OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

WASHINGTON, D.C. 20460

MEMORANDUM

SUBJECT: Environmental Risk Assessment and Biological Evaluation in Support of the Section 3 Registration of NSTKI-014, an End-Use Product Containing Two New Active Ingredients (Potassium Carbonate and Red Thyme Oil)

Action Code Case Number:	00132908; 00133037; 00133038
e-Submission Package ID:	Not Available
EPA File Symbol:	94218-G; 94218-R; 94218-E
PC Code:	073504 (potassium carbonate); 597801 (red thyme oil)
CAS Number:	584-08-7, 85085-75-2
A.I. Tolerance/Exemption:	40 CFR 180.950 (red thyme oil); OF8851 (Potassium Carbonate Petition Number)
MRID Numbers:	50898804, 50898812-50898817, 50898903, 50898915-50898918, 50898922, 50898923
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EXECUTIVE SUMMARY

Biofungitek, S.L. requests registration of NSTKI-014, an end use product (EP) containing potassium carbonate and red thyme oil, which are two new active ingredients (AIs). Thyme oil is a complex set of oils and other components found in thyme plants of the genus, *Thymus*. Red thyme oil (CAS number 85085-75-2) specifically comes from *Thymus zygis*, which is grown in southern Spain and northern Africa. White thyme oil (CAS number 8007-46-3) is similar to red thyme oil but comes from *Thymus vulgaris*. Both types of thyme oil contain thymol, but the amount of thymol may differ. The EP will be used as a fungicide on growing crops in agricultural, greenhouse, turf, and home and garden use sites.

The Agency has reviewed and evaluated the non-target organism data for the proposed product. All data requirements have been met. Potassium carbonate is expected to be practically non-toxic to birds, slightly toxic to mammals and fish, and practically non-toxic to aquatic and terrestrial invertebrates. Red thyme oil is expected to be practically non-toxic to birds, slightly toxic to mammals and fish, slightly to moderately toxic to aquatic invertebrates, and practically non-toxic to terrestrial invertebrates. Phytotoxicity was observed in the seedling emergence study conducted with an EP containing both AIs, 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 to all animal taxa.

Based on an application rate of 7.0 lb EP/acre, risk quotients for terrestrial and semi-aquatic plants range from <0.1 to 8.1. The results specifically indicate that there is potential for risk to non-listed and listed dicot plant species from exposure to the proposed EP. No adverse effects were observed to monocots; therefore, risk is expected to be low for monocots. Risk to dicot plants from spray applications is reduced through the incorporation of multiple mitigation measures on the label including requirement to use medium/coarse droplet size and spray height restrictions, as well as incorporation of spray drift buffers. The spray drift buffers are based on distances from the edge of the application area at which spray drift deposition alone is not expected to exceed the no observed adverse effect level (NOAEC) for dicots. With a buffer distance of 7 feet applied to the product label, risks are expected to be low for plants and all other non-target species.

To meet its obligations under section 7(a)(2) of the Endangered Species Act (ESA), the EPA conducted a more extensive assessment to make effect determinations for direct effects to listed plant species. In addition to toxicity and exposure considerations, the refined assessment considered overlap of listed species ranges and designated critical habitats (CHs) within the action area that encompasses all the proposed label uses.

Based on the results of the lack of overlap of species ranges and habitat requirements with the proposed action area, EPA made NE (No Effect) determinations for 1,377 listed species (Appendix B) and 771 designated CHs (Appendix C). NE determinations were made because

either a species or CH is outside of the action area (based on overlap analysis), or no direct or indirect effects are expected (including effects to physical or biological features of any CH).

EPA made may affect (MA) determinations for 465 listed species and 128 CHs. MA determinations were made because the range or critical habitat of these species has greater than 1% overlap with associated Use Data Layers (UDLs) and a maximum 30 m drift distance, indicating that there is a potential for potassium carbonate and red thyme oil exposure. The 30 m drift distance was selected prior to incorporation of a buffer on the label and provides a conservative list of species that may be exposed. Of these species and CHs, not likely to adversely affect (NLAA) determinations are made for all MA species with a greater than 1% overlap based on either direct effects or effects to the prey, pollination, habitat, and/or dispersal (PPHD) of the listed species. These potential effects were determined to be discountable after mitigation measures were incorporated. Table 1 summarizes the effects determinations by taxon for listed species and Table 2 summarizes the effects determinations for CHs.

Although overlap exceeded 1% for some listed aquatic invertebrates and fish, no effects are expected to fish and aquatic invertebrates because of the dissociation of potassium carbonate and the rapid degradation of red thyme oil, so a NE determination was made for all listed aquatic species. A MA, NLAA determination was made for 271 listed terrestrial/semi-aquatic plant species and 58 plant CHs. When examining habitat of listed plants, it was determined that agricultural and turf fields represent unsuitable habitat for the majority of listed plant species. One listed species, the Spring Creek bladderpod (*Lesquerella perforata*), has been identified to co-occur with agricultural crops due to its response to disturbances that are associated with agricultural practices. This species occurs in some agricultural fields in Wilson County, Tennessee. To minimize exposure to the Spring Creek bladderpod, mitigations have been incorporated into the label language and prohibit applications in this county from September 15 to May 15. The proposed home and garden, turf, and ornamental uses of the EP are not expected to result in discernible effects to listed species because the proposed label requires applications for these uses via a handheld sprayers only. Handheld sprayers are primarily designed for application to small, targeted areas at very close proximity to the infected plant. Thus, such applications via handheld sprayer are not expected to result in exposure to nontarget plants, including listed plants. Therefore, NLAA determinations have been made for all listed plants given MA determinations. Any potential effects on these plants are anticipated to be discountable.

Because exposure and effects to plants are expected to be discountable following mitigation, effects to non-plant taxa that interact with such plants are anticipated to be discountable as well. This is based on lack of direct toxicity at anticipated exposure concentrations for non-plant terrestrial taxa, including mammals, birds, insects, reptiles, and amphibians. The EPA made NLAA determinations based on discountable effects for certain non-plant listed species and CHs because of the potential interactions of these terrestrial species with plants in the action area.

Therefore, effects to listed terrestrial animals via effects on their PPHD are expected to be discountable as well.

Table 1. Number of Listed Species Effects Determinations and the EPA's Predictions of Potential Likelihood of Jeopardy by Taxon.

Taxon	Number of Species	NE	MA		
			NLAA	LAA, No J	LAA, J/AM
Amphibians	42	23	19	0	0
Aquatic Invertebrates	228	228	0	0	0
Birds	111	67	44	0	0
Fish	201	201	0	0	0
Mammals	102	56	46	0	0
Plants (Lichens, flowering plants, ferns and allies, conifers and cycads)	946	675	271	0	0
Reptiles	49	19	30	0	0
Terrestrial Invertebrates	163	108	55	0	0
Total	1,842	1,377	465	0	0

NE = No Effect; MA = May Affect; NLAA = Not Likely to Adversely Affect; LAA = Likely to Adversely Affect; No J = Not a Likelihood of Jeopardy; J = Likelihood of Jeopardy.

Table 2. Number of Designated Critical Habitat Effects Determinations and the EPA's Predictions of Potential Likelihood of Adverse Modification of the Designated Critical Habitat.

Taxon	Number of CHs	NE	MA		
			NLAA	LAA, No AM	LAA, AM
Amphibians	31	18	13	0	0
Aquatic Invertebrates	102	102	0	0	0
Birds	33	23	10	0	0
Fish	122	122	0	0	0
Mammals	46	32	14	0	0
Plants (Lichens, flowering plants, ferns and allies, conifers and cycads)	482	424	58	0	0
Reptiles	19	12	7	0	0

Taxon	Number of CHs	NE	MA		
			NLAA	LAA, No AM	LAA, AM
Terrestrial Invertebrates	64	38	26	0	0
Total	899	771	128	0	0

CH = designated critical habitat; NE = No Effect; MA = May Affect; NLAA = No Likely to Adversely Affect; LAA = Likely to Adversely Affect; No AM = Not a Likelihood of Adverse Modification; AM = Likelihood of Adverse Modification.

The conclusions conveyed in this assessment were developed in full compliance with the *EPA Scientific Integrity Policy for Transparent and Objective Science*, and the EPA Scientific Integrity Program's *Approaches for Expressing and Resolving Differing Scientific Opinions.* The full text of the *EPA Scientific Integrity Policy for Transparent and Objective Science*, as updated and approved by the Scientific Integrity Committee and the EPA Science Advisor can be found here: https://www.epa.gov/sites/default/files/2014-02/documents/scientific_integrity_policy_2012.pdf.
The full text of the EPA Scientific Integrity Program's *Approaches for Expressing and Resolving Differing Scientific Opinions* can be found here: https://www.epa.gov/scientific-integrity/approaches-expressing-and-resolving-differing-scientific-opinions.

