Proposed Registration Decision for the New Active Ingredient

Red Thyme Oil

fungicide for use on food crops, turf, ornamentals and greenhouses

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Approved by:

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1. Introduction

This document announces that the Environmental Protection Agency (EPA) has completed its initial evaluation of the new biochemical active ingredient (AI), red thyme oil, for use as a fungicide on crops, turf, and ornamentals and has concluded that it meets the regulatory and safety standards under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA). EPA is seeking public comments on its proposed decision during a 15-day public comment period.

Red thyme oil, also known as Spanish thyme oil, is an essential oil extracted from the thyme plant species *Thymus zygis*. It is a pale yellow liquid that is classified as an edible oil, and it is used as a flavor and fragrance ingredient. Red thyme oil is obtained from thyme plants grown in southern Spain and northern Africa. The primary components found in this active ingredient are thymol (~49-50%), γ-terpinene, p-cymene, linalool, and carvacrol. It is reported that some thyme oil from *Thymus zygis* may contain up to 90% thymol.

EPA has already registered "thyme oil" (also known as white thyme oil) as an active ingredient. The already registered thyme oil is from a different species - *Thymus vulgaris.* While the already registered thyme oil and the proposed new active ingredient, red thyme oil (*Thymus zygis*) differ in their species designation, both species belong to the same botanical genus *Thymus,* and the same botanical family Lamiaceae, and both contain the same major constituent thymol. Based on their similarities, data for thyme oil (from *Thymus vulgaris*) have been used in this assessment in some cases. Notably, the main constituent of the already registered thyme oil and red thyme oil is thymol, which is also a stand-alone active ingredient in federally registered pesticide products approved for use on food. Despite variable differences in the constituent compounds between the already registered thyme oil and red thyme oil, the Agency has determined that red thyme oil and thyme oil are substantially similar as the two oils are considered to be structurally and functionally similar.

The oils of thyme from the plant species *Thymus zygis* and *Thymus vulgaris* are known to have strong antimicrobial properties, which make them useful as ingredients in cosmetics, pharmaceuticals, and the food industry. Further, the U.S. Food and Drug Administration (FDA) has categorized the essential oils of thyme as Generally Recognized as Safe (GRAS) (21 CFR 582.20).

As an active ingredient in pesticidal end-use products (EPs), red thyme oil is intended for use as a contact foliar fungicide for application on food crops, turf, and ornamentals in both residential and agricultural settings, including greenhouses, orchards, nurseries, and agricultural fields. One manufacturing-use product (MP), Red Thyme Oil Technical (EPA File Symbol: 94218-R), and one EP, NSTKI-014 (EPA File Symbol: 94218-E), are proposed for registration. The EP is formulated as a wettable powder that is diluted in water and can be applied every 5 days at the first sight of

disease symptoms. The EP is mixed at a rate of 2-7 pounds (lbs.) product in 100 gallons (gal.) of water to obtain a solution with a pH of 7-10. Since the AI is present at a nominal concentration of 1.75% in the EP, it is applied at a maximum application rate of 0.1225 lbs. AI/acre (0.001225 lbs. AI/gallon) for a single application; therefore, with only 10 applications allowed per year the total annual application rate will be 1.225 lbs. AI/acre/year. The EP is intended to be applied using handheld sprayers and groundboom equipment with the option of adding a shield over the sprayers. The restricted-entry interval (REI) listed on the label is 4 hours from the time of application. All occupational applicators and handlers are required to wear the following personal protective equipment (PPE): long-sleeved shirts, long pants, shoes and socks, chemical-resistant gloves, and protective eyewear.

After reviewing the submitted and publicly available data and information for red thyme oil, EPA has concluded that there is a reasonable certainty of no harm from residues of this new active ingredient and that its use will not cause unreasonable adverse effects to human health or the environment. Therefore, the Agency is proposing to grant the unconditional registration of two products one MP and one EP: Red Thyme Oil Technical (EPA File Symbol: 92188-R) and NSTKI-014 (EPA File Symbol: 94218-E) containing the new active ingredient, red thyme oil, under FIFRA section 3(c)(5).

