



ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2018-0545; FRL-9761-01-OCSP]

Cell Walls of *Saccharomyces cerevisiae*; Tolerance Exemption

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes an exemption from the requirement of a tolerance for residues of cell walls of *Saccharomyces cerevisiae* (also known as yeast cell walls or YCWs) when used as a carrier inert ingredient in pesticide formulations in pre-harvest applications to crops. SciReg, Inc., on behalf of Eden Research, 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 cell walls of *Saccharomyces cerevisiae* on food or feed commodities 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-2018-0545, 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 OPP Docket 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. 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-2018-0545 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-2018-0545, 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 October 18, 2018 (83 FR 52787), EPA issued a document pursuant to FFDCA section 408, 21 U.S.C. 346a, announcing the receipt of a pesticide petition

(PP IN-11175) filed by SciReg, Inc. (12733 Director's Loop, Woodbridge, VA, 22192), on behalf of Eden Research. The petition requested that 40 CFR 180.920 be amended by establishing an exemption from the requirement of a tolerance for residues of cell walls of *Saccharomyces cerevisiae* (also known as yeast cell walls or YCWs) when used as a carrier inert ingredient in pesticide formulations applied pre-harvest to crops. That document included a summary of the petition prepared by the petitioner and solicited comments on the petitioner's request. The Agency did not receive any public comments.

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 the 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 the FFDCA defines "safe" to mean that EPA has determined 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 it 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 an exemption 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 shown 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 FFDC section 408(c)(2)(A), and the factors specified in FFDC section 408(c)(2)(B), 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. EPA has sufficient data to assess the hazards of and to make a determination on aggregate exposure to YCWs, including exposure resulting from the exemption established by this action. EPA's assessment of exposures and risks associated with YCWs follows.

A. Toxicological Profile

YCWs are obtained by hydrolyzing intact yeast (*Saccharomyces cerevisiae*) cells. Given the long history of safe dietary exposure to strains of *S. cerevisiae* through their use in food, beverages, and nutritional supplements, YCWs are expected to be non-toxic. Although no toxicity information is available for YCWs, data from the major chemical components of YCWs

(β -glucan and mannan) are used to assess the safety of YCWs.

The acute oral toxicity of β -glucan is low, with an $LD_{50} >2000$ mg/kg. The repeated-dose toxicity for the major components of YCWs is low. No adverse effects were observed in subchronic studies in mice or rats or in a screening reproductive toxicity study in rats with β -glucan.

No oral chronic or carcinogenicity studies are available for YCWs or its components. However, there is low concern for genotoxicity or mutagenicity, based on negative results in mammalian and bacterial genotoxicity tests with β -glucan and mannan. No evidence of neurotoxicity or immunotoxicity is seen in the available studies.

B. Toxicological Points of Departure/Levels of Concern

No toxicological endpoint of concern for YCWs has been identified in the database.

C. Exposure Assessment

1. Dietary exposure. Dietary exposure (food and drinking water) may occur from the current pesticidal uses of cell walls of *Saccharomyces cerevisiae* strain LAS117 as well as the proposed pre-harvest use of YCWs in crops (e.g., eating foods treated with pesticide formulations containing YCWs, and drinking water exposures). Dietary exposure may also occur from non-pesticidal exposure (e.g. YCW dietary supplements). However, no endpoint of concern was identified. Therefore, a quantitative acute or chronic dietary exposure assessment is not necessary for YCWs.

2. Residential exposure. The current pesticidal uses of cell walls of *Saccharomyces cerevisiae* strain LAS117 as well as the proposed pre-harvest use of YCWs in crops are not anticipated to result in residential exposure. Residential exposure may occur from non-pesticidal uses (e.g., skin care products). However, no toxicological endpoint of concern was identified. Therefore, a quantitative assessment for residential exposure was not performed.

3. Cumulative effects from substances with a common mechanism of toxicity.

Unlike pesticides for which EPA has followed a cumulative risk approach based on a common

mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to YCWs and any other substances, and YCWs do not appear to produce a toxic metabolite produced by other substances. For the purposes of this action, therefore, EPA has assumed that YCWs do not have a common mechanism of toxicity with other substances.

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. As part of its qualitative assessment, the Agency did not use safety factors for assessing risk to YCWs, and no additional safety factor is needed for assessing risk to infants and children. Based on the low toxicity in the available studies, 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 YCWs, EPA has determined that there is a reasonable certainty that no harm to the general population or any population subgroup, including infants and children, will result from aggregate exposure to YCW residues. Therefore, the establishment of an exemption from the requirement of a tolerance under 40 CFR 180.920 for residues of YCWs when used as a carrier inert ingredient in pesticide formulations in pre-harvest applications to crops is safe under FFDCA section 408.

V. Other Considerations

A. Analytical Enforcement Methodology

An analytical method is not required for enforcement purposes since the Agency is not establishing a numerical tolerance for residues of YCWs in or on any food commodities.

B. International Residue Limits

In making its tolerance decisions, EPA seeks to harmonize U.S. tolerances with

international standards whenever possible, consistent with U.S. food safety standards and agricultural practices. EPA considers the international maximum residue limits (MRLs) established by the Codex Alimentarius Commission (Codex), as required by FFDCA section 408(b)(4). Codex is a joint United Nations Food and Agriculture Organization/World Health Organization food standards program, and it is recognized as an international food safety standards-setting organization in trade agreements to which the United States is a party. EPA may establish a tolerance that is different from a Codex MRL; however, FFDCA section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level.

The Codex has not established a MRL for YCWs.

VI. Conclusion

Taking into consideration all available information on YCWs, EPA has determined that there is a reasonable certainty that no harm to the general population or any population subgroup, including infants and children, will result from aggregate exposure to YCW residues. Therefore, an exemption from the requirement of a tolerance is established under 40 CFR 180.920 for YCWs when used as an inert ingredient (carrier) in pesticide formulations.

VII. 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).

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 an entry for “Cell Walls of *Saccharomyces cerevisiae*” to read as follows:

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

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Table 1 to 180.920

Inert Ingredients	Limits	Uses
* * * * *		
Cell Walls of <i>Saccharomyces cerevisiae</i>		Carrier
* * * * *		