ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2018-0522; FRL-10130-01-OCSPP]

Eugenol; Exemption from the Requirement of a Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes an exemption from the requirement of a tolerance for residues of eugenol (2-methoxy-4-(-2-propenyl)phenol) in or on all food commodities when used in accordance with good agricultural practices. SciReg, Inc., on behalf of Eden Research PLC, submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting an exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for residues of eugenol when used in accordance with this exemption.

DATES: This regulation is effective [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Objections and requests for hearings must be received on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA-HQ-OPP-2018-0522, is available at *https://www.regulations.gov* or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave., NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room and the OPP Docket is (202) 566-1744. For the latest status information

on EPA/DC services, docket access, visit *https://www.epa.gov/dockets*.

FOR FURTHER INFORMATION CONTACT: Charles Smith, Biopesticides and Pollution Prevention Division (7511P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; main telephone number: (703) 305-7090; email address: *BPPDFRNotices@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How can I get electronic access to other related information?

You may access a frequently updated electronic version of 40 CFR part 180 through the Office of the Federal Register's e-CFR site at *https://www.ecfr.gov/current/title-40*.

C. How can I file an objection or hearing request?

Under FFDCA section 408(g), 21 U.S.C. 346a(g), any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2018-0522 in the subject line on the first page of your submission. All

objections and requests for a hearing must be in writing and must be received by the Hearing Clerk on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA-HQ-OPP-2018-0522, by one of the following methods:

• *Federal eRulemaking Portal*: *https://www.regulations.gov*. Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.

• *Mail*: OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

• *Hand Delivery*: To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *https://www.epa.gov/dockets*.

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *https://www.epa.gov/dockets*.

II. Background and Statutory Findings

In the *Federal Register* of August 24, 2018 (83 FR 42818) (FRL-9982-37), EPA issued a document pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide tolerance petition (PP8F8681) by Eden Research PLC, 6 Priory Ct., Priory Court Business Park, Poulton, Cirencester, GL7 5JB, United Kingdom (c/o SciReg, Inc., 12733 Director's Loop, Woodbridge, VA 22192). The petition requested that 40 CFR part 180 be amended by establishing an exemption from the requirement of a tolerance for residues of

eugenol (2-methoxy-4-(-2-propenyl)phenol) in or on raw agricultural commodities and processed foods when used in accordance with good agricultural practices. That document referenced a summary of the petition prepared by the petitioner Eden Research plc, c/o SciReg Inc., which is available in the docket, *https://www.regulations.gov*. There were no substantive comments received in response to the notice of filing.

III. Aggregate Risk Assessment and Determination of Safety

Section 408(c)(2)(A)(i) of FFDCA allows EPA to establish an exemption from the requirement for a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the exemption is "safe." Section 408(c)(2)(A)(ii) of FFDCA defines "safe" to mean that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." This includes exposure through drinking water and in residential settings but does not include occupational exposure. Pursuant to FFDCA section 408(c)(2)(B), in establishing or maintaining in effect an exemption from the requirement of a tolerance, EPA must take into account the factors set forth in FFDCA section 408(b)(2)(C), which require EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue...." Additionally, FFDCA section 408(b)(2)(D) requires that the Agency consider "available information concerning the cumulative effects of a particular pesticide's residues" and "other substances that have a common mechanism of toxicity."

EPA establishes exemptions from the requirement of a tolerance only in those cases where it can be clearly demonstrated that the risks from aggregate exposure to pesticide chemical residues under reasonably foreseeable circumstances will pose no harm to human health. If EPA is able to determine that a tolerance is not necessary to ensure that there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, an exemption

from the requirement of a tolerance may be established.

Consistent with FFDCA section 408(c)(2)(A), and the factors specified in FFDCA section 408(c)(2)(B), EPA has reviewed the available scientific data and other relevant information in support of this action. EPA has sufficient data to assess the hazards of and to make a determination on aggregate exposure for, including exposure resulting from the exemption established by this action. EPA's assessment of exposures and risks associated with eugenol follows.

IV. Toxicological Profile

Eugenol is a naturally occurring allyl chain-substituted guaiacol and a member of the phenylpropanoid class of chemicals. Eugenol is also the main constituent of clove bud oil (80 to 90%) and clove leaf oil (82 to 88%), and is also found in cinnamon bark and leaves, Tulsi leaves, turmeric, pepper, ginger, oregano and thyme and various other herbs. As such, eugenol has long been part of the normal human diet. It is currently approved by the U.S. Food and Drug Administration (FDA) for use as a food additive and generally recognized as safe (GRAS) by the FDA (21 CFR 184.1257).

In conducting its hazard assessment for eugenol, EPA relied on data from the open scientific literature which includes (1) a 19-week dietary study in rates, (2) a 13-week dietary study in rates, (3) five prenatal developmental toxicity studies, and (4) several mutagenicity studies. In these data, no adverse effects were seen at the highest dose test of 300 mg/kg/day. For guideline studies, EPA generally recommends testing at a limit dose of 1000 mg/kg/day. However, based on the data reviewed from the open literature along with a body of knowledge regarding eugenol such as its low toxicity; rapid degradation into the environment; natural occurrence and widespread use in herbs and a part of the human diet; EPA would not expect to see adverse effects at higher doses.