An exemption from the requirement of a tolerance is already established for red thyme oil. The regulations at 40 CFR 180.950 (Tolerance exemptions for minimal risk active and inert ingredients) states: "Unless specifically excluded, residues resulting from the use of the following substances as either an inert or an active ingredient in a pesticide chemical formulation … are exempted from the requirement of a tolerance under FFDCA section 408, if such use is in accordance with good agricultural or manufacturing practices." (See 67 FR 36537, May 24, 2002: https://www.federalregister.gov/documents/2002/05/24/02-12973/pesticides-tolerance-exemptions-for-minimal-risk-active-and-inert-ingredients. During the pre-application meetings and discussions with the applicant, EPA determined that red thyme oil is an "edible oil" per 40 CFR 180.950(c) and is therefore exempt from the requirement of a tolerance under FFDCA section 408. Background

2. Background

Thyme oil (derived from *Thymus vulgaris*) and its principal active constituent, thymol, were originally classified as biochemical pesticides by the Agency's Biochemical Classification Committee in 1997, due to their natural occurrence, history of exposure to humans and the environment, and non-toxic mode of action to the target pest(s). The Agency's current assessment confirms that red thyme oil qualifies as equivalent to the other approved thyme oil.

On June 9, 2020, EPA received applications from Biofungitek, S.L. for the registration of two pesticide products, one manufacturing product (MP), and one end-use product (EP), containing the new biochemical fungicide, red thyme oil. To support the FIFRA section 3 registration applications, Biofungitek, S.L. provided a combination of guideline studies, data waiver requests, and scientific rationales supported by information from the open scientific literature to address

product chemistry, human health, and ecological toxicity data requirements. A petition to establish a tolerance exemption for residues of red thyme oil on all food commodities was not submitted by the applicant. As previously stated, during the pre-application meetings and discussions with the applicant, EPA determined that red thyme oil is an "edible oil" per 40 CFR 180.950(c) and is therefore exempt from the requirement of a tolerance under FFDCA section 408. (See 67 FR 36537, May 24, 2002: https://www.federalregister.gov/documents/2002/05/24/02-12973/pesticides-tolerance-exemptions-for-minimal-risk-active-and-inert-ingredients.)

In the Federal Register of April 21, 2021, EPA published a Notice of Receipt (NOR) that announced receipt of two new product applications: one manufacturing-use product (MP), Red Thyme Oil Technical (EPA File Symbol: 94218-R), and one end-use product (EP), NSTKI-014 (EPA File Symbol: 94218-E), containing the new active ingredient, red thyme oil.

3. Evaluation

In evaluating a pesticide registration application, EPA assesses a variety of studies to determine the likelihood of adverse effects (i.e., risk) from exposures associated with the use of the pesticide product. Risk assessments are developed to evaluate how the active ingredient might affect a range of nontarget organisms, including humans and terrestrial and aquatic wildlife (plants and animals). Based on these assessments, EPA evaluates and approves language for each pesticide label to ensure the directions for use and safety measures are appropriate to mitigate any potential risk. In this way, the pesticide's label helps to communicate essential limitations and/or mitigations that are necessary for public and environmental safety. In fact, it is a violation of FIFRA to use a registered pesticide in a manner inconsistent with the label.

3.1 Assessment of Risk to Human Health

To assess risks to human health from use of biochemical pesticides, EPA evaluates the potential toxicity of a product, and the likelihood, amount, and types of exposure users and bystanders are likely to experience. In conducting a risk assessment, EPA must consider: (1) the hazards of a substance and (2) the direct or indirect human exposure to that substance as a consequence of use. EPA uses this information to assess and characterize the risk(s) and predict the probability, nature, and magnitude of the adverse health effects that may occur from use of the substance in the manner described.

To evaluate the toxicity of biochemical pesticides, EPA typically requires a range of Tier I data: acute toxicity data (acute oral toxicity, acute inhalation toxicity, acute dermal toxicity); irritation tests (primary eye irritation, primary dermal irritation, and dermal sensitization); subchronic testing (90-day oral, 90-day dermal, and 90-day inhalation); mutagenicity testing (bacterial reverse mutation test and in vitro mammalian cell assay); and developmental toxicity testing (prenatal development). Tiers II and III testing requirements are triggered only when there is indication, usually through lower tier testing, that a biochemical pesticide has unusual characteristics, such as subchronic toxicity, or is suspected or known to be a carcinogen.

3.1.1 Toxicological Data/Information

Adequate mammalian toxicology data/information are available to support the registration of red thyme oil. All toxicology data requirements for red thyme oil have been satisfied and a risk assessment is available in the regulatory docket (search for "EPA-HQ-OPP-2021-0219" at http://www.regulations.gov).

The toxicology database used for the biopesticide risk assessment for red thyme oil includes: 1) guideline acute toxicity studies; 2) rationales for the 90-day oral toxicity, 90-day dermal toxicity, 90-day inhalation toxicity, prenatal developmental toxicity, *in vitro* mammalian cell assay, bacterial reverse mutation test, and *in vivo* cytogenetics data requirements; and 3) a 26-week inhalation toxicity non-guideline study. The rationales for the 90-day oral, 90-day dermal, and 90-day inhalation requirements were accepted by OPP's Hazard and Science Policy Council (HASPOC) on December 14, 2022. Tier II and III data requirements have not been triggered at this time. Additionally, no relevant toxicity data for this active ingredient or related substances were found in a search of the literature. The toxicology data requirements and the toxicological profile are discussed in the following sections.