I. BACKGROUND

A. Active Ingredient Characterization

The AIs are proposed for use as broad spectrum, contact foliar fungicides in NSTKI-014, an end-use product formulation. Potassium carbonate (K_2CO_3) is a carbonate salt that is composed of two potassium monovalent salt ions (K^+) and one carbonate ion (CO_3^{-2}). When potassium carbonate is added to a spray tank, it will dissociate to the two ions, each of which are naturally occurring and ubiquitous in both living and non-living systems. Antifungal effects of potassium carbonate are likely associated with multiple mechanisms, such as pH elevation on the leaf surface and collapse of fungal cell walls due to K^+ imbalance or dehydration of fungal spores (Jabnoun-Khiareddine *et al*., 2016).

Thyme oil is a complex set of oils and other components found in thyme plants of the genus, *Thymus*. Red thyme oil specifically comes from *Thymus zygis*, which is grown in southern Spain and northern Africa. White thyme oil is similar to red thyme oil but comes from *Thymus vulgaris*. Both types of thyme oil contain thymol, but the amount of thymol may differ. Similar to potassium carbonate, thyme oil is likely to elicit antifungal effects through cell membrane disruption. This membrane activity is attributed to phenolic constituents (i.e., thymol, monoterpenes) present in the essential oil (Rota *et al.,* 2008; as cited in MRID 50898813).

B. Biopesticide Use Pattern

The proposed EP, NSTKI-014, is comprised of 58.04% potassium carbonate and 1.75% red thyme oil. The product is proposed for indoor and outdoor uses on growing crops and ornamentals in agricultural, greenhouse, turf, recreational, and home and garden use sites to control fungal diseases, such as powdery mildew and *Botrytis* spp. The product is a spray that is applied with conventional ground equipment at a rate of 2 to 7 lb EP/acre (potassium carbonate: 1.2 to 4.1 lb/acre, red thyme oil: 0.04 to 0.12 lb/acre).

II. ECOLOGICAL EFFECTS ASSESSMENT

Nontarget Organism Toxicity

All nontarget toxicity data requirements for NSTKI-014 have been satisfied per 40 CFR 158.2060. The information presented in Table 3 below is a summary of the nontarget toxicity data for potassium carbonate, red thyme oil, and NSTKI-014. If toxicity information for red thyme oil is not available (such as for fish and aquatic invertebrates), information on the toxicity of thymol was used as a surrogate because thymol is the major constituent in red thyme oil.

For potassium carbonate, to address data requirements for avian acute oral and dietary toxicity, the applicant submitted waiver rationale, which are discussed in sections 1 and 2 below. The applicant submitted an acute oral toxicity up-and-down test with female Sprague-Dawley-derived albino rats exposed to potassium carbonate, and the LD_{50} was determined to be 1,750 mg K_2CO_3/kg-bw, indicating that potassium carbonate is slightly toxic to wild mammals. To address data requirements for fish and aquatic invertebrate toxicity, the applicant submitted information including toxicity studies obtained from the scientific literature and European Chemicals Agency (ECHA) chemical dossier for potassium carbonate with LC/EC_{50} values ranging from 3.2 to 430 mg/L depending on the tested species and substance. Lastly, the applicant submitted a guideline study for honeybee acute contact toxicity testing with potassium carbonate. The study is considered acceptable and demonstrates that potassium carbonate is practically non-toxic (LD_{50} >100 µg ai/bee) to honeybees.

The Agency previously waived non-target organism toxicity data requirements for white thyme oil (USEPA, 2010). In a 2020 risk assessment of vegetable and flower oils, the EPA determined that adverse effects to nontarget organisms are not expected to result from applications of thyme oil when products are applied according to the labels (USEPA, 2020a; USEPA, 2020b). Although no risk concerns for animals were identified in these previous assessments of white thyme oil, the applicant submitted waiver rationale and toxicity data to address the data requirements for red thyme oil. To address data requirements for avian acute oral and dietary toxicity, the applicant submitted waiver rationale, which are discussed in sections 1 and 2 below and which the EPA determined to be acceptable. The applicant submitted an acute oral

toxicity up-and-down test with female Sprague-Dawley-derived albino rats exposed to red thyme oil, and the LD_{50} was determined to be 550 mg red thyme oil/kg-bw, indicating that red thyme oil is slightly toxic to wild mammals. To address data requirements for fish and aquatic invertebrate toxicity, the applicant submitted toxicity information obtained from the scientific literature and European Chemicals Agency (ECHA) chemical dossier for potassium carbonate; these findings indicate potassium carbonate and thyme oil are moderately to slightly toxic depending on the tested species and substance. Lastly, the applicant also submitted a guideline study for honeybee acute contact toxicity testing with red thyme oil. The study is considered acceptable and demonstrates that red thyme oil is practically non-toxic (LD_{50} >100 µg ai/bee) to honeybees.

For risks to mammals and plants from the proposed uses of NSTKI-014, the applicant submitted studies that tested the effects of applications of an EP containing 58% potassium carbonate and 1.75% thymol (equivalent to the ingredients in NSTKI-014). In the submitted acute oral toxicity up-and-down test with female Sprague-Dawley-derived albino rats exposed to the EP, the LD_{50} was determined to be 3,129 mg EP/kg-bw, indicating that the EP is practically non-toxic to wild mammals. In the submitted seedling emergence study, effects to two tested dicots (lettuce and tomato) were noted, whereas in the vegetative vigor study no adverse effects were observed.

Table 3. Non-Target Organism and Environmental Fate Information for Potassium Carbonate and Red Thyme Oil

Study/OCSPP Guideline #	Results[1]	MRID and Classification
Acute oral toxicity – rat [surrogate for wild mammals] (870.1110)	LD_{50} = 1,750 mg K_2CO_3/kg-bw	50898904; Slightly toxic; ACCEPTABLE
Acute oral toxicity – rat [surrogate for wild mammals] (870.1110)	LD_{50} = 550 mg red thyme oil/kg-bw	51739502; Slightly toxic; ACCEPTABLE
Acute oral toxicity – rat [surrogate for wild mammals] (870.1110)	LD_{50} = 3,219 mg EP/kg-bw Rats were exposed to an EP containing 58.04% K_2CO_3 and 1.75% red thyme oil.	50899002; Practically non-toxic; ACCEPTABLE
Freshwater fish acute toxicity (850.1075)	96-hour LC_{50} = 68 mg K_2CO_3/L NOAEC = 33 mg K_2CO_3/L	50898915; Slightly toxic; ACCEPTABLE
Freshwater fish acute toxicity (850.1075)	Thyme oil[2]: 96-hour LC_{50} = 16.1 – 20.5 mg thyme oil/L	50898812; Slightly toxic; ACCEPTABLE
	Thymol: 96-hour LC_{50} = 3.2 mg thymol/L	50898812; Moderately toxic; ACCEPTABLE
Aquatic invertebrate acute toxicity (850.1010)	48-hour EC_{50} = 430 mg K_2CO_3/L (95% C.I.: 190 – 940 mg K_2CO_3/L) NOAEC = 190 mg K_2CO_3/L	50898916; Practically non-toxic; ACCEPTABLE

Study/OCSPP Guideline #	Results[1]	MRID and Classification
Aquatic invertebrate acute toxicity (850.1010)	Thyme oil[2]: 48-hour EC_{50} = 5.94 – 12.2 mg thyme oil/L	50898813; Slightly to moderately toxic; ACCEPTABLE
	Thymol: 48-hour EC_{50} = 3.2 mg thymol/L	50898813; Moderately toxic; ACCEPTABLE
Nontarget plant studies-seedling emergence (850.4100)	Plants were exposed to an EP containing 58.04% K_2CO_3 and 1.75% red thyme oil. 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. The NOAEC and LOAEC values for all species (except for lettuce and tomato) were 7.0 and >7.0 lb EP/acre, respectively. Lettuce had a NOAEC value of 0.44 lb EP/acre for shoot height and dry weight and 3.5 lb EP/acre for emergence and survival. The LOAEC value for lettuce was 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 (*Lactuca sativa*) with an IC_{25} of 0.62 lb EP/acre for shoot dry weight.	50898922; ACCEPTABLE
Nontarget plant studies-vegetative vigor (850.4150)	Plants were exposed to an EP containing 58.04% K_2CO_3 and 1.75% red thyme oil. No significant adverse effects on survival, height, and/or dry weight of all tested plant species (monocots and dicots) after 21 days. The NOAEC and IC_{25} values for all endpoints were determined to be 7 and >7 lb EP/acre, respectively.	50898923; ACCEPTABLE
Honeybee acute contact toxicity (850.3020)	48-hour contact LD_{50} >100 µg K_2CO_3/bee	50898903; Practically non-toxic; ACCEPTABLE
Honeybee acute contact toxicity (850.3020)	48-hour contact LD_{50} >100 µg red thyme oil/bee	50898804; Practically non-toxic; ACCEPTABLE

[1] LC_{50} = median lethal concentration; NOAEC = no observed adverse effect concentration; EC_{50} = median effect concentration; LOAEC = lowest observed adverse effect concentration; EP = end use product; IC_{25} = inhibition concentration yielding 25% reductions relative to controls; LD_{50} = median lethal dose.

