



BILLING CODE 6560-50-P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2016-0378; FRL-9956-02]

Isoamyl acetate; 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 isoamyl acetate (CAS Reg. No. 123-92-2) when used as an inert ingredient (buffering agent) in pesticide formulations applied to growing crops and raw agricultural commodities after harvest. The Technology Sciences Group on behalf of the Jeneil Biosurfactant Company 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.

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-2016-0378, 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: Michael Goodis, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; main telephone number: (703) 305-7090; 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 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 FFDCFA 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-2016-0378 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-2016-0378, 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. Petition for Exemption

In the **Federal Register** of August 29, 2016 (81 FR 59165) (FRL-9950-22), EPA issued a document pursuant to FFDCA section 408, 21 U.S.C. 346a, announcing the filing of a pesticide petition (PP IN-10851) by the Technology Sciences Group, 1150 18th

Street, NW, Suite 1000, Washington, D.C. 20036, on behalf of the Jeneil Biosurfactant Company, 400 N. Dekora Woods Blvd., Saukville, WI 53080. The petition requested that 40 CFR 180.910 be amended by establishing an exemption from the requirement of a tolerance for residues of isoamyl acetate (CAS Reg. No.123-92-2) when used as an inert ingredient (buffering agent) in pesticide formulations applied to growing crops and raw agricultural commodities after harvest. That document referenced a summary of the petition prepared by the Technology Sciences Group on behalf of the Jeneil Biosurfactant Company the petitioner, which is available in the docket, <http://www.regulations.gov>. One comment was received and posted to this docket. The comment did not pertain to isoamyl acetate but to a totally unrelated compound.

This regulation eliminates the need to establish a maximum permissible level for residues of isoamyl acetate when applied in accordance with the conditions under 40 CFR 180.910.

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(b)(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 appreciable risks 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 finite 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 isoamyl acetate including exposure resulting from the exemption established by this action. EPA's assessment of exposures and risks associated with isoamyl acetate 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 isoamyl acetate as well as the no-observed-adverse-effect level (NOAEL) and the lowest-observed-adverse-effect level (LOAEL) from the toxicity studies are discussed in this unit.

Isoamyl acetate exhibits low levels of acute toxicity with oral lethal dose (LD)₅₀s for rats and rabbits being 16.6 grams/kilogram (g/kg) and 7.4 g/kg respectively. The dermal LD₅₀ for rabbits is > 5g/kg. It is not irritating to rabbit skin.

The National Toxicology Program reported dogs exposed to 5,000 parts per million (ppm) isoamyl acetate via inhalation for one hour showed drowsiness and nasal irritation. Cats exposed to 4,000 ppm isoamyl acetate for 20 minutes experienced eye and nose irritation.

The potential for eye irritation in rabbits was evaluated with a mixture of n-pentyl acetate and 2-methylbutyl acetate, two structural isomers of isoamyl acetate. Moderate conjunctival irritation, with no effects to the cornea or iris, resulted from ocular exposure and minor, transient conjunctival irritation was also observed. Conjunctival effects cleared up in 7 days.

There are no repeat-dose toxicity studies with isoamyl acetate. However, there are studies available regarding isoamyl alcohol. Isoamyl acetate readily metabolizes to isoamyl alcohol and toxicity data on isoamyl alcohol may be used as a surrogate for isoamyl acetate.

In a 4-week range-finding drinking water study, SPF-Wistar rats received isoamyl alcohol doses of 360 milligrams/kilogram/day (mg/kg/day) for two weeks and 1160 mg/kg/day for the next two weeks (20,000 and 16,000 ppm respectively). The higher concentration was unpalatable to the rats. Exposure to isoamyl alcohol did not affect body weight gain or food consumption and no effects were observed upon gross post-mortem examination. The NOAEL for this study is 1,160 mg/kg/day.

In a subsequent 90-day study, rats were given daily drinking water concentrations of 0, 1,000, 4,000 and 16,000 ppm isoamyl alcohol (males 0, 73, 295, 1,068 mg/kg/day and females 91, 385, 1,657 mg/kg/day, respectively). Treatment did not induce any

effect on mortality, body weight, various clinical chemistry parameters, or organ weights or any abnormality at gross and microscopic examination. There were marginal increases in red blood cell counts in the male animals of the mid- and high- dose groups and slight decreases in mean corpuscular volume and mean corpuscular hemoglobin content in the male animals of the high-dose group. The highest dose levels tested were the no observed-adverse-effect levels (NOAEL) in the drinking water study in rats (1,068 and 1,657 mg/kg/day in males and females respectively).

In a 17-week oral gavage study, Ash/CSE rats were administered daily doses of 0, 150, 500 or 1,000 mg/kg/day isoamyl alcohol. Parameters and endpoints evaluated included clinical observations, body weight, food and water consumption, hematology, clinical chemistry, urinalysis, organ weights (brain, liver, heart, spleen, stomach, small intestine, caecum, adrenals, gonads, pituitary and thyroid) and macroscopic and microscopic evaluations. Two high-dose rats died from lung congestion which was attributed to gavage error. No deaths or abnormalities in behavior occurred during the study in any of the test groups. After 17 weeks treatment, there were slight decreases in body weight gain in the high-dose males. That was ascribed to 5-10% lower food consumption compared to controls. No other consistent test-related effects were seen in any of the test groups. The NOAEL under the conditions of this study was 1,000 mg/kg/day.

