



ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2023-0561; FRL-12759-01-OCSP]

Vadescana Double-Stranded RNA; 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 Vadescana double-stranded (ds) RNA in or on honey and honeycomb if used according to the label and good agricultural practices. GreenLight Biosciences, Inc. submitted a petition to the 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 Vadescana dsRNA (Varroa destructor-Specific Recombinant Double-Stranded Interfering Oligonucleotide EP15) under FFDCA 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-2023-0561, is available at <https://www.regulations.gov>. Additional information about dockets generally, along with instructions for visiting the docket in-person, is available at <https://www.epa.gov/dockets>.

FOR FURTHER INFORMATION CONTACT: Shannon Borges, Biopesticides and Pollution Prevention Division (7511M), Office of Pesticide Programs, Environmental Protection Agency,

1200 Pennsylvania Ave. NW, Washington, DC 20460-0001; main telephone number: (202) 566-1400; 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:

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

If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. What is EPA's authority for taking this action?

EPA is issuing this rulemaking under section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a. FFDCA section 408(c)(2)(A)(i) 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." FFDCA section 408(c)(2)(A)(ii) 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, among other things, “available information concerning the cumulative effects of a particular pesticide's residues” and “other substances that have a common mechanism of toxicity.”

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. If you fail to file an objection to the final rule within the time period specified in the final rule, you will have waived the right to raise any issues resolved in the final rule. 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 the EPA, you must identify docket ID number EPA-HQ-OPP-2023-0561 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*]**.

EPA’s Office of Administrative Law Judges (OALJ), in which the Hearing Clerk is housed, urges parties to file and serve documents by electronic means only, notwithstanding any other particular requirements set forth in other procedural rules governing those proceedings. See “Revised Order Urging Electronic Filing and Service,” dated June 22, 2023, which can be found at <https://www.epa.gov/system/files/documents/2023-06/2023-06-22%20-%20revised%20order%20urging%20electronic%20filing%20and%20service.pdf>. Although EPA’s regulations require submission via U.S. Mail or hand delivery, EPA intends to treat submissions filed via electronic means as properly filed submissions; therefore, EPA believes the

preference for submission via electronic means will not be prejudicial. When submitting documents to the OALJ electronically, a person should utilize the OALJ e-filing system at https://yosemite.epa.gov/OA/EAB/EAB-ALJ_upload.nsf.

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 at <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. If you wish to include CBI in your request, please follow the applicable instructions at <https://www.epa.gov/dockets/commenting-epa-dockets#rules> and clearly mark the information that you claim to be CBI. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice.

II. Petitioned-for Exemption

In the *Federal Register* of December 19, 2023 (88 FR 87733) (FRL-10579-11-OCSPP), EPA issued a notice pursuant to FFDCa section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide tolerance exemption petition (PP 3F9054) by GreenLight Biosciences, Inc., 200 Boston Ave., Suite 1000, Medford, MA 02155. The petition requested that 40 CFR part 180 be amended by establishing an exemption from the requirement of a tolerance for residues of the miticide *Vadescana dsRNA* in or on honey and honeycomb. That notice referenced a summary of the petition prepared by the petitioner GreenLight Biosciences, Inc. and is available in the docket. EPA received two comments in response to the notice of filing. EPA's response to these comments is discussed in Unit III.C.

III. Final Tolerance Actions

A. EPA's Safety Determination

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 evaluated the available toxicological and exposure data on Vadescana dsRNA and considered their validity, completeness, and reliability, as well as the relationship of this information to human risk. A full explanation of the data upon which the EPA relied and its risk assessment based on those data can be found within the document entitled “Human Health Risk Assessment for a FIFRA Section 3 Registration Application for the Manufacturing Use Product EP15 (EPA File Symbol 94614-G), and the End Use Products EP15 Formulation (2 g/L) (EPA File Symbol 94614-U) and EP15 Formulation (4 g/L) (EPA File Symbol 94614-L), Containing a New Active Ingredient Vadescana (Varroa destructor-Specific Recombinant Double-Stranded Interfering Oligonucleotide EP15), and associated FFDCA Petition to Establish a Permanent Exemption from the Requirement of a Tolerance for Residues of Vadescana in or on Honey and Honeycomb” (Human Health Risk Assessment). This document, as well as other relevant information, are available in the docket for this action as described under **ADDRESSES**.