[2] The cited studies in the applicant's submission did not always specify if the tested thyme oil was white thyme oil (*Thymus vulgaris*) or red thyme oil (*Thymus zygis*).

1. Avian Acute Oral Toxicity

A waiver rationale for acute avian oral toxicity (MRID 50898917) was submitted for potassium carbonate. The rationale demonstrates that dietary potassium, which is often sourced from potassium carbonate for incorporation into avian dietary formulations, is involved in many physiological processes, including maintenance of water balance, maintenance of osmotic pressure, maintenance of acid base balances, activation of enzymes, metabolism of carbohydrate and proteins, regulation of neuromuscular activity, and regulation of heartbeat. Potassium also promotes the absorption of free neutral amino acids such as glycine. Due to its beneficial properties, potassium carbonate is sometimes incorporated into avian feed to provide additional potassium in a form that can also be used to combat the effects of heat stress, particularly in broiler chicken barns. Potassium itself is an important, though highly variable component in basal poultry feeds. The rationale further discussed several potassium carbonate nutritional dietary studies with broiler chickens, Japanese quails, and turkeys that lasted over 30 days and demonstrated that potassium carbonate was well tolerated and did not cause mortality in birds at doses ranging from 2,119 to 2,955 mg/kg body weight per day. Finally, the rationale demonstrated that the increase in potassium carbonate levels due to use of NSTKI-014 would not significantly increase avian exposure to potassium and carbonate after dissociation compared to levels that exist naturally in the environment. Potassium levels in soils frequently exceed 2%, and carbonate soil levels typically range from 0.5% to 15.3%. Applications of NSTKI-014 are estimated to contribute 0.000343% potassium and 0.000264% carbonate.

A waiver rationale for acute avian oral toxicity (MRID 50898817) was submitted for red thyme oil. In the rationale the applicant stated that considerable research has focused on the dietary effects of thymol and thyme oil on poultry because of the antimicrobial properties of these compounds. The studies presented in the rationale were designed to determine the potential effects of thymol or thyme oil supplements in avian diets rather than to determine toxicity endpoints specific to regulatory testing (*i.e.,* LD_{50} or NOEC). However, relevant endpoints were evaluated, including body weight gain, feed consumption, mortality, egg production, and general health parameters. None of the studies summarized in the waiver request resulted in toxic responses at any treatment level. Therefore, 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.

2. Avian Dietary Toxicity

Waiver rationale for acute avian dietary toxicity was submitted for potassium carbonate (MRID 50898918) and red thyme oil (MRID 50898816). The rationale for each AI is the same as the one submitted for avian acute oral toxicity and is considered acceptable for avian acute dietary toxicity. For further details, refer to the avian acute oral toxicity section above.

3. Mammalian Acute Oral Toxicity

A guideline study was submitted to assess effects of potassium carbonate on mammals from acute oral exposure (MRID 50898904). In the acute oral toxicity up-and-down procedure test, nine fasted female Sprague-Dawley-derived albino rats were given single oral gavage doses of ground Brenntag potassium carbonate (99.50% potassium carbonate) as a 50% (w/w) mixture with distilled water at dose levels of 175 mg K_2CO_3/kg-bw (1 animal), 550 mg K_2CO_3/kg-bw (1 animal), 1,750 mg K_2CO_3/kg-bw (3 animals), or 5,000 mg K_2CO_3/kg-bw (4 animals, including one used in an initial limit test). Treatment was on Day 0 with observations conducted for up to 14 days. The animals were 9-12 weeks old (161-203 g) at the time of dosing. Mortality occurred at 5,000 mg K_2CO_3/kg-bw (4/4 animals) and 1,750 mg K_2CO_3/kg-bw (1/3 animals). At 5,000 mg K_2CO_3/kg-bw, all four animals died within 3 to 24 hours of dosing; prior to death, all exhibited irregular respiration and one also exhibited hypoactivity and piloerection. At 1,750 mg K_2CO_3/kg-bw, one animal was found dead on Day 7 after appearing normal through Day 4, then exhibiting irregular respiration on Days 5-6 and hypoactivity and hunched posture on Day 6. One 1,750 mg K_2CO_3/kg-bw survivor exhibited irregular respiration and hypoactivity three hours after dosing; these signs resolved by Day 1, and the animal appeared active and healthy thereafter. No other abnormal clinical signs were seen, and all of the survivors gained weight during both weeks of the study. The estimated acute oral LD_{50} was 1,750 mg K_2CO_3/kg-bw.

A guideline study was submitted to assess effects of red thyme oil on mammals from acute oral exposure (MRID 51739502). In an acute oral toxicity up-and-down procedure test, 10 fasted female Sprague-Dawley-derived albino rats were given single oral gavage doses of undiluted Bordas Thyme Oil (80% to <100% red thyme oil) at dose levels of 175 mg red thyme oil/kg-bw (2 animals), 550 mg red thyme oil/kg-bw (4 animals), 1,750 mg red thyme oil/kg-bw (3 animals), or 5,000 mg red thyme oil/kg-bw (1 animal used in an initial limit test). Treatment was on Day 0 with observations conducted for up to 14 days. The animals were 9-12 weeks old (167-218 g) at the time of dosing. Mortality occurred at 550, 1,750, and 5,000 mg red thyme oil /kg-bw. The 5,000 mg red thyme oil/kg-bw animal died within 5 hours of dosing after exhibiting irregular respiration, hypoactivity, ataxia, and prone posture. All three 1,750 mg red thyme oil/kg-bw animals died within one day of dosing after exhibiting irregular respiration, prone posture, ataxia, and/or reduced fecal volume. One 550 mg red thyme oil/kg-bw animal was found dead on Day 3 after exhibiting irregular respiration and hypoactivity on Days 0 to 2, prone posture (on Day 0 only), and reduced fecal volume, anogenital staining, and/or hunched posture between Days 1 and 2. The surviving 550 mg red thyme oil/kg-bw animals exhibited hypoactivity, irregular respiration, hunched posture, ataxia, and/or piloerection on Day 0 with later onset of reduced fecal volume or anogenital staining on Day 1. The surviving 550 mg red thyme oil/kg-bw animals recovered by Day 4, gained weight during both weeks of the study, and were free of abnormal gross necropsy findings. Both animals dosed at 175 mg red thyme oil/kg-bw survived, gained weight during both weeks of the study, and were free of abnormal gross necropsy findings. The estimated acute oral LD_{50} was 550 mg red thyme oil/kg-bw.

A guideline study was submitted to assess effects of an EP containing 58.04% K_2CO_3 and 1.75%

red thyme oil (equivalent to the ingredients in NSTKI-014) on mammals from acute oral exposure (MRID 50899002). In an acute oral toxicity up-and-down procedure test, nine fasted female Sprague-Dawley-derived albino rats were given single oral gavage doses of the EP as a 50% (w/w) mixture with distilled water at dose levels of 175 mg EP/kg-bw (1 animal), 550 mg EP/kg-bw (1 animal), 1,750 mg EP/kg-bw (3 animals), or 5,000 mg EP/kg-bw (4 animals, including one used in an initial limit test). Treatment was on Day 0 with observations conducted for up to 14 days. The animals were 7-12 weeks old (160-207 g) at the time of dosing. At 5,000 mg EP/kg-bw, all four animals died within 24 hours of dosing; one died without preceding abnormal clinical signs, and the remaining three decedents exhibited irregular respiration and hypoactivity or prone posture, with ataxia noted in one animal. At the remaining dose levels, there were no mortalities or abnormal gross necropsy findings, and all of the survivors gained weight during both weeks of the study. One 1,750 mg EP/kg-bw animal had irregular respiration three hours after dosing; this resolved by Day 1, and the animal appeared active and healthy thereafter. No other abnormal clinical signs were observed in survivors. The estimated acute oral LD_{50} was 3,129 mg EP/kg-bw.