Isoamyl acetate was negative in bacteria cell and *in vitro* genotoxicity assays as well as one *in vivo* study. It did not induce reverse gene mutations in *Salmonella typhimurium* in the absence and presence of metabolic activation.

Prenatal toxicity to isoamyl alcohol was studied using Wistar rats and Himalayan rabbits exposed 6 hours/day on gestational days 6-15 and 7-19 respectively. Dose concentrations were 0, 500, 2500 and 10,000 mg/m³ (0, 135, 675, 2,700 ppm). All rats and rabbits were sacrificed on days 20 and 29 respectively. In both species, maternal toxicity was manifested by slight retardation of body weight gain during the first days of the exposure period in animals of the high-dose group. The rabbits of this group had eye irritation (reddish, lid closure, or slight discharge) during exposure. There were no compound-related signs of embryo/fetotoxicity or teratogenicity in any of the treated rat groups. In rabbits, there was a statistically significant increase incidence of total fetal soft tissue variations mainly caused by a significant increase in the incidence of 'separated origin of carotids'. However, the incidences of variations were within the range of biological variation and unexpectedly low in control animals. The NOAEL for maternal toxicity in both rats and rabbits was 2,500 mg/m³ (675 ppm; 1,013 mg/kg/day) and the NOAEL for developmental toxicity was 10,000 mg/m³ (2,700 ppm; 4,054 mg/kg/day).

An *in vitro* *Hydra attenuata* developmental toxicity assay was conducted with isoamyl acetate. It was equally toxic to adults and embryos indicating low concern for developmental toxicity.

The Joint FAO/WHO Expert Committee on Food Additives summarized a chronic study where male and female rats received 2% isoamyl alcohol in their drinking water. No adverse effects or tumors were observed up to 2,000 mg/kg/day in rats given isoamyl alcohol in their drinking water for 53-56 weeks.

A DEREK analysis conducted on the isoamyl acetate structure did not reveal any structural alerts for possible carcinogenicity with regard to systemic and organ toxicity or mutagenicity. Therefore, based on the results of the DEREK analysis, the lack of toxicity in the submitted studies, and the lack of mutagenicity, isoamyl acetate is not expected to be carcinogenic to humans.

B. Toxicological Points of Departure/Levels of Concern

Due to the lack of adverse effects in the available data, no toxicological endpoint of concern has been identified. Therefore, a quantitative assessment of human exposure and risk is not necessary and have not been conducted.

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* In evaluating dietary exposure to isoamyl acetate, EPA considered exposure under the proposed exemption from the requirement of a tolerance. EPA assessed dietary exposures from isoamyl acetate in food as follows:

Under this exemption from the requirement of a tolerance, residues of isoamyl acetate may be found on foods from crops that were treated with pesticide formulations containing isoamyl acetate. However, a quantitative dietary exposure assessment was not conducted since an endpoint for risk assessment was not identified.

2. *Dietary exposure from drinking water.* Since a hazard endpoint of concern was not identified for the acute and chronic dietary assessment, a quantitative dietary exposure risk assessment for drinking water was not conducted, although exposures may be expected from use on food crops.

3. *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).

Isoamyl acetate may be used in pesticide products and non-pesticide products that may be used around the home. Based on the discussion in Unit IV.B., a quantitative residential exposure assessment for isoamyl acetate was not conducted.

4. *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.”

EPA has not found isoamyl acetate to share a common mechanism of toxicity with any other substances, and isoamyl acetate does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that isoamyl acetate 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 <http://www.epa.gov/pesticides/cumulative>.

D. Safety Factor for Infants and Children

1. *In general.* Section 408(b)(2)(C) of FFDCA provides that EPA shall apply 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 FQPA Safety Factor (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.

As part of its qualitative assessment, the Agency did 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 isoamyl acetate, 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

Because no toxicological endpoints of concern were identified, EPA concludes that aggregate exposure to residues of isoamyl acetate will not pose a risk to the U.S. population, including infants and children, and that there is a reasonable certainty that no harm will result to the general population, or to infants and children from aggregate exposure to isoamyl acetate residues.

V. 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.

VI. Conclusions

Therefore, an exemption from the requirement of a tolerance is established under 40 CFR 180.910 for isoamyl acetate (CAS Reg. No. 123-92-2) when used as an inert ingredient (buffering agent) in pesticide formulations applied to growing crops and raw agricultural commodities after harvest.

VII. Statutory and Executive Order Reviews

This action establishes an exemption from the requirement of a tolerance under FFDCFA 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).

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: February 13, 2017.

Michael Goodis,

Director, Registration Division, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 180--[AMENDED]

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

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

2. In §180.910, add alphabetically the inert ingredient to the table to read as follows:

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

Inert ingredients	Limits	Uses
* * *	*	***
Isoamyl acetate (CAS Reg. No. 123-92-2)		Buffering Agent
* * *	*	***

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