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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 174

[EPA-HQ-OPP-2014-0834; FRL-9926-99]

Defensin Proteins (SoD2 and SoD7) derived from spinach (*Spinacia oleracea* L.) in Citrus Plants; Temporary Exemption from the Requirement of a Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes a temporary exemption from the requirement of a tolerance for residues of SoD2 and SoD7, two defensin proteins derived from spinach (*Spinacia oleracea* L.), in or on citrus when used as plant-incorporated protectants (PIPs) in accordance with the terms of Experimental Use Permit (EUP) No. 88232-EUP-1. Southern Gardens Citrus submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting the temporary tolerance exemption. This regulation eliminates the need to establish a maximum permissible level for residues of SoD2 and SoD7 in or on citrus. The temporary tolerance exemption expires on April 18, 2018.

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-2014-0834, is available at <http://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 is (202) 566-1744, and the telephone number for the OPP Docket is (703) 305-5805. Please review the visitor instructions and additional information about the docket available at <http://www.epa.gov/dockets>.

FOR FURTHER INFORMATION CONTACT: Robert McNally, 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 Government Printing Office's e-CFR site at http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl.

C. How Can I File an Objection or Hearing Request?

Under FFDCa section 408(g), 21 U.S.C. 346a, 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-2014-0834 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-2014-0834, by one of the following methods:

- *Federal eRulemaking Portal*: <http://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 <http://www.epa.gov/dockets/contacts.html>.

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

II. Background and Statutory Framework

In the **Federal Register** of January 28, 2015 (80 FR 4525) (FRL-9921-55), EPA issued a document pursuant to FFDCIA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide tolerance petition (PP 4F8289) by Southern Gardens Citrus, 1820 Country Road 833, Clewiston, FL 33440. The petition requested that 40 CFR part 174 be amended by establishing a

temporary exemption from the requirement of a tolerance for residues of spinach defensin (SoD2 and SoD7) proteins in or on citrus. That document referenced a summary of the petition prepared by the petitioner Southern Gardens Citrus, which is available in the docket, <http://www.regulations.gov>. A comment was received on the notice of filing. EPA's response to this comment is discussed in Unit VII.C.

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 performs a number of analyses to determine the risks from aggregate exposure to pesticide residues. First, EPA determines the toxicity of pesticides. Second, EPA examines

exposure to the pesticide through food, drinking water, and through other exposures that occur as a result of pesticide use in residential settings.

III. Toxicological Profile

Consistent with FFDCa section 408(b)(2)(D), EPA has reviewed the available scientific data and other relevant information in support of this action and considered its validity, completeness and reliability, and the relationship of this information to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children.

Diverse defensin proteins are expressed by most eukaryotic species to combat various bacterial and fungal organisms. Homologous proteins have also diverged in evolution to provide functions related to plant stresses such as heat and drought.

There is a long history of mammalian consumption of the entire spinach plant (both raw and cooked) as food, without causing any known deleterious human health effects or any evidence of toxicity. Spinach plant leaves have long been part of the human diet and there have been no findings that indicate toxicity or allergenicity of spinach proteins. Spinach is commonly regarded as a “super food” that serves as an excellent source of vitamins, minerals, and antioxidants. Recent U.S. consumption statistics indicate that, on average, 2 lbs. of spinach are consumed per person per year in the United States. “Spinach Profile,” Agricultural Marketing Resource Center (June 2013)

(http://www.agmrc.org/commodities_products/vegetables/spinach-profile/). Similarly, citrus whole fruits and juices have been an important part of the American and international diets for centuries. “History of Citrus,” All Foods Natural (2013) (available online at: <http://www.allfoodnatural.com/article/history-of-citrus.html>). Available studies demonstrate

that spinach defensin 2 (SoD2) and spinach defensin 7 (SoD7) proteins have very low oral toxicity. In an acute oral toxicity study conducted with a single dose of 5,000 milligram/kilogram (mg/kg) of microbial-produced SoD2 protein, no evidence of toxic or adverse effects was observed. Due to the high similarity between SoD2 and SoD7, the toxicity assessment is applicable to both proteins.

In an *in vitro* study, microbial-produced SoD2 and SoD7 proteins were rapidly and extensively hydrolyzed in stimulated gastric and intestinal conditions in the presence of pepsin (at pH 1.2) and pancreatin, respectively. Both microbial-produced SoD2 and SoD7 proteins demonstrated half-lives of approximately five minutes when subjected to pepsin digest, and both proteins were completely proteolyzed to amino acids and small peptide fragments in less than one minute in the presence of 0.15 milligram/liter (mg/ml) pancreatin. These results indicate that both the SoD2 and SoD7 proteins are highly susceptible to degradation in conditions similar to the human digestive tract.

A literature search was performed to identify any published studies that might implicate these spinach proteins as allergens. No scientific references were found to suggest possible allergenicity associated with these spinach proteins. Sequence comparisons were made between the novel proteins from spinach, SoD2 and SoD7, against those of known and putative allergens using FASTA3 to search the *AllergenOnline.org* database using full-length matches, sliding window of 80 amino acids and finally 8-mer identity searches. In addition, the sequences were searched against the National Center for Biotechnology Information (NCBI) Protein database without keyword limits to identify highly related proteins and with the keyword limit of allergen, to find any high scoring identity matches to proteins annotated as allergens, as a check on the *AllergenOnline.org* data. No significant sequence matches were found between

either SoD2 or SoD7 and any allergens. Thus there are no potential safety concerns related to allergenicity that would require further testing.