4. Freshwater Fish Toxicity

A study following FIFRA Guideline 72-1 (which is one source for the 2016 OCSPP 850.1075 guideline) from the ECHA chemical dossier was submitted to address the potassium carbonate data requirement for acute freshwater toxicity (MRID 50898915; ECHA, 2011). The study was a 96-hour acute toxicity test with potassium carbonate. In this study, groups of 30 rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance at nominal concentrations of 0, 18, 30, 50, 83, 140, and 230 mg K_2CO_3/L under flowthrough conditions. Mean measured concentrations were <LOQ (negative control), 7, 33, 54, 85, 150 and 230 mg K_2CO_3/L. Based on mean measured concentrations, the 96-hr LC_{50} was 68 mg K_2CO_3/L. The NOAEC based on mortality was 33 mg K_2CO_3/L. No exposure-related sublethal effects were reported.

The applicant submitted toxicity information demonstrating the potential effects of red thyme oil to freshwater fish (MRID 50898812). In the submission, the applicant included 96-hour LC_{50} values for rainbow trout, coho salmon, and fathead minnows exposed to thyme oil or thymol (a surrogate for thyme oil) in the open literature. The 96-hour LC_{50} values were 16.1 mg thyme oil/L for rainbow trout, 20.5 mg thyme oil/L for coho salmon, and 3.2 mg thymol/L for fathead minnows. Thyme oil and thymol would be classified as slightly and moderately toxic, respectively, to freshwater fish.

5. Aquatic Invertebrate Toxicity

A study following FIFRA Guideline 72-2 (which is one source for the 2016 OCSPP 850.1010 guideline) was submitted to address the potassium carbonate data requirement for aquatic invertebrate acute toxicity (MRID 50898916). The study, which was attained from the ECHA chemical dossier (ECHA, 2021), was a 48-hour acute toxicity test with potassium carbonate. In this static renewal toxicity test, groups of 20 daphnids (*Daphnia magna*) were exposed to

nominal concentrations of 0, 110, 180, 300, 510 and 850 mg K_2CO_3/L. Mean measured concentrations of the active ingredient were <LOQ (negative control), 120, 190, 320, 530 and 940 mg K_2CO_3/L. Based on mean measured concentrations, the 48-hour EC_{50} for mortality/immobilization was 430 mg K_2CO_3/L. The 48-hour NOAEC based on mortality/immobilization was 190 mg K_2CO_3/L.

The applicant submitted toxicity information demonstrating the potential effects of red thyme oil to freshwater invertebrates (MRID 50898813). In the submission, the applicant included 48-hour EC/LC_{50} values for *Daphnia magna* from the open literature and those values range from 5.94 to 12.2 mg thyme oil/L. The submission also included EC/LC_{50} values for thymol (which is a surrogate for thyme oil), which ranged from 3.2 to 5.7 mg thymol/L. Thyme oil would be classified as slightly to moderately toxic to freshwater invertebrates, and thymol would be classified as moderately toxic to freshwater invertebrates.

6. Nontarget Plant Toxicity

Guideline seedling emergence and vegetative vigor studies were submitted for the EP.

In the seedling emergence study (MRID 50898922), a definitive test was conducted on the effects of the test substance (58.04% K_2CO_3, 1.75% red thyme oil) on seedling emergence, survival, dry weight, and height of four monocot crops (*Allium cepa* (onion), *Lolium perenne* (ryegrass), *Triticum aestivum* (wheat), *Zea mays* (corn)) and six dicot crops (*Beta vulgaris* (sugarbeet), *Brassica rapa* (turnip), *Brassica oleracea* (cabbage), *Glycine max* (soybean), *Lycopersicon esculentum* (tomato), *Lactuca sativa* (lettuce)). Nominal application rates were 0.44, 0.88, 1.8, 3.5, and 7.0 lb EP/acre for all tested species. Plants were observed for emergence, mortality, and morphological abnormalities beginning on Day 7, and daily thereafter if needed to establish the 50% emergence date. At test termination (Day 21), shoot height and shoot dry weights were measured. At study termination, mean control plant emergence was ≥70% for all test species except ryegrass, which had 65% mean emergence in the negative control. Mean plant survival based on the number of seeds planted in the control groups ranged from 65 to 95% across all test species. Mean plant survival based on the number of seedlings that emerged in control groups was >90% for all test species. For all test species except for lettuce and tomatoes, measured endpoints were not significantly different from negative controls and no compound-related phytotoxic effects were reported, resulting in NOAEC and LOAEC values of 7.0 and >7.0 lb EP/acre, respectively, for percent survival, shoot height, shoot dry weight, and percent emergence. For tomato, dry weight and seedling height were affected, and the NOAEC and LOAEC values were 3.5 and 7 lb EP/acre, respectively. Lettuce emergence, survival (based on number of seeds planted), dry weight, and seedling height were all affected. The NOAEC and LOAEC values for lettuce shoot height and dry weight were 0.44 and 0.88 lb EP/acre, respectively. The NOAEC and LOAEC values for emergence and survival were 3.5 and 7.0 lb EP/acre, respectively. Overall, the most sensitive endpoint was lettuce dry weight with a 39% effect at the LOAEC (0.88 lb EP/acre) and an IC_{25} value 0.62 lb EP/acre.

In the vegetative vigor study (MRID 50898923), a definitive test was conducted on the effects of the test substance (58.04% K_2CO_3, 1.75% red thyme oil) on survival, growth, and condition of four monocot crops (*Allium cepa* (onion), *Lolium perenne* (ryegrass), *Triticum aestivum* (wheat), *Zea mays* (corn)) and six dicot crops (*Beta vulgaris* (sugarbeet), *Brassica rapa* (turnip), *Brassica oleracea* (cabbage), *Glycine max* (soybean), *Lycopersicon esculentum* (tomato), *Lactuca sativa* (lettuce)). Nominal test substance concentrations were 0.44, 0.88, 1.8, 3.5, and 7.0 lb EP/acre for all tested species. Plants were treated with the test substance and negative control approximately 2-3 weeks after planting, allowing them to reach the 2- to 4-leaf stage at the time of application. The condition of test plants was assessed prior to application and weekly thereafter. Shoot heights were measured and recorded on days 14 and 21. On day 21, the above ground portions of the plants were harvested, dried, and weighed to determine the shoot dry weights. For all species, there were no significant differences in plant survival, shoot height, or shoot dry weight at 21 days after treatment with either the test substance or the negative control. The NOAEC values and EC/IC_{25} values were 7 and >7 lb EP/acre, respectively for survival, shoot height, and shoot dry weight.

7. Nontarget Insect Toxicity

A honeybee acute contact toxicity study (MRID 50898903) was submitted for potassium carbonate. In the 48-hour contact toxicity study, honeybees (*Apis mellifera*) were exposed to potassium carbonate at nominal doses of 6.3, 13, 25, 50, and 100 µg K_2CO_3/bee by topical application. Negative, solvent (Tween 80 solution), and positive (0.05, 0.10, and 0.30 µg dimethoate/bee) controls were used. Analytical concentrations of the test substance were not determined for this study. Mortality and behavioral abnormalities were recorded at 4, 24, and 48 hours. No mortalities occurred in any control or treatment group during the study. Additionally, no abnormal behaviors were noted. Based on these results, the 48-hour contact LD_{50} value for potassium carbonate was determined to be > 100 µg K_2CO_3/bee. The NOAEC value, based on mortality, was 100 µg K_2CO_3/bee.

A honeybee acute toxicity study (MRID 50898804) was submitted for red thyme oil. In the 48-hour contact toxicity study, honeybees (*Apis mellifera*) were exposed to red thyme oil at nominal doses of 6.3, 13, 25, 50, and 100 µg red thyme oil/bee by topical application. Negative, solvent (acetone), and positive (0.05, 0.10, and 0.30 µg dimethoate/bee) controls were used. Analytical concentrations of the test substance were not determined for this study. Mortality and behavioral abnormalities were recorded at 4, 24, and 48 hours. No mortalities occurred in the negative control and 3.3% mortality occurred in the solvent control. In the treatment groups, 0% mortality occurred in the four lowest doses with 7% mortality in the 100 µg red thyme oil/bee treatment group. Additionally, no abnormal behaviors were noted except for one immobile bee in the 100 µg red thyme oil/bee treatment group at 24 hours. Based on these results, the 48-hour contact LD_{50} value for red thyme oil was determined to be > 100 µg red thyme oil/bee. The NOAEC value, based on mortality, was 100 µg red thyme oil/bee.