Vadescana (CAS Reg. No. 2643947-26-4) consists of double-stranded ribonucleic acid (dsRNA) that induces mortality of the Varroa mite (*Varroa destructor*) via a gene silencing mode of action. EPA used a weight-of-evidence approach, considering available hazard and exposure data to assess the risk to human health from the use of the end-use products containing the active ingredient Vadescana dsRNA. When Vadescana dsRNA is ingested by Varroa mites, it causes the inhibition of expression of the Varroa calmodulin protein by interfering with its messenger RNA stability or translation. Loss of functional calmodulin in Varroa mites leads to disruption of important cellular processes and interferes with the mites' reproductive success. The active ingredient is intended for direct applications into beehives and dietary exposure may result from consumption of honey and/or honeycomb-derived foods from treated beehives. Based on a weight-of-evidence approach, considering all available Vadescana hazard and exposure data, the agency conducted a qualitative dietary risk assessment. Vadescana dsRNA may be consumed with honey and/or honeycomb-derived food from treated beehives. Dietary risk from Vadescana is considered negligible for the following reasons: (1) Vadescana was found to have low toxicity via the oral route of exposure (EPA Toxicity Category IV); (2) Vadescana concentration is expected to decrease during honey processing in the hive; (3) While binding of a small number of potential Vadescana 21-mers to transcripts of two genes could not be excluded through bioinformatics alone, Vadescana exposure is expected to be negligible because it is rapidly degraded in simulated gastric and intestinal fluids, which also indicates that the formulation does not impact stability of the RNA in the mammalian gut. This degradation pattern was also highly similar to food-derived RNA indicating it would not be digested differently than naturally occurring RNA found in food; (4) Physiological barriers present in mammals (i.e., nucleases in saliva and gastrointestinal tract, acidic conditions in the stomach, presence of multiple membrane barriers) impede the uptake of naked, unmodified dsRNA, like Vadescana, further minimizing exposure, and thus risks, via the oral route. Together, any potential dietary risk from the use of Vadescana to human health is considered negligible. The petitioned-for tolerance exemption is

only for in-hive uses; therefore, dietary exposure to Vadescana dsRNA through drinking water is expected to be negligible. No residential applications are proposed for the EP15 products based on the product labels.

Although FFDCA section 408(b)(2)(C) provides for an additional tenfold margin of safety for infants and children in the case of threshold effects, EPA has determined that there are no such effects due to the lack of toxicity of Vadescana dsRNA. As a result, an additional margin of safety for the protection of infants and children is unnecessary.

B. Analytical Enforcement Methodology

An analytical method is not required for Vadescana dsRNA because the EPA is establishing an exemption from the requirement of a tolerance without any numerical limitation.

C. Response to Comments

The Agency received two comments in response to the Notice of Filing. A Response to Comments document has been written to best summarize and respond to the comments received. The first comment contained several human health concerns and questions. The concerns outlined in the comments have been considered as part of the Human Health Risk Assessment. The second comment expressed several ecological concerns surrounding the registration of products containing Vadescana dsRNA. As tolerances and tolerance exemptions under the FFDCA are concerned with human safety, the ecological concerns raised in this comment are not relevant to and EPA did not consider them in the establishment of this tolerance exemption. EPA has nevertheless prepared separate responses in the Response to Comments document apart from its response to the Notice of Filing. All documents, including the Human Health Risk Assessment, the Ecological Risk Assessment and the Response to Comments will be available in the <https://regulations.gov> docket EPA-HQ-OPP-2023-0561.