Acute Toxicity

The acute toxicity data requirements were all satisfied by guideline studies on the MP and indicated a range of acute toxicity profiles. The data submitted for undiluted red thyme oil support the active ingredient being classified as Toxicity Category IV for inhalation toxicity; toxicity Category III for acute oral toxicity and dermal irritation; and toxicity Category II for acute dermal toxicity and eye irritation. The available data also suggest it is a skin sensitizer. The signal word "Warning" will be used on the MP label as a result of the eye irritation and the indications that it is a dermal sensitizer.

Subchronic Toxicity

90-day oral toxicity

The rationale submitted to fulfill the 90-day oral toxicity data requirement was assessed by the HASPOC, using a weight of the evidence (WOE) approach that considered all of the available hazard and exposure information. The rationale was determined to be acceptable based on the following considerations: (1) two repeat dose studies were performed on rats that were fed thymol (the major component in red thyme oil and an acceptable surrogate for these studies) at varying doses above the limit dose; and no adverse effects were observed in either study; (2) low acute oral toxicity (Toxicity Category III); (3) red thyme oil is naturally occurring and has been part of the human diet in food products and used in a variety of cosmetic products; (4) red thyme oil is categorized as an edible oil, so it is exempt from the requirement of a tolerance when used as an inert or active ingredient in pesticide chemical formulations (40 CFR 180.950); (5) the proposed active ingredient, red thyme oil, is a mixture of organic compounds known to

be rapidly degraded in the environment to elemental compounds by normal biological, physical and/or chemical processes; and (6) thymol is currently exempt from the requirement of a tolerance in the U.S. in or on food commodities.

90-day dermal toxicity

The rationale submitted to fulfill the 90-day dermal toxicity data requirement was assessed by the HASPOC, using a WOE approach that considered all of the available hazard and exposure information. The rationale was determined to be acceptable based on the following considerations: (1) thyme oil and thymol, as surrogates for red thyme oil, are naturally occurring with a history of use without adverse reactions seen from their uses in cosmetics and foods approved by the FDA; (2) the essential oils of thyme (including *Thymus zygis*) are recognized as GRAS by the FDA (21 CFR 582.20); (3) there were no adverse effects observed in three repeat-dose tests on surrogates for red thyme oil, which included two thymol repeat oral (gavage) dose toxicity studies up to the highest dose tested (HDT) (667 mg/kg/day) and one prenatal development toxicity study for thyme oil in rats dosed at 375 mg/kg/day (HDT); and (4) the repeat-dose oral studies approached the limit dose without adverse effects and the identification of endpoints.

90-day inhalation toxicity

The rationale submitted to fulfill the 90-day inhalation toxicity data requirement was assessed by the HASPOC, using a WOE approach that considered all of the available hazard and exposure information. The rationale was determined to be acceptable based on the following considerations: (1) the low acute inhalation toxicity for red thyme oil (Toxicity Category IV); (2) a 26-week repeat dose study on thymol (an acceptable surrogate for red thyme oil), wherein no adverse effects were observed on body weights, organ weights, food intake, appearance and functional behaviors; (3) the natural occurrence and long history of human exposure in food and cosmetics to thyme oil, an acceptable surrogate for red thyme oil; and (4) no adverse effects or endpoints were observed in a 19-week repeat-dose oral study on rats.

Developmental Toxicity

The rationale submitted to fulfill the developmental toxicity data requirement was assessed by the HASPOC, using a WOE approach that considered all of the available hazard and exposure information. The rationale was determined to be acceptable based on the following considerations: (1) prenatal developmental studies were found in the public literature for the several acceptable surrogates - thyme extract *(Thymus vulgaris)*, thyme oil *(Thymus vulgaris)*, and thymol and no adverse effects were reported in any of the repeat dose developmental studies; (2) all species of thyme oil (including red thyme oil) are naturally occuring and humans have a long history of exposure to these substances in food and cosmetic products; (3) red thyme oil is of low acute oral toxicity (Toxicity Category III); (4) red thyme oil is categorized as an edible oil and is exempt from the requirement of a tolerance when used as an inert or active ingredient in pesticide chemical formulations (40 CFR 180.950); (5) a non-guideline prenatal 2-week development study on mice using the surrogate thyme oil demonstrated no adverse

effects on embryo development at 375 mg/kg/day; and (6) a developmental safety assessment was conducted on pregnant rats who were administered thyme extract (*Thymus vulgaris)* and pure thymol, two acceptable surrogates for red thyme oil. No signs of external toxicity or mortality were observed in all groups treated with thyme extract and thymol.