III. ECOLOGICAL EXPOSURE AND RISK CHARACTERIZATION

A. Terrestrial Exposure and Risk Characterization

A quantitative risk assessment was not conducted for birds, terrestrial-phase amphibians, reptiles, mammals, and terrestrial invertebrates, including listed endangered/threatened species in these taxa. Potassium carbonate has a history of beneficial and common use in avian diets, and considerable research has focused on the effects of thymol and thyme oil on poultry because of the antimicrobial properties of these compounds. Because adverse effects of potassium carbonate, thyme oil, and thymol in avian diets have not been observed, both potassium carbonate and red thyme oil are expected to be practically non-toxic to birds, which serve as a surrogate for terrestrial-phase amphibians and reptiles. Based on the submitted acute oral toxicity study with rats, NSTKI-014 is practically non-toxic to wild mammals. No toxic effects were observed up to the limit dose in the honeybee acute contact toxicity studies with potassium carbonate and red thyme oil. Additionally, potassium carbonate will dissociate in environmental matrices and terrestrial vertebrates are likely exposed to naturally occurring potassium and carbonate at levels that are several orders of magnitude higher than expected exposures from proposed applications of NSTKI-014. The amount of red thyme oil and thymol to which a terrestrial animal is expected to be exposed is low given the low concentration (1.75% (w/w)) of red thyme oil in the NSTKI-014. Therefore, when the EP is used in accordance with the proposed label use directions, risks to terrestrial animals are expected to be low, and direct effects to listed terrestrial animals are not expected.

A quantitative risk assessment was conducted for nontarget plants due to phytotoxic effects observed in the seedling emergence study. In this study, effects on shoot height and dry weight were observed in lettuce and tomato and effects on emergence and survival were noted for lettuce. The most sensitive NOAEC and IC_{25} values were determined for lettuce dry weight and were 0.44 and 0.62 lb EP/acre, respectively. To evaluate potential exposure and estimate risk to nontarget plants, the EPA used the terrestrial plant model, TerrPlant[1] (version 1.2.2). Developed by the Office of Pesticide Program's Environmental Fate and Effects Division, TerrPlant derives estimated environmental concentrations (EECs) and risk quotients (RQs) for a pesticide via runoff and spray drift exposure from a single application. Table 4 summarizes the modeled EECs from runoff and spray drift to off-field dry and semi-aquatic areas for a ground application of NSTKI-014 at the maximum single application rate of 7 lb EP/acre. For details on model inputs and outputs, refer to **Appendix A**.

[1] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#terrestrial

Table 4. TerrPlant EECs (lb EP/A) for terrestrial plant exposure to NSTKI-014 from application rates of 7.0 lb EP/acre

Description of Area	EEC (lb EP/A)
Runoff to dry areas	0.35
Runoff to semi-aquatic areas	3.50
Spray drift	0.07
Total for dry areas	0.42
Total for semi-aquatic areas	3.57

Risk quotients are developed for non-listed and listed species of monocots and dicots inhabiting dry and semi-aquatic areas that are adjacent to treatment sites. The model compares the combined deposition estimates from runoff and spray drift to adverse effect levels determined in toxicity studies. The RQs are derived by dividing the total EEC by the relevant toxicity value (*i.e.,* IC_{25} or NOAEC). The IC_{25} values for the most sensitive tested monocot and dicot species are used to determine the potential risk of the pesticide to non-listed species. The corresponding NOAEC values for the same species and biological endpoint are used to determine the potential risk of the pesticide to listed plants. The Level of Concern (LOC) for non-listed and listed plant species is 1.0. Risk quotient values exceeding 1.0 indicate potential risk to plants. Risk quotient values less than or equal to 1.0 indicate that potential risk is low. In other words, if a pesticide exposure estimate (EEC) does not exceed the toxicity value (IC_{25} or NOAEC), the RQ is ≤ 1.0 and is below the LOC. Therefore, potential risk to that plant group is considered to be low.

No toxic effects were observed in the vegetative vigor study. As summarized in the ECOLOGICAL EFFECTS ASSESSMENT section above, lettuce and tomatoes were the only affected plant species in the seedling emergence study. In this study, effects on shoot height and dry weight were observed, with the most sensitive NOAEC equaling 0.44 lb EP/acre. At the LOAEC (0.88 lb EP/acre), lettuce shoot weight was reduced by 39%. Based on the seedling emergence study, IC_{25} values were determined for lettuce dry weight (0.62 lb EP/acre) and tomato shoot height (6.5 lb EP/acre). Based on effects to the most sensitive plant species (lettuce), the predicted exposures from the TerrPlant model indicate that there is risk to non-listed and listed semi-aquatic dicot species because calculated RQs (non-listed: 5.8, listed: 8.1) exceed the LOC. For monocot species, the LOC is not exceeded. Tables 5 summarizes the results from the TerrPlant model.

Table 5. Risk Quotients (RQs) from Applications of NSTKI-014 via Runoff and Spray Drift Exposure in Dry Areas, Runoff and Spray Drift in Semi-Aquatic Areas, and Spray Drift only*.

Plant Type (Test Species)	Listed Status (RQ Endpoint)	RQ (Dry areas)	RQ (Semi-aquatic areas)	RQ (Spray drift)
Most sensitive test species				
Monocot (All Species)	Non-listed (EC/IC_{25})	N/C	N/C	N/C
Monocot (All Species)	Listed (NOAEC)	<0.1	0.51	<0.1
Dicot (Lettuce)	Non-listed (IC_{25})	0.68	**5.8**	0.11
Dicot (Lettuce)	Listed (NOAEC)	0.95	**8.1**	0.16
Less sensitive test species				
Dicot (Tomato)	Non-listed (IC_{25})	<0.1	0.55	<0.1
Dicot (Tomato)	Listed (NOAEC)	0.12	1.0	<0.1

*RQs exceeding the LOCs shown in bold text.
NC = not calculated because a definitive EC/IC_{25} value was not determined (*i.e.,* all EC/IC_{25} values > 7 lb EP/acre)

To further characterize the potential risks to plants, the EPA also compared the EECs to less sensitive endpoints from the seedling emergence test. For example, the most sensitive LOAEC can be compared to the EECs to characterize risk at application rates where adverse effects actually occurred. Based on the most sensitive LOAEC value (instead of the NOAEC), a lower RQ value of 4.1 for listed dicot species in semi-aquatic areas results, but the listed species LOC is still exceeded. If the next most sensitive NOAEC (based on effects on tomato growth or lettuce emergence and survival) is used, the listed species LOC is not exceeded (RQ = 1.0; Table 5). Similarly, if the IC_{25} for tomato shoot height is used instead of the IC_{25} for lettuce dry weight, the RQs for non-listed dicots do not exceed the LOC (RQ = 0.55; Table 5). Lastly, the EPA noted that for the other eight test species in the seedling emergence study and all 10 test species in the vegetative vigor study, growth inhibition and effects on survival/emergence did not exceed 25% at the maximum single application rate, resulting in the EC/IC_{25} values > 7 lb EP/acre. Although risks cannot be precluded based on the most sensitive endpoints for lettuce dry weight, there is potential that effects to nontarget plants may vary across species when responses across all plant test species (not only the most sensitive) are considered. This is particularly important for understanding the potential effects and risks to animal species that depend on plants for food or habitat.

To further analyze the potential risk from use of NSTKI-014 to non-target dicot species, the EPA used the AgDRIFT[2] (version 2.1.1) model to predict spray drift deposition and to determine the distance from the edge of the treated site where the RQ from spray drift alone is equal to the

[2] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#AgDrift

LOC for listed and non-listed plants. It is important to recognize, though, that risk from runoff is not considered in this spray drift analysis. However, risk to plants from runoff exposure from spray applications may also be reduced through the incorporation of spray drift buffers. In this analysis, EPA determined the distances to where the spray drift deposition equals the seedling emergence IC_{25} for evaluating risk to non-listed plants and to where the spray drift deposition equals the seedling emergence NOAEC for evaluating risk to listed plants. Beyond these distances, exposure from spray drift alone is not expected to result in exceedances of the LOC. Table 6 provides buffer distances for dicots based on fine to medium droplet size distributions in the AgDRIFT model for ground applications (droplet sizes per the American Society of Agricultural and Biological Engineers or ASABE). The applications are modeled with both high and low boom applications (1.27 and 0.5 meters above the ground, respectively).