IV. Aggregate Exposures

In examining aggregate exposure, FFDCa section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

The Agency has considered available information on the aggregate exposure levels of consumers (and major identifiable subgroups of consumers) to the pesticide chemical residue and to other related substances. These considerations include dietary exposure under the tolerance exemption and all other tolerances or exemptions in effect for the plant-incorporated protectant chemical residue, and exposure from non-occupational sources. The Agency anticipates that there may be dietary exposure to the pesticide from the consumption of citrus products. In addition, people have a long history of consumption of spinach and will continue to be exposed to defensin proteins through consumption of spinach. Since the PIP is integrated into the plants genome, the Agency has concluded, based upon previous science reviews, that residues in drinking water will be extremely low or non-existent. Non-occupational exposure via the skin or inhalation is not likely since the plant-incorporated protectant is contained within

plant cells, which essentially eliminates these exposure routes or reduces these exposure routes to negligible. In any event, there are no non-dietary non-occupational uses of SoD2 and SoD7 as it is only used in agricultural settings.

V. 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, modify, or revoke a tolerance, the Agency consider “available information” concerning the cumulative effects of a particular pesticide’s residues and “other substances that have a common mechanism of toxicity.”

Since SoD2 and SoD7 proteins do not act through a toxic mode of action nor do the SoD2 and SoD7 proteins appear to produce a toxic metabolite produced by other substances, the proteins do not have a common mechanism of toxicity with other substances; therefore, the requirements of section 408(b)(2)(D)(v) do not apply.

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

FFDCA section 408(b)(2)(C) provides that, in considering the establishment of a tolerance or tolerance exemption for a pesticide chemical residue, EPA shall assess the available information about consumption patterns among infants and children, special susceptibility of infants and children to pesticide chemical residues, and the cumulative effects on infants and children of the residues and other substances with a common mechanism of toxicity. In

addition, FFDCA section 408(b)(2)(C) provides that EPA shall apply an additional tenfold (10X) margin of exposure (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 that a different margin of exposure (safety) will be safe for infants and children. This additional margin of exposure (safety) is commonly referred to as the Food Quality Protection Act Safety Factor (FQPA SF). 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.

Based on the information discussed in Unit III., EPA concludes that there are no threshold effects of concern to infants, children, or adults from exposure to the spinach defensin proteins SoD2 and SoD7. As a result, EPA concludes that no additional margin of exposure (safety) is necessary to protect infants and children and that not adding any additional margin of exposure (safety) will be safe for infants and children.

Therefore, based on the discussion in Units III and IV, 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 the residues of spinach defensin proteins SoD2 and SoD7 in citrus, when it is used as a plant-incorporated protectant. Such exposure includes all anticipated dietary exposures and all other exposures for which there is reliable information. The Agency has arrived at this conclusion based on a lack of toxicity and allergenicity of the SoD2 and SoD7 proteins.

VII. Other Considerations

A. Endocrine Disruptors

The pesticidal active ingredient is a protein, derived from a source that is not known to exert an influence on the endocrine system. Therefore, the Agency is not requiring information on the endocrine effects of the plant-incorporated protectant at this time.

B. Analytical Enforcement Methodology

A standard operating procedure for an enzyme-linked immunosorbent assay for the detection and quantification of spinach defensin proteins SoD2 and SoD7 in citrus plant tissue has been judged useful for its intended purpose.

C. Response to Comments

EPA received one comment relevant to this petition. The comment supports this tolerance exemption and therefore warrants no response.

VIII. Conclusion

The Agency concludes that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure residues of spinach defensin SoD2 and SoD7 proteins in or on citrus. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. The Agency has arrived at this conclusion because, as discussed previously no toxicity to mammals has been observed, nor is there any indication of allergenicity potential for the plant-incorporated protectant.

Therefore, an exemption is established for residues of spinach defensin SoD2 and SoD7 proteins in or on citrus when the protein is used as a PIP in citrus plants.

IX. Statutory and Executive Order Reviews

This action establishes a temporary 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 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).

X. 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 174

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

Dated: April 28, 2015.

Robert McNally,

Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 174--[AMENDED]

1. The authority citation for part 174 continues to read as follows:

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

2. Add § 174.535 to subpart W to read as follows:

§ 174.535 Spinach Defensin proteins; temporary exemption from the requirement of a tolerance.

(a) Residues of the defensin protein SoD2 derived from spinach (*Spinacia oleracea* L.) in or on citrus food commodities are temporarily exempt from the requirement of a tolerance when used as a plant-incorporated protectant in citrus plants in accordance with the terms of Experimental Use Permit No. 88232-EUP-1. This temporary exemption from the requirement of a tolerance expires on April 18, 2018.

(b) Residues of the defensin protein SoD7 derived from spinach (*Spinacia oleracea* L.) in or on citrus food commodities are temporarily exempt from the requirement of a tolerance when used as a plant-incorporated protectant in citrus plants in accordance with the terms of Experimental Use Permit No. 88232-EUP-1. This temporary exemption from the requirement of a tolerance expires on April 18, 2018.