Genotoxicity

Acceptable publicly available genotoxicity data were submitted on red thyme oil (*Thymus zygis*) and two acceptable surrogates, thyme oil (*Thymus vulgaris*) and thymol. In an Ames test, all three substances tested negative and did not induce mutations in the *Salmonella typhimurium TA 1535, TA 1537, TA98, and TA100* strains tested. For the required *in vitro* mammalian cell assays on mice and hamsters, the surrogates, thyme oil (*Thymus vulgaris*), and thymol, tested negative for mutations. Finally, for the *in vivo* micronucleus test requirement, the surrogate thyme oil (*Thymus vulgaris*) did not produce an increase in micronuclei in the bone marrow of rats during an *in vivo* micronucleus test. All available data indicate that red thyme oil and its surrogates are not genotoxic.

3.1.2 Dietary and Occupational Exposure and Risks

Dietary and Drinking Water Exposure and Risk Characterization

Dietary risk assessment incorporates both exposure (food and drinking water) and toxicity of a given pesticide. For red thyme oil, the Agency has conducted a qualitative dietary risk assessment in lieu of a quantitative assessment. Dietary risk is expected to be not of concern, as significant residues of the substance are not anticipated on treated commodities at the time of consumption based on red thyme oil's rapid biodegradability. Moreover, red thyme oil is an edible oil that occurs naturally in food commodities, is of low toxicity, and is exempt from the requirement of tolerance when used as an active ingredient in a pesticide chemical formulation if its use is in accordance with good agricultural and manufacturing practices under 40 CFR 180.950(c). Relatedly, its major component, thymol, is also currently exempt from the requirement of a tolerance in or on food commodities when used in accordance with good agricultural practices (40 CFR 180.1240(a)) and in or on food commodities when applied/used in/on public eating places, dairy processing equipment, and/or food processing equipment and utensils (40 CFR 180.1240(b)).

Residential (Non-occupational) Exposure and Risk Characterization

Red thyme oil is intended for use in residential (non-occupational) settings. Residential uses are anticipated to result in minimal residential risk based on the following: (1) the dilution of the EP in water will further reduce the concentration of the TGAI and minimize any potential exposure; and (2) humans have a history of exposure to thyme oil, including red thyme oil, because it is found in a variety of food and cosmetic products, red thyme oil is an edible oil and is exempt from the requirement of a tolerance under 40 CFR 180.950(c); and (3) there was a lack of systemic toxicity reported in the toxicological database does not indicate any systemic toxicity. Given these factors, residential handler and post-application risks are not expected.

Occupational Exposure and Risk Characterization

Short- (1 to 30 days) and intermediate-term (1 to 6 months) dermal and inhalation exposures to red thyme oil are expected for occupational handlers from application of the proposed product. There is potential for post-application exposure for agricultural workers re-entering treated areas. Occupational handlers are required to wear the following PPE: long-sleeved shirts, long pants, shoes, and socks, chemical resistant gloves, and protective eyewear which are listed on the proposed label. Use of shielded sprayers will help reduce drift and exposure. There is a 4-hour REI for occupational workers. Occupational handler risk and post-application risk to red thyme oil are expected to be negligible based on the natural occurrence and long history of human exposure, low application rates, physical chemical properties (the proposed active ingredientis a mixture of organic compounds known to be rapidly degraded in the environment to elemental compounds by normal biological, physical and/or chemical processes), lack of toxicological concerns, and PPE requirements; therefore, a qualitative risk assessment has been conducted in lieu of a quantitative assessment.

3.1.3 Cumulative Risk

EPA has not made a common mechanism of toxicity finding for red thyme oil and any other substances, and this biopesticide does not appear to produce a toxic metabolite produced by other substances. Therefore, EPA has not assumed that red thyme oil has a common mechanism of toxicity with other substances.

3.1.4 Human Health Conclusions

EPA concludes that the use of red thyme oil will not result in unreasonable adverse effects to human health and that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of red thyme oil. EPA does not expect dietary (food and drinking water) or other non-occupational risks of concern from the use of red thyme oil. Data demonstrates that red thyme oil is of low toxicity for all routes of exposure when formulated into an EP. Occupational exposure for individuals handling red thyme oil or entering treated areas are not expected to result in risks of concern.

The database of studies required to support the hazard assessment to human health is complete. For more information on the human health hazard assessment of red thyme oil, see the supporting documentation provided in the associated regulatory docket (search for "EPA-HQ-OPP-2021-0219" at http://www.regulations.gov).