D. Conclusion

Based upon its evaluation in the Human Health Risk Assessment, which concluded that Vadescana dsRNA residues in or on honey and honeycomb are not toxic to mammals, the EPA

concludes that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of Vadescana dsRNA. Therefore, EPA is finalizing the tolerance exemption that was petitioned for by GreenLight Biosciences, Inc. An exemption from the requirement of a tolerance is established for residues of Vadescana dsRNA in or on honey and honeycomb when used according to the label and good agricultural practices.

IV. Statutory and Executive Order Reviews

Additional information about these statutes and Executive Orders can be found at <https://www.epa.gov/laws-regulations/laws-and-executive-orders>.

A. Executive Order 12866: Regulatory Planning and Review

This action is exempt from review under Executive Order 12866 (58 FR 51735, October 4, 1993), because it establishes or modifies a pesticide tolerance or a tolerance exemption under FFDCA section 408 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.

B. Executive Order 14192: Unleashing Prosperity Through Deregulation

Executive Order 14192 (90 FR 9065, February 6, 2025) does not apply because actions that establish a tolerance under FFDCA section 408 are exempted from review under Executive Order 12866.

C. Paperwork Reduction Act (PRA)

This action does not impose an information collection burden under the PRA, 44 U.S.C. 3501 et seq., because it does not contain any information collection activities.

D. Regulatory Flexibility Act (RFA)

This action is not subject to the RFA, 5 U.S.C. 601 *et seq.* The RFA applies only to rules subject to notice and comment rulemaking requirements under the Administrative Procedure Act (APA), 5 U.S.C. 553, or any other statute. This rule is not subject to the APA but is subject to

FFDCA section 408(d), which does not require notice and comment rulemaking to take this action in response to a petition.

E. Unfunded Mandates Reform Act (UMRA)

This action does not contain an unfunded mandate of \$100 million or more (in 1995 dollars and adjusted annually for inflation) as described in UMRA, 2 U.S.C. 1531–1538, and does not significantly or uniquely affect small governments. The action imposes no enforceable duty on any State, local or Tribal governments or the private sector.

F. Executive Order 13132: Federalism

This action does not have federalism implications as specified in Executive Order 13132 (64 FR 43255, August 10, 1999), because it will not have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government.

G. Executive Order 13175: Consultation and Coordination with Indian Tribal Governments

This action does not have tribal implications as specified in Executive Order 13175 (65 FR 67249, November 9, 2000), because it will not have substantial direct effects on tribal governments, on the relationship between the Federal Government and the Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes.

H. Executive Order 13045: Protection of Children from Environmental Health Risks and Safety Risks

This action is not subject to Executive Order 13045 (62 FR 19885, April 23, 1997) because it is not a significant regulatory action under section 3(f)(1) of Executive Order 12866 (See Unit IV.A.), and because EPA does not believe the environmental health or safety risks addressed by this action present a disproportionate risk to children.

However, EPA's 2021 Policy on Children's Health applies to this action. This rule finalizes an exemption from the requirement of a tolerance under the FFDCA, which requires

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 ...” (FFDCA 408(b)(2)(C)). The Agency’s consideration is documented in Unit III.A.

I. Executive Order 13211: Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution or Use

This action is not subject to Executive Order 13211 (66 FR 28355) (May 22, 2001) because it is not a significant regulatory action under Executive Order 12866.

J. National Technology Transfer Advancement Act (NTTAA)

This action does not involve technical standards that would require Agency consideration under NTTAA section 12(d), 15 U.S.C. 272.

K. Congressional Review Act (CRA)

This action is subject to the CRA, 5 U.S.C. 801 et seq., and EPA will submit a rule report to each House of the Congress and to the Comptroller General of the United States. This action 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: June 9, 2025.

Edward Messina,

Director, Office of Pesticide Programs.

For the reasons stated in the preamble, the 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 § 180.1417 to subpart D to read as follows:

§180.1417 Vadescana double-stranded RNA (CAS Reg. No. 2643947-26-4); exemption from the requirement of a tolerance.

An exemption from the requirement of a tolerance is established for residues of Vadescana dsRNA in or on honey and honeycomb when used in accordance with label directions and good agricultural practices.

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