevant components of TGAI are not expected to dissociate.	47730401 and 47730409

TABLE 5. Physical and Chemical Properties for Tea Tree Oil (40 CFR § 158.2030)

OCSPP Guideline Reference No./Property	Description of Result	MRID
830.7550 Partition Coefficient (n-Octanol/ Water) 830.7560 830.7570	Not known for TGAI. Component — log K_{ow} terpinen-4-ol — 2.643 — 3.33 γ-terpinene — 4.47 α-terpinene — 4.75 p-cymene — 4.44 1,8-cineole — 3.13	47730401 and 47730409
830.7840 Water Solubility	Not known for TGAI. Component — Temp (˚C) — Solubility terpinen-4-ol — - — 1767 mg/L γ -terpinene — 22-25 — 8.72 mg/L α-terpinene — - — 5.92 mg/L p-cymene — - — 5.0 mg/L 1,8-cineole — - — 552 mg/L	47730401 and 47730409
830.7950 Vapor Pressure	Not known for TGAI. Component — Temp (˚C) — VP (Pa) terpinen-4-ol — 20 — 53.2 (-terpinene — 20 — 93.1 — 23.5 — 103 α-terpinene — 20 — 106.4 p-cymene — 25 — 199.5 1,8-cineole — 25 — 253	47730401 and 47730409

Table 6: Mammalian Toxicology Data Requirements for Tea Tree Oil (40 CFR § 158.2050)			
Study/OCSPP Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Acute oral toxicity (rat) (870.1100)	LD_{50} = 1752 mg/kg (1752-2450 mg/kg)	Toxicity Category III	47730404
Acute dermal toxicity (rat) (870.1200)	LD_{50} > 2000 mg/kg	Toxicity Category III	47730404
Acute inhalation toxicity (rat) (870.1300)	LC_{50} = 3.64 mg/L	Toxicity Category IV	48598701 48878201
Primary eye irritation (rabbit) (870.2400)	Waived: MP is corrosive to skin. A chorioallantioic membrane vascular assay (chicken egg) was submitted, but is unacceptable as EPA has not established this assay to be appropriate to fulfill the primary eye irritation data requirement.	Toxicity Category I	47730405
Primary dermal irritation (rabbit) (870.2500)	Corrosive. Well-defined to severe erythema and barely perceptible to slight edema were noted on the intact sites of 6/6 rabbits at the 24- and 72-hour evaluations. Well-defined to severe erythema and barely perceptible to moderate edema were noted on the abraded sites of 6/6 rabbits at the 24 and 72 hour evaluations. Three animals had erosion on abraded sites at the 72-hour evaluation. The primary irritation index (PII) was 5.0.	Toxicity Category I	47730404
Dermal sensitization (guinea pig) (870.2600)	Waived: MP is corrosive to skin. A skin sensitization study was submitted. After intradermal and epidermal inductions, the test and control animals showed no signs of reactivity 24 hours after challenge. However, study classification is unacceptable due to the lack of positive control data.	-	47730404
90-Day oral toxicity (870.3100)	LOAEL = 60 mg/kg/day based on testicular toxicity in males and increased liver to body weight ratios in females NOAEL = 30 mg/kg/day for males and females	-	48598702 48878202
90-Day dermal toxicity (870.3250)	Waived: prolonged dermal exposure not anticipated. TGAI is corrosive to skin and adequate PPE is required on the label. Undiluted tea tree oil caused severe irritation to the skin on the first day of a non-guideline 30-day dermal irritation study on rabbits. For the remainder of the study, a 25% solution in paraffin oil was applied to the skin which did not result in visible irritation; however, non-specific microscopic dermatitis consistent with irritation was observed.	-	47730411 47730404
90-Day inhalation toxicity (870.3465)	The data from the 90-data oral toxicity study has been bridged to satisfy this data requirement. A route to route extrapolation will be employed using a 100% absorption assumption.	-	48598704 48878201

Table 6: Mammalian Toxicology Data Requirements for Tea Tree Oil (40 CFR § 158.2050)			
Study/OCSPP Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Developmental toxicity (870.3700)	Maternal: NOAEL = 30 mg/kg/day LOAEL = 60 mg/kg/day based on treatment related decreased body weight gain and food intake Developmental: NOAEL = 60 mg/kg/day LOAEL = 120 mg/kg/day based on decreased fetal weights	-	49166401
Mutagenicity – Tier I (870.5100, 5300 and 5375) Mutagenicity – Tier II (870.5395)	Not mutagenic in *Salmonella* reverse mutation assay at doses below 50 µg. Negative in *in vivo* mouse bone marrow micronucleus assay.	-	47730404 47730407 47730409