With regard to the overall toxicological profile of eugenol, the active ingredient is of minimal toxicity. Where data was not available on eugenol for acute inhalation and primary eye

irritation toxicity, it was provided on isoeugenol. Isoeugenol is structurally and physiochemically similar to eugenol. Based on data provided for eugenol and isoeugenol, eugenol is of low acute oral toxicity (Toxicity Category III) and inhalation toxicity (Toxicity Category III). The active ingredient shows moderate dermal toxicity (Toxicity Category II). It is a mild eye (Toxicity Category III), a severe dermal irritant (Toxicity Category II), and a weak dermal sensitizer.

With regard to subchronic toxicity, developmental toxicity, reproductive toxicity and mutagenicity data requirements for the active ingredient eugenol, all data requirements were satisfied by a combination of guideline and non-guideline studies, data waivers, and citations to studies from the Agency database as well as to the open literature. For the 90-day oral data requirement, data was provided on isoeugenol. There were no adverse subchronic effects for any oral or dermal routes of exposure. Regarding subchronic dermal and subchronic inhalation, EPA granted waivers for these data requirements based on weight of evidence approach (WOE). Specific to subchronic dermal, eugenol is the main constituent of clove bud oil and clove leaf oil. It is used extensively in dentistry for its analgesic and anti-inflammatory activities. In addition, the dermal margin of exposure (MOE) is based on a 300 mg/kg/day point of departure (POD) range from 460-33,000. This is well above the Agency's Level of Concern (LOC) of 100.

In terms of subchronic inhalation toxicity, eugenol has low inhalation toxicity. Eugenol is used in spray perfumes up to a concentration of 10%, in air fresheners up to 5%, and oil of clove in massage products and perfumes up to 30%. Despite its broad usage in cosmetics and air fresheners, no or few adverse incidents have been reported. Lastly, the occupational handler inhalation MOEs are more than ten times the LOC of 100, ranging from 550,000 to 12,000,000.

In terms of mutagenicity, the active ingredient was determined to be non-mutagenic, and no adverse effects were identified relative to either developmental toxicity or reproductive toxicity.

In conclusion, there were no adverse subchronic effects for any oral, dermal, inhalation, or developmental routes of exposure and as stated previously, EPA has granted a waiver of these

data requirements based on a WOE approach for the subchronic toxicity testing considering all the available eugenol hazard and exposure data. This WOE approach includes the following rationale:

1. Exposure from all routes and in all scenarios is considered to be negligible due to the following reasons: (1) eugenol is moderately volatile with a vapor pressure of 2.7 Pa @ 25oC; volatilization from both moist and dry soil surfaces is expected due to thymol's Henry's Law Constant of 1.92 x 10-6 atm-cu m/mol and vapor pressure; eugenol is expected to exist solely as a vapor in the ambient atmosphere, which would be readily degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in the air is estimated to be 5.9 hours; vapor phase eugenol is also degraded in the atmosphere by reaction with ozone, the half-life for this reaction is estimated to be 23 hours; Eugenol also absorbs UV light and therefore is likely susceptible to direct photolysis by sunlight; and (2) eugenol is expected to readily biodegrade as demonstrated in guideline ready biodegradability studies.

2. Eugenol is naturally occurring and has long been part of the normal human diet. It is currently FDA-approved for use as a food additive (21 CFR 175.105). FDA also considers eugenol as GRAS (21 CFR 184.1257). Eugenol is commonly used in foods, air fresheners, cosmetics, and perfumes.

3. Eugenol demonstrates low toxicity throughout its toxicity database. No adverse effects were observed to highest dose tested (300 mg/kg/day) (exception is one eugenol study with no-observed-adverse-effect level (NOAEL) of 300 mg/kg/day and lowest-observed-adverse-effect-level (LOAEL) of 625 mg/kg/day based on decreased body weight) in the eugenol toxicity database. The database includes a 19-week dietary study in rats, a 13-week dietary study in rats, five prenatal developmental toxicity studies, and several genotoxicity studies. Data from the open literature indicates that eugenol is rapidly metabolized as well as rapidly excreted.

A. Toxicological Points of Departure/Levels of Concern

Based on the toxicological profile, EPA did not identify any toxicological endpoints of concern for eugenol.

B. Exposure Assessment

1. *Dietary exposure from food, feed uses, and drinking water*. Eugenol is naturally occurring and has long been part of the normal human diet. As part of its qualitative risk assessment for eugenol, the Agency considered the potential for any additional dietary exposure to residues of eugenol from its proposed use as a fungicide and nematicide on agricultural use sites. EPA expects dietary (food and drinking water) exposures from the proposed use of eugenol to be negligible due to its short half-life and biodegradable nature. A quantitative dietary exposure assessment was not conducted since a toxicological endpoint for risk assessment was not identified.