Determination of Safety for U.S. Population, Infants, and Children U.S. Population:

Infants and Children:

With particular regard to infants and children, FFDCA section 408(b)(2)(C) provides that, in

establishing or modifying a tolerance or tolerance exemption for a pesticide chemical residue, EPA shall assess risk considering the available information about consumption patterns among infants and children, special susceptibility of infants and children to pesticide chemical residues, and the cumulative effects on infants and children of the residues and other substances with a common mechanism of toxicity and ensure there is a reasonable certainty of no harm to infants and children from aggregate exposure to the pesticide chemical residue. In addition, FFDCA section 408(b)(2)(C) requires that, in the case of threshold effects, EPA apply an additional tenfold (10X) margin of safety for infants and children to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure, unless EPA determines, based on reliable data, that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the Food Quality Protection Act (FQPA) Safety Factor. In applying this provision, EPA either retains the default value of 10X or uses a different safety factor when reliable data available to EPA support the choice of a different factor. An FQPA safety factor is not required at this time for red thyme oil because EPA performied a qualitative dietary assessment based on negligible toxicological and exposure concerns.

3.2 Assessment of Ecological Exposure and Risk

To assess ecological risks from use of biochemical pesticides, EPA evaluates the likely environmental impacts as a result of exposure of the chemical to plants and animals in the environment and whether that exposure will cause harm or ecological effects. EPA uses this combined information and considers the overall toxicity to characterize the risk(s) in order to identify what levels may cause harmful effects on the plants and animals of concern from use of the substance in the manner described.

To evaluate toxicity, EPA initially requires that a wide range of studies including Tier I testing be done on the following nontarget organisms: mammalian (acute, sub-chronic, prenatal developmental, and mutagenicity), birds (acute oral and dietary), aquatic animals (acute freshwater fish and aquatic invertebrates), terrestrial plants, and nontarget insects. Testing is organized in a tiered structure, where Tier I studies test worst-case exposure scenarios and higher tiers (Tiers II and III) generally encompass definitive risk determinations and longer-term greenhouse or field testing. Higher tier testing is implemented only when unacceptable effects are seen at the Tier I screening level.

The database of studies required to support the hazard assessment to the environment is complete for red thyme oil. All data requirements for avian, mammalian, aquatic taxa, terrestrial plants, and nontarget insects were satisfied with acceptable studies or waiver rationales. All submitted information for red thyme oil indicate that red thyme oil is expected to be practically non-toxic to birds, slightly toxic to mammals, slightly to moderately toxic to freshwater fish, slightly to moderately toxic to freshwater invertebrates, and practically non-toxic to terrestrial invertebrates. Based on the submitted acute oral toxicity study with rats, the EP is practically non-toxic to wild mammals. Phytotoxicity was observed in the seedling emergence study conducted with the EP, whereas no effects were observed in any species tested in a vegetative

vigor study conducted with the same EP. Overall, risks from the proposed uses of the EP are expected to be low for all animal taxa. Furthermore, given the low concentration (1.75% (w/w)) of red thyme oil in the EP, the amount of red thyme oil and thymol to which an animal is expected to be exposed from the proposed uses is low. Therefore, when the EP is used in accordance with the proposed label use directions, direct effects and effects to the diet and habitat of federally listed threatened and endangered terrestrial and aquatic animals are expected to be discountable (as explained in 'Section 3.2.3' of this document).

For more information on the environmental hazard assessment of red thyme oil, please see the supporting documentation provided in the associated regulatory docket (search for "EPA-HQ-OPP-2021-0219" at http://www.regulations.gov).

3.2.1 Terrestrial Animals and Plants

Terrestrial Vertebrates

Terrestrial vertebrates (including birds, mammals, amphibians, and reptiles) may be exposed to red thyme oil as a result of the proposed applications; however, the submitted data indicate that no significant effects are anticipated for terrestrial vertebrates. Acceptable scientific rationales for acute avian oral toxicity and avian dietary toxicity were submitted for red thyme oil. In the rationales, the applicant examined studies from the scientific literature on the dietary effects of white thyme oil and thymol, which are regularly used as feed additives for poultry. None of the studies summarized in the rationale resulted in toxic responses at any treatment level. The highest concentrations tested may be considered the NOAEC (No Observed Adverse Effect Concentration) for each study, resulting in NOAECs ranging from 100 to 4,000 mg thymol/kg-feed and 60 to 5,000 mg thyme oil/kg-feed. Because adverse effects of thyme oil and thymol in avian diets have not been observed, red thyme oil is expected to be practically non-toxic to birds, which serve as a test species surrogate for terrestrial-phase amphibians and reptiles.

