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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2018-0204; FRL-9556-01-OCSPP]

Hydrolyzed Vegetable Proteins from Soy; 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 hydrolyzed vegetable proteins from soy when used as an inert ingredient (pH adjusting agent, surfactant, or adhesive) in pesticide products applied to growing crops pre-harvest, limited to 25% in the pesticide formulation. SciReg, Inc. on behalf of Italpollina USA, Inc. submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting establishment of an exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for residues of hydrolyzed vegetable proteins from soy 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-2018-0204, 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 is (202) 566-1744.

Due to the public health concerns related to COVID-19, the EPA Docket Center (EPA/DC) and Reading Room is open to visitors by appointment only. For the latest status information on EPA/DC services and access, visit *https://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: Marietta Echeverria, Registration Division (7505T), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; main telephone number: (202) 566-1030; email address: *RDFRNotices@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-2018-0204 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-2018-0204, 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/contacts.html.

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

II. Petition for Exemption

In the *Federal Register* of April 19, 2019 (84 FR 16430) (FRL-9991-14), EPA issued a document pursuant to FFDCA section 408, 21 U.S.C. 346a, announcing the filing of a pesticide petition (PP IN-11079) by SciReg, Inc. (12733 Director's Loop, Woodbridge, VA 22192) on behalf of Italpollina USA, Inc. (name changed to Hello Nature USA, Inc.)(1100 South Tower, 225 Peachtree Street, N.E., Atlanta, GA 30303). The petition requested that 40 CFR 180.920 be amended by establishing an exemption from the requirement of a tolerance for residues of hydrolyzed vegetable proteins when used as an inert ingredient (pH adjusting agent, surfactant, or adhesive) in pesticide products applied to growing crops pre-harvest under 40 CFR 180.920. That document referenced a summary of the petition prepared by SciReg, Inc. on behalf of Italpollina USA, Inc., the petitioner, which is available in the docket ID number EPA-HQ-OPP-2018-0204, *https://www.regulations.gov*. There were no relevant comments received in response to the notice of filing. The petitioner subsequently requested a limitation of not more than 25% hydrolyzed vegetable proteins from soy in pesticide formulations for use under 40 CFR 180.920.

III. Inert Ingredient Definition

Inert ingredients are all ingredients that are not active ingredients as defined in 40 CFR 153.125 and include, but are not limited to, the following types of ingredients (except when they have a pesticidal efficacy of their own): solvents such as alcohols and hydrocarbons; surfactants such as polyoxyethylene polymers and fatty acids; carriers such as clay and diatomaceous earth; thickeners such as carrageenan and modified cellulose; wetting, spreading, and dispersing agents; propellants in aerosol dispensers;

microencapsulating agents; and emulsifiers. The term "inert" is not intended to imply nontoxicity; the ingredient may or may not be chemically active. Generally, EPA has exempted inert ingredients from the requirement of a tolerance based on the low toxicity of the individual inert ingredients.

IV. 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 tolerance 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. Section 408(b)(2)(C) of FFDCA 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...."

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. In order to determine the risks from aggregate exposure to pesticide inert ingredients, the Agency considers the toxicity of the inert in conjunction with possible exposure to residues of the inert ingredient through food, drinking water, and through other exposures that occur as a result of pesticide use in residential settings. 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 inert

ingredient, 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 hydrolyzed vegetable proteins from soy including exposure resulting from the exemption established by this action. EPA's assessment of exposures and risks associated with hydrolyzed vegetable proteins from soy follows.

A. Toxicological Profile

EPA has evaluated the available toxicity data and considered their validity, completeness, and reliability as well as the relationship of the results of the studies 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. Specific information on the studies received and the nature of the adverse effects caused by hydrolyzed vegetable proteins from soy as well as the no-observed-adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from the toxicity studies can be found at http://www.regulations.gov in the document titled “Hydrolyzed Vegetable Proteins from Soy; Human Health Risk Assessment and Ecological Effects Assessment to Support Proposed Exemption from the Requirement of a Tolerance When Used as an Inert Ingredient in Pesticide Formulations” in docket ID number EPA-HQ-OPP-2018-0204.

Hydrolyzed vegetable proteins (also referred to as vegetable hydrolysates) are produced through hydrolysis of proteins derived from plants such as soybeans, peas, corn, alfalfa, potatoes or chickpeas. This process breaks the protein down to small peptides, reduces the molecular weight of the original protein and reduces the antigenicity and allergenicity of the protein. It is expected that systemic toxicity is

similar for all hydrolyzed vegetable proteins regardless the vegetable source. Since toxicity data on hydrolyzed vegetable proteins from soy are limited, toxicity data on hydrolyzed vegetable proteins from various sources are used to bridge data gaps. Acute and repeated dose toxicity studies summarized were conducted with a variety of hydrolyzed vegetables including soybean, potatoes, lupine, avocado, casein and hemp seed meal.