Spray drift buffer distances that resulted from low boom ground applications ranged from 4 ft for non-listed species to 7 ft for listed species (Table 6). These buffer distances increased for high boom applications and ranged from 7 ft for non-listed species to 10 ft for listed species. Application of NSTKI-014 with a low boom and a fine to medium/coarse droplet spectrum results in the narrowest buffer distance in which listed and non-listed plant LOCs are not exceeded. The proposed label indicates that ground boom applications are required to use a medium or coarser droplet size (ASABE S572.1), which is expected to help mitigate risk. Compared to high boom applications, low boom applications have less spray drift, ultimately resulting in lower risk to non-target plant species and smaller buffer distances required to mitigate risk. With the incorporation of the identified buffer distances, risks from spray drift exposure are expected to be low for off-field plants.

Although the EECs in Table 4 indicate that runoff exposure is the driver for the TerrPlant estimates, the runoff EECs are expected to be overestimates of the actual runoff of potassium carbonate and red thyme oil off a treated use site. For NSTKI-014, exposure and risk from runoff is expected to be low for plants that are off-field due to: 1) dissociation of potassium carbonate with concentrations of the ions in runoff being lower than naturally occurring concentrations, 2) the low concentration of red thyme oil in the EP (1.75% (w/w)), and 3) the rapid degradation of thyme oil (USEPA, 2020a) and thymol (USEPA, 2019) in the environment. The EPA expects naturally occurring potassium and carbonate ions to be present in off-field soil and water bodies at levels that are several orders of magnitude higher than estimated exposure from proposed applications of NSTKI-014. Additionally, the EPA expects that applied red thyme oil (which contains approximately 48% thymol) will rapidly degrade in the environment by normal biological, physical and/or chemical processes (USEPA, 2020a). Lastly, the label includes a 7-ft buffer to the treated field, which the EPA expects to further decrease any potential off-field runoff exposure.

Table 6. Modeled Spray Drift Buffer Distances Needed to Mitigate Risk from Ground Applications of Fine to Medium/Coarse Droplet Sizes.

Plant type	Listed Status	Spray Drift Buffer Distances (ft)	
		Fine to Medium/Coarse Droplet Spectrum	
		High Boom (1.27 m height)	Low Boom (0.5 m height)
Dicot	Non-listed[1]	7	4
	Listed[2]	10	7

[1] Based on the distance where the deposition equals the most sensitive dicot IC_{25} (0.62 lb EP/acre)

[2] Based on the distance where the deposition equals the most sensitive dicot NOAEC (0.44 lb EP/acre)

B. Aquatic Exposure and Risk Characterization

A quantitative risk assessment was conducted for fish and aquatic invertebrates due to the toxic effects observed in the available potassium carbonate and thyme oil nontarget organism toxicity studies. In the studies with potassium carbonate, significant treatment related mortalities were observed in rainbow trout and daphnids at 54 and 320 mg K_2CO_3/L, respectively, resulting in NOAEC values of 33 and 190 mg K_2CO_3/L, respectively. The corresponding LC/EC_{50} values were 68 and 430 mg K_2CO_3/L, respectively. In studies with thyme oil, the LC/EC_{50} values ranged from 16.1 to 20.5 mg thyme oil/L for fish and from 5.94 to 12.2 mg thyme oil/L for aquatic invertebrates. The LC/EC_{50} was equal to 3.2 mg/L in the aquatic animal studies with thymol.

Potassium carbonate and red thyme oil may be introduced to water bodies via runoff or spray drift. A worst-case scenario EEC is calculated for a direct application of the EP to water. Based on the highest application rate (7 lb EP/acre) and an application to a one-acre water body that is six inches deep[3], the EEC is 5.1 mg EP/L. Based on the composition of NSTKI-014, this EEC equates to 3.0 mg K_2CO_3/L and 0.09 mg red thyme oil/L. Because red thyme oil is 48-50% thymol, the EEC in terms of thymol would be approximately 0.05 mg thymol/L.

Results of the exposure modeling and toxicity effects data (LC/EC_{50}) were used to evaluate the likelihood of adverse ecological effects to aquatic species. To calculate RQs, the worst-case scenario EEC was divided by the toxicity values (LC/EC_{50} or NOAEC) for fish and invertebrates. The acute RQs were compared to the Agency's acute LOC, which is 0.5 and 0.05 for non-listed and listed aquatic species, respectively. The chronic RQs were compared to the chronic LOC, which is 1.0 for both listed and non-listed species. The aquatic RQs for the proposed product, NSTKI-014, are all below the LOC (Table 7). Therefore, risks to aquatic animals are low and direct effects to listed aquatic organisms are not anticipated when the product is used in accordance with the proposed label directions.

[3] A one-acre wetland that is 6 inches deep contains 21,780 ft^3 of water, which equals 6.17 x 10^8 mL.

Table 7. Risk Quotients (RQs) for Fish and Aquatic Invertebrates from Applications of NSTKI-014

Taxa	Worst-Case Scenario EEC (mg/L)	Acute		Chronic	
		LC/EC_{50} (mg/L)	RQ	NOAEC (mg/L)	RQ
Fish	K_2CO_3: 3.0	68	0.04	33	0.09
	Red thyme oil: 0.09	16.1	0.01	Not available	N/A
	Thymol: 0.05	3.2	0.02	Not available	N/A
Invertebrate	K_2CO_3: 3.0	430	0.01	190	0.02
	Red thyme oil: 0.09	5.94	0.02	Not available	N/A
	Thymol: 0.05	3.2	0.02	Not available	N/A

IV. ENDANGERED SPECIES ASSESSMENT

A quantitative risk assessment was not conducted for listed birds, terrestrial-phase amphibians, reptiles, mammals, and terrestrial invertebrates, including endangered/threatened species. Potassium carbonate, thyme oil, and thymol have a history of common use in avian diets and are considered practically non-toxic based on the submitted information. Based on the submitted acute oral toxicity study with rats, NSTKI-014 is practically non-toxic to wild mammals. No toxic effects were observed for potassium carbonate and red thyme oil up to the limit dose in the honeybee acute contact toxicity studies, and both AIs are considered non-toxic to terrestrial invertebrates. Furthermore, wild birds, terrestrial-phase amphibians, reptiles, and mammals are likely exposed to naturally occurring potassium and carbonate ions at levels that are several orders of magnitude higher than expected exposures to these ions after dissociation following proposed applications of NSTKI-014. Additionally, the amount of red thyme oil and thymol to which a terrestrial animal is expected to be exposed is low given the low concentration (1.75% (w/w)) of red thyme oil in the NSTKI-014. Therefore, when the EP is used in accordance with the proposed label use directions, direct effects and effects to the prey and habitat of listed terrestrial animals are expected to be discountable. Due to the phytotoxic effects observed in the available seedling emergence study conducted with NSTKI-014 and the submitted toxicity information for fish and aquatic invertebrates, a quantitative risk assessment was conducted for these species. This assessment is described in briefly below. For full details of the risk assessment, refer to the ECOLOGICAL EXPOSURE AND RISK CHARACTERIZATION section.