A guideline study was submitted to assess effects of red thyme oil on mammals from acute oral exposure. Mortalities occurred at 550, 1,750, and 5,000 mg red thyme oil /kg-bw. The acute oral toxicity test indicated that red thyme oil was slightly toxic with an estimated acute oral LD_{50} of 550 mg red thyme oil/kg-bw. A guideline acute oral toxicity study conducted with the EP indicated that the EP containing red thyme oil was practically non-toxic to mammals through acute oral exposure with estimated acute oral LD_{50} was 3,129 mg EP/kg-bw. All data indicate no direct effects to terrestrial vertebrates are anticipated.

Nontarget Terrestrial Invertebrates

The nontarget insect data requirement was satisfied with an acceptable honeybee acute contact toxicity study for red thyme oil. No mortality occurred in the four lowest doses with 7% mortality in the 100 µg red thyme oil/bee treatment group. No abnormal behaviors were noted except for one immobile bee in the 100 µg red thyme oil/bee treatment group at 24 hours. The study indicated that red thyme oil is practically non-toxic to honeybees with a 48-hour contact LD_{50} value > 100 µg red thyme oil/bee.

Nontarget Plants

The nontarget plant data requirements were satisfied through the submission of acceptable guideline seedling emergence and vegetative vigor studies using the EP (1.75% red thyme oil). In the seedling emergence study, the test indicated some phytotoxicity. For all plant species except for lettuce and tomatoes, measured endpoints were not significantly different from negative controls and no compound-related phytotoxic effects were reported after 21 days. Lettuce had NOAEC values of 0.44 lb EP/acre for shoot height and dry weight and 3.5 lb EP/acre for emergence and survival. The LOAEC (Lowest Observed Adverse Effect Concentration) values for lettuce were 0.88 lb EP/acre for height and weight and 7 lb EP/acre for emergence and survival. For effects on tomato height and dry weight, the NOAEC and LOAEC values were 3.5 and 7.0 lb EP/acre, respectively. The most sensitive dicot species was lettuce with an IC_{25} value of 0.62 lb EP/acre for shoot dry weight.

In the vegetative vigor study, the effects of the EP on survival, growth, and condition of terrestrial plants were measured. Plants were treated with the test substance approximately 2-3 weeks after planting, allowing them to reach the 2- to 4-leaf stage at the time of application. For all species, there were no significant effects on plant survival, shoot height, or shoot dry weight at 21 days after treatment. The NOAEC and EC/IC_{25} values were 7 and >7 lb EP/acre, respectively, for survival, shoot height, and shoot dry weight.

3.2.2 Aquatic Organisms

Freshwater Fish, Aquatic-Phase Amphibians, Aquatic Invertebrates and Aquatic Plants

The applicant satisfied the freshwater fish acute toxicity data requirement by using acceptable scientific information from the public literature on two substantially similar compounds – white thyme oil and thymol - to demonstrate that red thyme oil is expected to be slightly to moderately toxic to freshwater fish. Acute toxicity studies on rainbow trout, coho salmon, and fathead minnows exposed to thyme oil and thymol (accepted surrogates for red thyme oil) indicated 96-hour LC_{50} values of 16.1 mg white thyme oil/L for rainbow trout, 20.5 mg white thyme oil/L for coho salmon, and 3.2 mg thymol/L for fathead minnows.

The applicant satisfied the aquatic invertebrate acute toxicity data requirement by using acceptable scientific information from the public literature on two substantially similar compounds – white thyme oil and thymol - to demonstrate that red thyme oil is expected to be slightly to moderately toxic to freshwater invertebrates. Publicly available scientific data indicate 48-hour EC/LC_{50} values of 5.94 to 12.2 mg for white thyme oil/L for *Daphnia magna* and 3.2 to 5.7 mg for thymol/L for *Daphnia magna*.

With regard to aquatic plants, no significant exposure is anticipated given the low estimated environmental concentration of red thyme oil and the rapid degradation of thyme oil and thymol in the environment. As such, no significant risks are anticipated for any aquatic plants.

3.2.3 Listed Threatened and Endangered Species Conclusions

Red thyme oil is proposed as a new active ingredient that has a fungicidal mode of action. Based on lack of adverse effects at the low estimated environmental concentrations of red thyme oil, direct effects are not expected for all federally listed threatened and endangered ("listed") mammals, birds, amphibians, reptiles, terrestrial invertebrates, and aquatic taxa when the proposed EP is used in accordance with the label use directions. Based on the phytotoxic effects on lettuce and tomato in the submitted seedling emergence study conducted with the proposed EP, impacts are possible for listed terrestrial and semi-aquatic plants via spray drift exposure. For the proposed EP, risk to off-field plants from runoff exposure is expected to be low due to the low concentration of red thyme oil in the EP (1.75% (w/w)) and the rapid degradation of thyme oil and thymol in the environment.

