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## ENVIRONMENTAL PROTECTION AGENCY

### 40 CFR Part 180

[EPA-HQ-OPP-2018-0088; FRL-9997-10]

### Emamectin Benzoate; Pesticide Tolerances

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Final rule.

**SUMMARY:** This regulation establishes tolerances for residues of emamectin benzoate (referred to as emamectin in this document) in or on multiple commodities which are identified and discussed later in this document. Interregional Research Project No. 4 (IR-4) and Syngenta Crop Protection, LLC requested these tolerances under the Federal Food, Drug, and Cosmetic Act (FFDCA).

**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-2018-0088, 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](mailto: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 EPA's tolerance regulations at 40 CFR part 180 through the Government Publishing Office's e-CFR site at [http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab\\_02.tpl](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-2018-0088 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-2018-0088, 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. Summary of Petitioned-For Tolerance**

In the **Federal Register** of July 24, 2018 (83 FR 34968) (FRL-9980-31), EPA issued a document pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide petition (PP 7E8644) by IR-4, IR-4 Project Headquarters, Rutgers, The State University of New Jersey, 500 College Road East, Suite 201W, Princeton, NJ 08540. The petition requested that 40 CFR part 180 be amended by establishing tolerances for residues of emamectin, including its metabolites and degradates in or on the raw agricultural commodities: Artichoke, globe at 0.06 parts per million (ppm), *Brassica*, leafy greens, subgroup 4-16B at 0.050 ppm, Celtuce at 0.100 ppm, Cherry subgroup 12-12A at 0.10 ppm, Fennel, Florence at 0.100 ppm, Fruit, pome, group 11-10 at 0.025 ppm, Herb subgroup 19A at 0.50 ppm, Kohlrabi at 0.050 ppm, Leafy greens subgroup 4-16A at 0.100 ppm, Leaf petiole vegetable subgroup 22B at 0.100 ppm, Nut, tree, group 14-12 at 0.02 ppm, Vegetable, *brassica*, head and stem, group 5-16 at 0.050 ppm, and Vegetable, fruiting, group 8-10 at 0.020 ppm. The petition also proposed to amend 40 CFR 180.505 by removing the tolerances for residues of emamectin, including its metabolites and degradates, in or on the raw agricultural

commodities: Fruit, pome, group 11 at 0.025 ppm, Nut, tree, group 14 at 0.02 ppm, Pistachio at 0.02 ppm, Turnip, greens at 0.050 ppm, Vegetable, leafy, except *brassica*, group 4 at 0.100 ppm, Vegetable, brassica, leafy, group 5 at 0.050 ppm, and Vegetable fruiting, group 8 at 0.020 ppm.

That document referenced a summary of the petition prepared by Syngenta, the registrant, which is available in the docket, <http://www.regulations.gov>. There were no comments received in response to the notice of filing.

In the **Federal Register** of August 24, 2018 (83 FR 42818) (FRL-9982-37), EPA issued a document pursuant to FFDCFA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide petition (PP 7F8640) by Syngenta Crop Protection, LLC, P.O. Box 18300 Greensboro, NC 27419-8300. The petition requested that 40 CFR part 180 be amended by establishing a tolerance for residues of emamectin, including its metabolites and degradates in or on vegetable, cucurbit, group 9 at 0.03 ppm. That document referenced a summary of the petition prepared by Syngenta, the registrant, which is available in the docket, <http://www.regulations.gov>. There were no comments received in response to the notice of filing.

Based upon review of the data supporting the petition, EPA is establishing tolerances that vary from what the petitioner requested, as authorized under FFDCFA section 408(d)(4)(A)(i). EPA's explanation for those variations are contained in Unit IV.C.

### **III. Aggregate Risk Assessment and Determination of Safety**

Section 408(b)(2)(A)(i) of FFDCFA allows EPA to establish 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....”

Consistent with FFDCA section 408(b)(2)(D), and the factors specified in FFDCA section 408(b)(2)(D), 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 emamectin including exposure resulting from the tolerances established by this action. EPA's assessment of exposures and risks associated with emamectin follows.

#### *A. Toxicological Profile*

EPA has evaluated the available toxicity data and considered its 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.

The main target organ for emamectin is the nervous system; treatment-related clinical signs (tremors, ptosis, ataxia, mydriasis, and hunched posture) and

neuropathology (neuronal degeneration in the brain and in peripheral nerves and muscle fiber degeneration) were found in most of the emamectin studies in rats, dogs, rabbits, and mice. Decreased body weight was also a frequent finding.