2. *Residential exposure*. The term "residential exposure" is used in this document to refer to non-occupational, non-dietary exposure. Eugenol is not proposed to be registered for any pesticidal uses that would result in residential exposure. Residential exposure may occur from non-pesticidal uses such as air fresheners, cosmetics, and perfumes. However, a quantitative residential exposure assessment was not conducted since a toxicological endpoint for risk assessment was not identified.

3. *Cumulative effects from substances with a common mechanism of toxicity*. Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish a tolerance exemption, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." EPA has not found that eugenol shares a common mechanism of toxicity with any other substances, and eugenol does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed eugenol does not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to

evaluate the cumulative effects of such chemicals, see EPA's website at *https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/cumulative-assessment-risk-pesticides*.

C. Safety Factor for Infants and Children

FFDCA Section 408(b)(2)(C) provides that EPA shall retain an additional tenfold (10X) margin of safety for infants and children in the case of threshold effects 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 additional safety factor when reliable data available to EPA support the choice of a different factor. The Agency has determined that a qualitative risk assessment rather than a quantitative risk assessment would be most appropriate for the proposed use based on the toxicity profiles of eugenol along with its long history of human exposure. For this reason, a FQPA safety factor is not required at this time. EPA has concluded there are no toxicological endpoints of concern for the U.S. population, including infants and children.

D. Aggregate Risks

Based on the available data and information, EPA has concluded that a qualitative aggregate risk assessment is appropriate to support this action, and that risks of concern are not anticipated from aggregate exposure to eugenol. This conclusion is based on the low toxicity of eugenol, long history of human exposure to eugenol via the normal human diet and expected rapid degradation of eugenol in the environment.

A full explanation of the data upon which EPA relied and its risk assessment based on those data can be found in the December 15, 2021, document entitled “Risk Assessment for FIFRA Section 3 Registrations of Eugenol Technical Containing 99.62% Eugenol as an Active Ingredient, Mevalone, Containing 3.21% Eugenol as an Active Ingredient. Tolerance Exemption Petition for Eugenol”. This document, as well as other relevant information, is available in the

docket for this action as described under **ADDRESSES**.

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

Based on the Agency's assessment, EPA concludes that there is reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of eugenol. Therefore, the establishment of an exemption from the requirement of a tolerance for residues of eugenol (2-methoxy-4-(-2-propenyl)phenol) in or on all food commodities when used in accordance with good agricultural practices is safe under FFDCA section 408.

VI. Other Considerations

Analytical Enforcement Methodology

An analytical method is not required for enforcement purposes since the Agency is establishing an exemption from the requirement of a tolerance without any numerical limitation.

VII. Conclusions.

Therefore, an exemption from the requirement of a tolerance is established for residues of eugenol (2-methoxy-4-(-2-propenyl)phenol) in or on all food commodities when used in accordance with good agricultural practices.

VIII. Statutory and Executive Order Reviews

This action establishes an exemption from the requirement of a tolerance under FFDCA section 408(d) in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled "Regulatory Planning and Review" (58 FR 51735, October 4, 1993). Because this action has been exempted from review under Executive Order 12866, this action is not subject to Executive Order 13211, entitled "Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use" (66 FR 28355, May 22, 2001), or Executive Order 13045, entitled "Protection of Children from Environmental Health Risks and Safety Risks" (62 FR 19885, April 23, 1997). This action does not contain any information collections subject to OMB

approval under the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq*., nor does it require any special considerations under Executive Order 12898, entitled "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations" (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerance exemption in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq*.), do not apply. This action directly regulates growers, food processors, food handlers, and food retailers, not States or Tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4). As such, the Agency has determined that this action will not have a substantial direct effect on States or Tribal Governments, on the relationship between the National Government and the States or Tribal Governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian Tribes. Thus, the Agency has determined that Executive Order 13132, entitled "Federalism" (64 FR 43255, August 10, 1999), and Executive Order 13175, entitled "Consultation and Coordination with Indian Tribal Governments" (65 FR 67249, November 9, 2000), do not apply to this action. In addition, this action does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act (UMRA) (2 U.S.C. 1501 *et seq*.).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act (NTTAA) (15 U.S.C. 272 note).

IX. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq*.), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of

Representatives, and the Comptroller General of the United States prior to publication of the rule in the *Federal Register*. This action is not a "major rule" as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: September 12, 2022.

Edward Messina,

Director, Office of Pesticide Programs.

Therefore, for the reasons stated in the preamble, EPA is amending 40 CFR chapter I as follows:

PART 180—TOLERANCES AND EXEMPTIONS FOR PESTICIDE CHEMICAL RESIDUES IN FOOD

1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

2. Add § 180.1395 to subpart D to read as follows:

§180.1395 Eugenol; exemption from the requirement of a tolerance.

An exemption from the requirement of a tolerance is established for eugenol (2-methoxy-4-(-2-propenyl)phenol) in or on all food commodities when used in accordance with good agricultural practices.

[FR Doc. 2022-20041 Filed: 9/15/2022 8:45 am; Publication Date: 9/16/2022]