Acute toxicity studies conducted with vegetable hydrolysates from various vegetables are limited. The acute oral toxicity is low in rats treated with soy protein hydrolysates (also known as hydrolyzed vegetable protein from soy). The lethal dose, LD_{50} is >5,000 milligrams per kilogram bodyweight (mg/kg). Vegetable hydrolysates from soy and lupine proteins do not cause skin irritation in rabbits. *In vitro* studies with human skin show no irritation with vegetable hydrolysates from potatoes. No eye irritation is observed in rabbits treated with vegetable hydrolysates from soy, nor in *in vitro* studies with human cornea treated with vegetable hydrolysates from potatoes. Slight eye irritation is observed in rabbits treated with vegetable hydrolysates from lupine. Vegetable hydrolysates from avocado and lupine proteins are not dermal sensitizers in the mouse local lymph node assay (LLNA) or the guinea pig maximization test, respectively.

An 8-week oral toxicity study in rats treated with hydrolysates from hemp seed meal show no adverse effects up to 1,000 milligrams/kilogram/day (mg/kg/day), the limit dose. Also, no toxicity is seen in rats treated with approximately 20,000 mg/kg/day of hydrolysates from *Lupinus albus* and *L. luteus* for 112 days via the diet.

No developmental, reproduction or carcinogen toxicity studies are available for review. However, as stated above, no toxicity is seen in repeated dose studies with hydrolysates of vegetable proteins in rats up to 20,000 mg/kg/day. No evidence of neurotoxicity or immunotoxicity is seen in the available studies.

Mutagenicity studies are available with hydrolyzed vegetable protein from potato, lupine and pea proteins. Ames tests conducted with these hydrolyzed vegetable proteins were negative. Therefore, hydrolyzed vegetable proteins are not expected to be mutagenic.

To assess the immunologic response against hydrolyzed vegetable proteins from soy, dogs were sensitized to non- hydrolyzed soy protein over a 90-day period then were exposed to either non-hydrolyzed or hydrolyzed soy intradermally (30 days after sensitization) and orally (8 months after sensitization). Dogs intradermally exposed to hydrolyzed soy protein experienced an inflammatory response that was half the response detected after injection of non-hydrolyzed soy protein. Dogs orally exposed to hydrolyzed soy protein up to 17.75 grams over the course of 150 minutes did not experience clinical signs or reactions.

While hydrolyzed vegetable proteins from soy are not toxic, there is a potential for allergenicity from soy proteins. The concern is low for the potential for allergenicity from hydrolyzed vegetable proteins from soy due to dietary exposure because the hydrolysis process breaks down the protein structure to reduce allergenicity to hydrolyzed vegetable proteins from soy. Enzymatic hydrolysis of soybean proteins is a common process used by industry to improve functional properties and has been used to reduce allergenicity in making hypoallergenic soybean products. Soybean products are well known products that have been used as food for a very long time. The methods for elimination of allergenicity are always the same: denaturation by heat or pH change and hydrolysis by any means that degrade the protein structures. In the current petition, the proprietary method used to hydrolyze soybean proteins is such that no allergenic protein is expected to remain intact in the finished product. Although, the hydrolysis process is partial, any non-hydrolyzed soy proteins, which are those presenting a residual risk of allergenicity, are removed by centrifugation from the solution.

To further demonstrate that the enzymatic hydrolysis of soy proteins is effective in reducing antigenicity and allergenicity, a Soy ELISA (enzyme-linked immunosorbent assay) was conducted with hydrolyzed soy proteins extracted from soybean oil cake. The Soy ELISA test is a highly sensitive detection system used to detect soy residues in foodstuffs and has a level of quantification of 1.7 mg/kg soy. Through the detection of reactive robust indicator proteins called soy trypsin inhibitors, soy content and allergenic potential can be evaluated in test samples. The concentration of soy trypsin inhibitor proteins is directly proportional to the concentration of soy in a test sample. No soy trypsin inhibitors were found in any samples of vegetable hydrolysates from soy, indicating a negative result for the presence of residual soy allergenic proteins in hydrolyzed vegetable proteins from soy within the LOQ of the ELISA assay. Although the LOQ for the ELISA test is 1.7 mg/kg of soy, the soy protein hydrolysates contain only hydrolyzed protein, which has been shown to have low allergenic potential as explained above. Therefore, there is low concern for allergenicity from soy protein hydrolysates at levels below the LOQ.

Moreover, residues of hydrolyzed vegetable proteins from soy used in pesticide formulations in accordance with the tolerance exemption established in this action will be exposed to the effects of weather and microbial degradation before the treated crop enters the food chain. Therefore, based on the hydrolysis process, the negative ELISA assay and the expected effects of weather and microbial degradation, the concern is low for the potential allergenicity of hydrolyzed vegetable proteins from soy.