The EPA made "no effect" (NE) determinations for 1,377 listed species and 771 designated CHs. These NE determinations were made because either a species or critical is outside of the action area (based on an overlap analysis) or because no direct effects and no effects to the species' prey, pollination, habitat, and dispersal are expected (including effects to physical or biological features of any designated critical habitat). For the remaining 465 listed species and 128 designated critical habitats, EPA made a "may affect" (MA) determination.

Although effects to listed plants from spray drift exposure are possible, EPA does not anticipate any adverse effects to nontarget plants as a result of the proposed applications of the EP due to incorporation of multiple mitigations to minimize exposure for nontarget plants. The EPA expects that most listed plant species are not present on agricultural fields or highly managed, non-agricultural use sites (such as golf courses or managed residential lawns), because agronomic/management practices make these use sites highly unlikely habitats for listed plants. Additionally, the incorporation of mitigation measures on the proposed label minimizes off-field exposure for listed plants in the vicinity of proposed use sites. These mitigation measures are outlined in 'Section 7' of this document and include spray height restrictions, droplet size restrictions, and a 7-foot buffer to minimize spray drift. Additionally, the proposed label includes use restrictions for Wilson County, Tennessee, to avoid on-field exposure for the listed Spring Creek bladderpod (*Lesquerella perforata*) that may be present on agricultural lands.

Based on the proposed label mitigations, the Agency does not expect any on field or off-field risk to listed plants and is making a "may affect, not likely to adversely affect" (NLAA) determination based on discountable effects for all listed plants and their designated critical habitats within the action area. Because exposure and effects to plants are not anticipated following mitigation, effects to listed animals that depend on such plants for food or habitat are anticipated to be discountable as well. Direct effects to animals are not expected, and the EPA expects that any effects to listed animals are discountable, even if the animal species relies on plants for its food or habitat. Therefore, the EPA made NLAA determinations for the remaining 465 listed species and 128 designated critical habitats.

Pursuant to the requirements of section 7(a)(2) of the Endangered Species Act (16 U.S.C. § 1536(a)(2)) and 50 C.F.R. § 402.13, EPA initiated consultation with the U.S. Fish and Wildlife Service (FWS) on June 28, 2024.

The database of studies required to support the assessment of risk to the environment is complete at this time. For more information on the environmental risk assessment of red thyme oil, please see the supporting documentation provided in the associated regulatory docket (search for "EPA-HQ-OPP-2021-0219" at www.regulations.gov).

4. Benefits

Red thyme oil is a fungicide with a low toxicity profile. It is a lower toxicity alternative to conventional fungicides such as ferbam, ziram, zineb, maneb, mancozeb captafol, captan, folpet and chlorothalonil. End-use products containing red thyme oil can also be used in Integrated Pest Management (IPM) programs as a complement or replacement for the aforementioned conventional fungicides. Of additional note, red thyme oil biodegrades more rapidly than most alternative conventional pesticides, potentially making it a more environmentally protective choice. Altogether, pesticides containing red thyme oil have both environmental and human health benefits relative to many conventional fungicides, making them a valuable addition to the pesticide tool kit and an attractive alternative to conventional fungicides.

5. Public Comments

In the Federal Register of April 21, 2021 (86 FR 20692), EPA published a Notice of Receipt (NOR) that announced receipt of two new product applications: one manufacturing-use product (MP), Thyme Oil, Red (EPA File Symbol: 94218-R) and one end-use product (EP), NSTKI-014 (EPA File Symbol: 94218-E), containing the new biochemical active ingredient, red thyme oil. No comments were received in response to this NOR.

Because the pesticide products contain a new active ingredient, red thyme oil, EPA is opening a 15-day public comment period. EPA is taking this action in accordance with a policy, first implemented in October 2009, designed to provide a more meaningful opportunity for the public to participate in major registration actions.

6. Proposed Registration Decision

The red thyme oil database is comprised of studies and information that meet the data requirements and support the labeled uses. In considering the assessed risk to human health and the environment, EPA concluded that red thyme oil meets the regulatory standard under the FIFRA. Therefore, EPA is proposing to grant the registration of the red thyme oil pesticide products under FIFRA section 3(c)(5).

EPA is proposing to register one MP and one EP. The MP will be for manufacturing and formulating and contains red thyme oil at 100%. The EP contains red thyme oil at 1.75%. The EP

will be applied to a variety of crops, turf, and ornamental plants as a fungicide. Notably, red thyme oil is an edible oil; and as such, a tolerance exemption for red thyme oil is already established, provided its use is in accordance with good agricultural or manufacturing practices.