Table 7: Nontarget Organism Toxicity Data Requirements for Tea Tree Oil (40 CFR § 158.2060)			
Study/OCSPP Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Avian acute oral toxicity (850.2100)	Adequate information to support data requirement: significant exposure to birds is not expected due to volatilization and rapid degradation of the active ingredient in the environment. Additionally, components of the TGAI are already found in a multitude of plants.	Significant exposure not expected	47730411
Avian dietary toxicity (850.2200)	Adequate information to support data requirement: significant exposure to birds is not expected due to volatilization and rapid degradation of the active ingredient in the environment. Additionally, components of the TGAI are already found in a multitude of plants.	Significant exposure not expected	47730411
Aquatic invertebrate acute toxicity, freshwater (850.1010)	48-hour EC_{50} = 0.591 mg/L (95% CL: 0.499-0.700 mg/L)	Highly toxic	48598703
Fish acute toxicity, freshwater (850.1075)	LC_{50} > 100 mg/L	Practically non-toxic	47730408
Terrestrial plant toxicity, Seedling emergence/Vegetative vigor (850.4100 and 850.4150)	Adequate information to support data requirement: using the proposed EP in efficacy trials on squash, potatoes, apples, no phytotoxicity was observed. Minor phytotoxicity was observed in one South African grape variety (brown spots) in one trial; however, in nine other trials in grapes no phytotoxicity was observed. Minor phytotoxicity was observed in one trial in tomatoes and cucumbers (small necrotic spots); however, no phytoxicity was observed in eleven other trials in tomatoes. The components of tea tree oil are volatile and are also already found in a multitude of plants.	Not phytotoxic	47730521
Nontarget insect testing	*Apis millifera*: oral LD_{50} > 98.5 µg a.i./bee;		47730520[1]

Table 7: Nontarget Organism Toxicity Data Requirements for Tea Tree Oil (40 CFR § 158.2060)			
Study/OCSPP Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
(880.4350)	contact LD_{50} > 331 μg a.i./bee *Bombus terrestris:* oral LD_{50} > 105.49 μg a.i./bee; contact LD_{50} > 100 μg a.i./bee *Aphidius rhopalosiphi*: ER_{50} and LR_{50} >1.08 L **EP**/ha *Typhlodromus pyri*: ER_{50} = 1.78 L EP/ha (95% c.i., 1.54-2.09 L **EP**/ha); 7d LR_{50} >4.32 L EP/ha	Practically non-toxic	47730519[2] 47730518[3] 47730517[3]

[1]Study conducted on the proposed EP, Timorex Gold (EPA File Symbol No. 86182-R), at target doses of 100 μg a.i./bee (oral) and 18, 32, 56, 100, 180, and 320 μg a.i./bee (contact)
[2] Study conducted on the proposed EP, Timorex Gold (EPA File Symbol No. 86182-R), at a target dose of 100 μg a.i./bee (nominally equivalent to 423.73 μg EP/bee)
[3] Supplemental data. Values reported are based on the proposed EP, Timorex Gold (EPA File Symbol No. 86182-R), and have not been corrected for active ingredient concentration.

VIII. APPENDIX B.

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

IX. APPENDIX C.

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X. GLOSSARY OF ACRONYMS AND ABBREVIATIONS

a.i.	active ingredient
ARS	Agricultural Research Service (USDA)
Biomor	Biomor Israel, Ltd.
BPPD	Biopesticides and Pollution Prevention Division
BRAD	Biopesticide Registration Action Document
bw	body weight
CBI	Confidential Business Information
CFR	Code of Federal Regulations
cm^3	cubic centimeter

CSF	Confidential Statement of Formula
cSt	centistokes
°C	degrees Celsius
DEEM-FCID	Dietary Exposure Evaluation Model - Food Commodity Intake Database
EC_{50}	median effective concentration. A statistically derived single concentration in environmental medium that can be expected to cause an effect in 50% of the test animals when administrated by the route indicated (inhalation). It is expressed as a concentration in air or water (e.g. mg/L).
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EP	end-use product
EPA	Environmental Protection Agency (the "Agency")
FDA	U.S. Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
FR	Federal Register
g	gram
ha	hectare
kg	kilogram
Kow	octanol-water partition coefficient
L	liter
LC_{50}	median lethal concentration. A statistically derived single concentration in air or water that can be expected to cause death in 50% of the test animals when administrated by the route indicated (inhalation and environment). It is expressed as a concentration in air or water (e.g. mg/L).
LD_{50}	median lethal dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral and dermal). It is expressed as a weight of substance per unit weight of animal (e.g., mg/kg).
LOAEL	lowest-observed-adverse-effect-level
LOC	level of concern
LOQ	limit of quantification
MOE	margin of exposure
MRID No.	Master Record Identification Number
mg	milligram
mPa	millipascal
mL	milliliter
MP	manufacturing-use product
N/A	not applicable
NE	"No Effect"
nm	nanometer
NOAEL	no-observed-adverse-effect-level
NOEL	no-observed-effect-level
NOF	notice of filing
NOR	notice of receipt

OPP	Office of Pesticide Programs
OCSPP	Office of Chemical Safety and Pollution Prevention
pa	pascal
PHI	pre-harvest interval
PMRA	Canada's Pesticide Management Regulatory Authority
POD	point of departure
PPE	personal protective equipment
PR Notice	Pesticide Registration Notice
REI	restricted-entry interval
RfD	reference dose
TGAI	technical grade of the active ingredient
TSG	Technology Sciences Group, Inc.
UF	uncertainty factor
ug	microgram
USDA	United States Department of Agriculture
UV	ultra-violet