Based on the maximum single application rate proposed on the label, environmental exposure concentrations were derived for NSTKI-014 in runoff and spray drift for plant species inhabiting dry and semi-aquatic areas that are adjacent to treatment sites. These EECs were compared to plant toxicity endpoints to develop RQs. No toxic effects were observed in the vegetative vigor

study. Lettuce and tomatoes were the only affected plant species in the seedling emergence study, with effects on emergence and survival noted for lettuce and effects on shoot height and dry weight noted for lettuce and tomato. The most sensitive species was lettuce with NOAEC and IC_{25} values of 0.44 and 0.62 lb EP/acre, respectively. At the LOAEC (0.88 lb EP/acre), lettuce shoot weight was reduced by 39%. For tomato, the NOAEC and LOAEC for dry weight and height were 3.5 and 7 lb EP/acre, respectively, and the LOAEC was based on a 34% reduction in dry weight and a 28% reduction in shoot height. Based on effects to the most sensitive plant species (lettuce), the EPA used the TerrPlant model and determined that there is potential risk to non-listed and listed semi-aquatic plant species because the calculated RQs exceed the Level of Concern. Although risks cannot be precluded based on the most sensitive endpoints for lettuce dry weight, there is potential that effects to nontarget plants may vary across species when responses across all plant test species (not only the most sensitive) are considered. This is particularly important for understanding the potential effects and risks to animal species that depend on plants for food or habitat. Results from the AgDRIFT model indicate that buffer distances are required to mitigate the spray drift to plants and range from 4 to 10 feet depending on application method (Tables 4). Application of NSTKI-014 with a low boom and a fine to medium droplet spectrum results in the narrowest buffer distance in which listed and non-listed plant LOCs are not exceeded based on drift exposure alone (Table 4). The proposed label indicates that ground boom applications require use a medium or coarser droplet size, which should help reduce offsite drift. For NSTKI-014, exposure and risk from runoff is expected to be low for plants that are off-field due to: 1) dissociation of potassium carbonate with concentrations of the ions in runoff being lower than naturally occurring concentrations, 2) the low concentration of red thyme oil in the EP (1.75% (w/w)), and 3) the rapid degradation of thyme oil (USEPA, 2020a) and thymol (USEPA, 2019) in the environment. Additionally, the label includes a 7-ft buffer to the treated field, which the EPA expects to further decrease potential off-field runoff exposure and risk.

For aquatic animal species RQs developed from toxicity data and EECs range from 0.01 to 0.09 and are below the listed and non-listed species LOC. Therefore, direct effects to nontarget listed aquatic organisms are not anticipated when the product is used in accordance with the proposed label directions.

Although adverse effects were observed in dicots in the submitted seedling emergence study, the Agency 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 of nontarget plants. Therefore, NLAA determinations have been made for all the listed plants in the action area based on discountable effects as a result of minimal potential exposure. The EPA has also made an NLAA determination based on discountable effects to listed animals and designated CHs for species that are in the action area and rely on plants for food or habitat. The effects to listed animals' PPHD are expected to be discountable. Exposure and effects to off-field plants are expected to be discountable; therefore, the EPA expects that any effects to non-plant taxa are discountable, even if the animal species relies on plants for its food or habitat.

This section presents the rationale supporting the EPA's effects determinations for NSTKI-014 (58.04% K2CO3 and 1.75% red thyme oil), which were made for all 1,842 currently listed, candidate, and proposed species and the 899 designated or proposed CHs. This assessment considers all listed, proposed, and candidate species and designated/proposed CHs as of February 16, 2022. The effects determinations considers both direct effects and effects to the PPHD of listed species from the proposed uses of NSTKI-014. A spatial overlap analysis was conducted to determine where listed species and their designated CHs may be present in relation to the proposed use sites. The EPA conducted a more extensive, refined assessment to make effect determinations for direct effects to listed plant species. In addition to toxicity and exposure considerations, the refined assessment considered overlap of listed species' ranges and designated critical habitats within the action area that encompasses the proposed label uses.

The location of species' ranges and designated critical habitats in relation to the proposed agricultural uses were identified through the generation of agricultural use data layers (UDLs) from the U.S. Department of Agriculture (USDA) cropland data layer (CDL). The EPA uses USDA's CDL for the agricultural use sites found in the conterminous United States (CONUS) and the 2016 U.S. Geological Survey National Land Cover Dataset (NLCD) for many non-agricultural uses (when available). Where NLCD was not available, the EPA uses the National Oceanic and Atmospheric Administration (NOAA) Coastal Change Analysis Program (C-CAP) dataset and corresponding landcover classes for non-agricultural uses. For Alaska and Puerto Rico, the EPA uses the NLCD, and for Hawaii, American Samoa, Guam, Commonwealth of the Marianas, and the U.S. Virgin Islands, the EPA uses the C-CAP data. These publicly available datasets include a robust accuracy assessment which is used by the EPA to ensure the UDLs used in the biological evaluations (BEs) are of sufficient accuracy for decision making. Use data layers spatially represent application sites for agricultural and non-agricultural uses in the EPA's ESA analyses and BEs. These data layers leverage several different landcover and land use datasets acquired from remote sensing technology to create a spatial footprint for a given label use.

The endangered and threatened species' range and designated CH locations were provided by the U.S. Fish and Wildlife Service (USFWS) and the National Marine Fisheries Service (NMFS). The overlap or co-occurrence analysis compares the exposure area for each UDL and the range/designated CH locations resulting in a percent overlap. The percent overlap is the acres of the exposure area for the UDL divided by the total acres for the species' range/designated CH.

The action area is defined as the area represented by the spatial locations of NSTKI-014's proposed use sites and other areas where effects are reasonably expected to occur (due to the transport of the AIs from the use sites to offsite areas). A species or designated CH is within the action area if it is found within one or more of the UDL exposure areas identified using the maximum overlap across UDLs. Given the known spatial relationship and correlation across the

landscape and the accuracy[4] of the available UDLs, the species or designated CH is considered outside of the action area if the resulting maximum overlap is <1%[5], including the offsite exposure area. Therefore, the Agency made NE determinations for species with <1% overlap of the range and each UDL. For all species with ≥1% overlap, EPA made MA determinations unless EPA was able to determine that no discernible effects to a species were expected based on the habitat characteristics and life histories of the species (i.e., cave dwelling species). For all species with MA determinations, EPA evaluated if it was the proposed uses were NLAA or LAA an individual of the listed species.

The EPA made NE determinations for 1,377 listed species (Appendix B) and 771 designated or proposed CHs (Appendix C). The NE determinations were made because either a species or designated CH is outside of the action area (<1% overlap), or no direct effects or effects to the species' PPHD are expected (including effects to physical or biological features of designated CHs). The latter is applicable for the NE determinations for listed fish, aquatic-phase amphibians, and aquatic invertebrates regardless of overlap. As outlined in the screening-level risk assessment in the ECOLOGICAL EXPOSURE AND RISK CHARACTERIZATION section, the aquatic EECs are very low compared to the toxicity endpoints, resulting in low RQs. Therefore, for these aquatic taxa, direct effects, effects to the species' PPHD, and effects to the physical or biological features of the designated CHs are not expected.

EPA made MA determinations for 465 listed species and 128 designated/proposed CHs. These MA determinations were made because the range or designated CH has greater than 1% overlap with at least one UDL and the offsite exposure area that is represented by a 30-m buffer added to the UDLs to account for potential drift exposure. Because overlap exceeds 1%, there is a potential for exposure to the AIs in NSTKI-014 and the EPA was unable to otherwise rule out potential effects to these species and designated CHs. The 30 m drift distance was selected prior to incorporation of a buffer on the label and provides a conservative list of species that may be exposed. Of these species and designated CHs, NLAA determinations are made for all MA species with a greater than 1% overlap based on potential direct effects and/or effects to the species' PPHD that were determined to be discountable after mitigation measures were incorporated. For the total numbers of species with NE vs. NLAA determinations, refer to Table 1 and Table 2 in the EXECUTIVE SUMMARY section.

A MA, NLAA determination was made for 271 listed terrestrial/semi-aquatic plant species and 58 designated/proposed plant CHs. When examining the habitats of listed plants, the EPA

[5] EPA has used this 1% overlap criteria because a known source of error within spatial datasets is positional accuracy and precision. The National Standard for Spatial Data Accuracy outlines the accepted method for calculating the horizontal accuracy of a spatial dataset (FGDC, 1998). To prevent false precision when calculating area and the percent overlap it rounded to whole numbers to account for significant digits, where <0.44% overlap is represented as 0% overlap and 0.45 – 0.99% overlap is represented as 1% overlap.

[5] The overlap is rounded to whole numbers due to the precision of the remotely sensed data; therefore <1% overlap represents <0.44% overlap with anything between 0.45 and 0.99% overlap rounding up to 1% overlap.

determined that agricultural and turf fields that represent the proposed use sites are unsuitable habitat for the majority of listed plant species. Additionally, the proposed home and garden and turf and ornamental uses of NSTKI-014 are not expected to result in discernible effects to listed species due to the requirement on the proposed label that applications for these uses be made using handheld sprayers, which are not expected to result in exposure to nontarget, offsite plants because these sprayers are primarily designed for application to small, targeted areas at very close proximity to the infected plant. One listed species, the Spring Creek bladderpod (*Lesquerella perforata*), has been identified to co-occur with agricultural crops due to its response to disturbance that is associated with agricultural practices. This species occurs in some agricultural fields in Wilson County, Tennessee. To minimize exposure to the Spring Creek bladderpod, mitigations have been incorporated into the label language. There are use restrictions placed on the label for Wilson County where this species occurs. Given the mitigations on the label (as discussed below in the Minimization of Exposure through Mitigation section), the EPA has made NLAA determinations for all listed plants and their designated CHs given MA determinations. Any effects on these plants and their designated CHs are anticipated to be discountable.