In the endangered species assessment portion of its review of the proposal to register red thyme oil pesticide products, EPA made a "may affect, not likely to adversely affect" (NLAA) determination for discountable effects to listed terrestrial invertebrates and to taxa that depend upon terrestrial invertebrates (e.g., for diet or pollination), including listed birds, mammals, amphibians, reptiles, insects, arachnids, and plants. Therefore, as part of the registration of the MP and EP containing red thyme oil, EPA initiated consultation with the FWS on June 28, 2024, and we are proposing to require the following term on both registrations:

"If, following consultation with the United States Fish and Wildlife Service, the Service identifies additional issues or needed modifications, EPA will determine whether any changes are needed to this registration or labeling and will notify Biofungitek, S.L. in writing if any changes are necessary and whether they are required to submit an amendment application incorporating any required data or modification, including an amended label. Alternatively, Biofungitek S.L. must submit a request for voluntary cancellation of the product. If this term of registration is not met, EPA may cancel the registration under an expedited process under FIFRA 6(e)."

The risk assessments and labels supporting this proposed decision can be found in the associated regulatory docket (search for "EPA-HQ-OPP-2021-0219" http://www.regulations.gov).

7. Proposed Registration Requirements

The EPA is proposing to register the following products:

An MP: Red Thyme Oil Technical (EPA File Symbol: 94218-R)
- 100% Red Thyme Oil
- The following statements and directions for use must appear on the MP label:
"ONLY FOR FORMULATION INTO FUNGICIDE PRODUCTS INTENDED FOR:
(1) AGRICULTURAL APPLICATIONS (GREENHOUSE, ORCHARD, NURSERY, AND FIELD): For Berries, Bulb Vegetables, Citrus Fruits, Cole Crops (Brassicas), Corn, Cucurbits, Edible Gourds, Fruiting Vegetables, Leafy Vegetables, Pome Fruits, Stone Fruits, Strawberry. Tree Nuts, Tropical Fruits.
(2) FOR CONTROL OF CERTAIN DISEASES IN TURF AND ORNAMENTALS.
(3) FOR RESIDENTIAL USES
(4) Uses for which US EPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and
(5) Uses for experimental purposes that are in compliance with US EPA requirements."

An EP: NSTKI-014 (EPA File Symbol# 94218-E)
- 1.75% Red Thyme Oil
- The following statements and directions for use must appear on the EP label:
"Applicators, mixers, loaders, and other handlers must wear: Long-sleeved shirt; Long pants; Chemical-resistant gloves made of any waterproof material; Protective eyewear; Socks plus shoes"
"RESTRICTIONS
Do not make more than 10 applications (70 lbs/A) in a year.
Do not apply NSTKI-014 through any type of irrigation system.
Do not apply when wind speeds exceed 10 miles per hour at the application site.
Do not apply during temperature inversions."
"In California: Do not apply via high-pressure hand wand to more than 2.8 acres per day per applicator."
"Do not apply NSTKI-014 within Wilson County, Tennessee from September 15 to May 15. The restricted-entry interval (REI) is 4 hours from the time of application."
"BE AWARE OF NEARBY NON-TARGET SITES AND ENVIRONMENTAL CONDITIONS."
"IMPORTANCE OF DROPLET SIZE
An effective way to reduce spray drift is to apply large droplets. Use the largest droplets that provide target pest control. While applying larger droplets will reduce spray drift, the potential for drift will be greater if applications are made improperly or under unfavorable environmental conditions."

Required Labeling Mitigations to Minimize Off-field Exposure:
1) The height of application is to be no more than 3 feet from the target vegetation in order to minimize drift.
2) The product must be applied with nozzles that dispense medium to coarse droplet sizes (Dv0.5 of 341 µm) to minimize drift distances.
3) Applicators must maintain a 7-foot buffer strip between the point of direct application and the closest downwind edge of off-field habitats in order to minimize drift.
4) For home and garden uses label and the turf and ornamental uses, the label has the following language: "apply directly to turf, ornamental plants, and fruit or vegetable plants via handheld sprayer only."

8. Supporting Documents

The risk assessments supporting this proposed decision and the draft product labels for the MP, Thyme Oil, Red (EPA File Symbol: 94218-R) and the EP, NSTKI-014 (EPA File Symbol: 94218-E), can be found in the associated regulatory docket (search for "EPA-HQ-OPP-2021-0219" at http://www.regulations.gov).

9. Future Data Requirements

Should the formulation of the end-use products or the application methods described in ‘Section 7’ of this document change in the future, or if new products are proposed containing red thyme oil, additional data may be required, and new risk assessments may need to be performed.