B. Toxicological Points of Departure/Levels of Concern

The available toxicity studies indicate that vegetable hydrolysates from soy have very low overall toxicity. Since no toxicity is observed in the available studies, an endpoint of concern for risk assessment purposes was not identified. Therefore, a qualitative risk assessment was conducted for acute and chronic dietary exposures and

short- and intermediate-term incidental oral, dermal and inhalation exposures.

C. Exposure Assessment

1. *Dietary exposure from food and feed uses*. In evaluating dietary exposure to hydrolyzed vegetable proteins from soy, EPA considered exposure under the proposed exemption from the requirement of a tolerance and from existing uses. EPA assessed dietary exposures from hydrolyzed vegetable proteins from soy in food as follows.

Dietary exposure (food and drinking water) to hydrolyzed vegetable proteins from soy may occur following ingestion of foods with residues from their use in accordance with this exemption. Dietary exposure may also occur after ingestion of food residues from their use in fertilizer products, dietary treatment for specific health conditions and use as a food additive (plant protein products) according to the U.S. Food and Drug Administration (FDA) under 21 CFR 170.3(n)(33). However, a quantitative dietary exposure assessment was not conducted since a toxicological endpoint for risk assessment was not identified.

2. *From non-dietary exposure*. The term "residential exposure" is used in this document to refer to non-occupational, non-dietary exposure (e.g., textiles (clothing and diapers), carpets, swimming pools, and hard surface disinfection on walls, floors, tables).

Hydrolyzed vegetable proteins from soy may be used in pesticide products and non-pesticide products that may be used in and around the home (e.g., for lawn and garden pest control, indoor pest control, cosmetics and personal care products). 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, 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."

Based on the lack of toxicity in the available data, hydrolyzed vegetable proteins from soy and its metabolites are not expected to share a common mechanism of toxicity with other chemicals; therefore, section 408(b)(2)(D)(v) does not apply.

D. Safety Factor for Infants and Children

Section 408(b)(2)(C) of FFDCA provides that EPA shall apply an additional tenfold 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 unless EPA concludes that a different margin of safety will be safe for infants and children. Based on the lack of threshold effects, EPA has not identified any toxicological endpoints of concern and is conducting a qualitative assessment of hydrolyzed vegetable proteins from soy. The qualitative assessment does not use safety factors for assessing risk, and no additional safety factor is needed for assessing risk to infants and children. Based on an assessment of hydrolyzed vegetable proteins from soy, EPA has concluded that there are no toxicological endpoints of concern for the U.S. population, including infants and children.

E. Aggregate Risks and Determination of Safety

Taking into consideration all available information on hydrolyzed vegetable proteins from soy, EPA has determined that there is a reasonable certainty that no harm will result to the general population, or to infants and children, from aggregate exposure to hydrolyzed vegetable proteins from soy residues. Therefore, the establishment of an exemption from the requirement of a tolerance under 40 CFR 180.920 for residues of hydrolyzed vegetable proteins from soy when used as an inert ingredient in pesticide formulations applied to growing crops pre-harvest limited to 25% in the final formulation, is safe under FFDCA section 408.

V. Other Considerations

Analytical Enforcement Methodology

An analytical method is not required for enforcement purposes since the Agency is not establishing a numerical tolerance for residues of hydrolyzed vegetable proteins from soy in or on any food commodities. EPA is establishing a limitation on the amount of hydrolyzed vegetable proteins from soy that may be used in pesticide formulations applied to growing crops pre-harvest. This limitation will be enforced through the pesticide registration process under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"), 7 U.S.C. 136 et seq. EPA will not register any such pesticide formulation that exceeds 25% of hydrolyzed vegetable proteins from soy.

VI. Conclusions

Therefore, an exemption from the requirement of a tolerance is established under 40 CFR 180.920 for hydrolyzed vegetable proteins from soy when used as an inert ingredient (pH adjusting agent, surfactant, or adhesive) in pesticide formulations applied to growing crops pre-harvest limited to 25% in the formulation.

VII. Statutory and Executive Order Reviews

This action establishes a tolerance exemption 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).

VIII. 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: April 29, 2022.

Marietta Echeverria,

Acting Director, Registration Division, 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. In §180.920, amend table 1 to 180.920, by adding in alphabetical order "Hydrolyzed vegetable proteins from soy" to read as follows:

§ 180.920 Inert ingredients used pre-harvest; exemptions from the requirement of a tolerance.

* * * * *

Table 1 to 180.920

Inert ingredients	Limits	Uses
* * *	*	* * *
Hydrolyzed vegetable proteins from soy	Not to exceed 25% of pesticide formulation	pH adjusting agent, surfactant, adhesive
* * *	*	* * *

[FR Doc. 2022-09655 Filed: 5/4/2022 8:45 am; Publication Date: 5/5/2022]