Because exposure and effects to plants are not anticipated following mitigation, effects to non-plant species that depend on such plants for food or habitat are anticipated to be discountable as well. This is based on lack of direct toxicity for birds, reptiles, terrestrial-phase amphibians, and terrestrial invertebrates. For mammals and aquatic animals, this is based on low exposure estimates relative to the toxicity endpoints. Any effects to the PPHD of listed animals that depend on plants or on plant-based physical or biological features of designated CHs are expected to be discountable.

Minimization of Exposure through Mitigation

The Agency made NLAA determinations for all the listed plant species and their designated CHs within the action areas for the proposed uses of NSTKI-014. This is primarily due to the EPA's assumption that most listed plant species are not present on agricultural fields (USEPA, 2023) 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 (as described below) minimizes off-field exposure for listed plants in the vicinity of proposed use sites, supporting the EPA's NLAA determination.

The proposed label includes the following mitigation measures to minimize off-field exposure, particularly via spray drift.

1. Apply with the nozzle height recommended by the manufacturer, but no more than 3 feet above the ground or crop canopy. For all other ground applications, the nozzle must be no more than 3 feet from the target vegetation.
2. Applicators are required to use a medium or coarser droplet size (ASABE S572.1).

3. Do not apply when wind speeds exceed 10 miles per hour at the application site.
4. Do not apply during temperature inversions.
5. Maintain a 7-foot buffer strip between the point of direct application and the closest downwind edge of sensitive habitats.
6. Apply directly to turf and ornamental plants via handheld sprayer only.

At the specified application parameters (*e.g.,* release height <3 ft, medium or coarser droplet size, etc.), off-field drift is expected to be minimized. For non-agricultural uses, the application equipment restriction to handheld sprayers only is expected to minimize off-field movement of the AIs because these sprayers are primarily designed for application to small, targeted areas at very close proximity to the infected plant.

The Agency identified one species that may be present on agricultural lands, the Spring Creek bladderpod (*Lesquerella perforata*). While agricultural fields represent unsuitable habitat for most listed plant species, the Spring Creek bladderpod has been identified to co-occur with agricultural crops due to its response to disturbances that are associated with agricultural practices. This species occurs in some agricultural fields in Wilson County, Tennessee. The Spring Creek bladderpod is expected to germinate in the winter and senesce in the spring. In order to reduce exposure during the vegetative stage, the proposed label contains a species-specific conservation measure, which prohibits applicators from using NSTKI-014 during the germination phase for this species in areas where it occurs. This restriction is expected to sufficiently reduce exposure so that adverse effects are unlikely even in rare instances where some Spring Creek bladderpods germinate or senesce outside of the expected time frame. The following restriction language has been added by the manufacturers to the proposed label after consulting with the EPA, "Do not apply NSTKI-014 within Wilson County, Tennessee from September 15 to May 15". This mitigation step is expected to reduce if not completely eliminate on-field exposure for the Spring Creek bladderpod.

For NSTKI-014, off-field effects are expected to result from contact exposure via spray drift rather than via runoff. For NSTKI-014, exposure and risk from runoff is expected to be low for plants that are off-field due to: 1) dissociation of potassium carbonate with concentrations of the ions in runoff being lower than naturally occurring concentrations, 2) the low concentration of red thyme oil in the EP (1.75% (w/w)), and 3) the rapid degradation of thyme oil (USEPA, 2020a) and thymol (USEPA, 2019) in the environment. The EPA expects naturally occurring potassium and carbonate ions to be present in off-field soil and water bodies at levels that are several orders of magnitude higher than estimated exposure from proposed applications of NSTKI-014. Additionally, the EPA expects that applied red thyme oil (which contains approximately 48% thymol) will rapidly degrade in the environment by normal biological, physical and/or chemical processes (USEPA, 2020a). Lastly, the label includes a 7-ft buffer to the treated field, which the EPA expects to further decrease any potential off-field runoff exposure.

Based on the mitigation steps for exposure and drift reduction, and application restrictions in Wilson County Tennessee, 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 determination based on

discountable NLAA for effects for all the plants including spring creek bladderpod.

LIST OF SUBMITTED STUDIES/RATIONALE WITH THE EPA'S CLASSIFICATION

MRID 50898804: ACCEPTABLE

MRID 50898812: ACCEPTABLE

MRID 50898833: ACCEPTABLE

MRID 50898814: ACCEPTABLE

MRID 50898815: ACCEPTABLE

MRID 50898816: ACCEPTABLE

MRID 50898817: ACCEPTABLE

MRID 50898923: ACCEPTABLE

MRID 50899002: ACCEPTABLE

MRID 50898813: ACCEPTABLE

MRID 50898903: ACCEPTABLE

MRID 50898915: ACCEPTABLE

MRID 50898916: ACCEPTABLE

MRID 50898917: ACCEPTABLE

MRID 50898918: ACCEPTABLE

MRID 50898922: ACCEPTABLE

MRID 50898913: ACCEPTABLE

MRID 50898904: ACCEPTABLE

MRID 51739502: ACCEPTABLE

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US EPA (2020a) Registration Review Assessment for Vegetable Oils (Case No. 8201): Canola Oil, Castor Oil, Soybean Oil and Jojoba Oil; and Flower Oils (Case No. 8202): Oil of Mustard, Oil of Citronella, Indole, Lavandin Oil, Oil of Lemongrass, Oil of Eucalyptus, Oil of Orange, Eugenol, Bergamot Oil, Alpha-lonone, Balsam Fir Oil, and Geraniol. By Shannon Borges, Chief. Signed January 10, 2020. Available at https://www.regulations.gov/document/EPA-HQ-OPP-2011-0628-0008.

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USEPA (2023) Draft Herbicide Strategy Framework to Reduce Exposure of Federally Listed Endangered and Threatened Species and Designated Critical Habitats from the Use of Conventional Agricultural Herbicides. Herbicide Strategy Framework Document; Docket No. EPA-HQ-OPP-2023-0365

Appendix A: TerrPlant Input and Output Data

TerrPlant v. 1.2.2
Green values signify user inputs (Tables 1, 2 and 4).
Input and output guidance is in popups indicated by red arrows.

Table 1. Chemical Identity.	
Chemical Name	**Potassium carbonate + thyme oil RED**
PC code	**073504, 597801**
Use	**Fungicide (many use sites)**
Application Method	**Ground**
Application Form	**Spray**
Solubility in Water (ppm)	**assumed >100 ppm**

Table 2. Input parameters used to derive EECs.			
Input Parameter	**Symbol**	**Value**	**Units**
Application Rate	A	**7**	**lb EP/A**
Incorporation	I	**1**	none
Runoff Fraction	R	**0.05**	none
Drift Fraction	D	**0.01**	none

Table 3. EECs for Potassium carbonate + thyme oil RED. Units in lb EP/A.		
Description	**Equation**	**EEC**
Runoff to dry areas	(A/I)*R	0.35
Runoff to semi-aquatic areas	(A/I)*R*10	3.50
Spray drift	**A*D**	**0.07**
Total for dry areas	**((A/I)*R)+(A*D)**	**0.420**
Total for semi-aquatic areas	**((A/I)*R*10)+(A*D)**	**3.57**

Table 4. Plant survival and growth data used for RQ derivation. Units are in lb EP/A.				
	Seedling Emergence		**Vegetative Vigor**	
Plant type	**EC_{25}**	**NOAEC**	**EC_{25}**	**NOAEC**
Monocot	**7**	**7**	**7**	**7**
Dicot	**0.62**	**0.44**	**7**	**7**

Table 5. RQ values for plants in dry and semi-aquatic areas exposed to Potassium carbonate + thyme oil RED through runoff and/or spray drift.*				
Plant Type	**Listed Status**	**Dry**	**Semi-Aquatic**	**Spray Drift**
Monocot	non-listed	<0.1	0.51	<0.1
Monocot	listed	<0.1	0.51	<0.1
Dicot	non-listed	0.68	5.76	0.11
Dicot	listed	0.95	8.11	0.16
*If RQ > 1.0, the LOC is exceeded, resulting in potential for risk to that plant group.				