Integral to the dose-response assessment in mammals for this class of compounds is the role of P-glycoprotein (P-gp) in target tissues. P-gp is a member of the adenosine triphosphate (ATP) binding cassette transporter protein class/group, which reside in the plasma membrane and function as a transmembrane efflux pump, moving xenobiotics from the intracellular to the extracellular domain. P-gp is found in the canalicular surface of hepatocytes, the apical surface of proximal tubular cells in the kidneys, brush border surface of enterocytes, luminal surface of blood capillaries of the brain (blood brain barrier), placenta, ovaries, and the testes. As an efflux transporter, P-gp acts as a protective barrier to keep xenobiotics out of the body by excreting them into bile, urine, and intestinal lumen, and prevents accumulation of these compounds in the brain and gonads, as well as in the fetus. Therefore, test animals with genetic polymorphisms that compromise P-gp expression are particularly susceptible to emamectin and abamectin induced neurotoxicity.

In this connection, some CF-1 mice have a polymorphism for the gene encoding P-gp and are either devoid (homozygous) or have diminished (heterozygous) levels of P-gp. These mice are found to be uniquely sensitive to the neurotoxic effects of emamectin and abamectin. In addition, the neonatal rat is also particularly sensitive to emamectin and abamectin as P-gp is undetectable in the neonatal rat brain. The first detection of P-gp is on post-natal day (PND) 7 and does not reach adult levels until approximately PND 28. As shown in the reproductive and DNT studies, neonatal rats are sensitive to the

effects of abamectin-induced pup body weight reductions and death. In contrast, in the developing human fetus, the presence of P-gp was found as early as 22 weeks of gestation. Based on the difference in the ontogeny of P-gp in neonatal rats and human newborns, the Agency does not believe that the early post-natal findings in the rat are relevant to human newborns or young children, at this time.

The human multidrug resistance (*MDR-1*) gene encoding P-gp and polymorphism of *MDR-1* gene are well studied. The literature data are inconclusive with respect to the functional significance of the genetic variance in P-gp in humans. Currently, the reported cases of polymorphism of the *MDR-1* gene in human populations have not been shown to result in a loss of P-gp function similar to that found in CF-1 mice. Given the ontogeny of P-gp and the lack of convincing evidence from the literature on human polymorphism of *MDR-1* gene resulting in diminished P-gp function, the Agency considers the results of the studies with CF-1 mice not relevant for human health risk assessment. Therefore, the Agency is using results from toxicological studies conducted in the species that do not have diminished P-gp function for selecting toxicity endpoints and PODs for risk assessment. Among the test animals with fully functional P-gp, the beagle dog is the most sensitive species.

Emamectin did not elicit increased fetal sensitivity in developmental toxicity studies in rats and rabbits. In the reproductive toxicity study, emamectin produced neuronal degeneration in the brain and spinal in parental and offspring animals at similar dose level (1.8 mg/kg/day), and no increase in quantitative sensitivity was found in the pup with respect to the neurotoxicity. However, in the developmental neurotoxicity study in rats, there was an increase in both quantitative and qualitative sensitivity in the pups as

no adverse effect was seen at the highest dose tested (3.6/2.5 mg/kg/day) in parental animals, while at 0.6 mg/kg/day, the pups showed a dose-related decrease in open field motor activity at post-natal day 17. Body tremors, hind-limb extension, and auditory startle were also observed in the high dose pups (3.6/2.5 mg/kg/day).

The carcinogenicity and mutagenicity studies provide no indication that emamectin is carcinogenic or mutagenic. Emamectin is classified as “not likely to be carcinogenic to humans.”

Specific information on the studies received and the nature of the adverse effects caused by emamectin 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 “*Emamectin (Emamectin Benzoate). Human Health Risk Assessment in Support of Establishing Permanent Tolerances on Globe Artichoke, Cherry Subgroup 12-12A, Herb Subgroup 19A, and Crop Group Conversions and Expansions to include Pome Fruit Group 11-10, Tree Nut Group 14-12, Brassica Vegetable Head and Stem Group 5-16, Brassica Leafy Greens Subgroup 4-16B, Leafy Greens Subgroup 4-16A, Leaf Petiole Vegetable Subgroup 22B, Fruiting Vegetable Group 8-10, and individual tolerances for Florence Fennel, Kohlrabi, Celtuce, and Cucurbit Vegetables Group 9*” on pages 42-48 in docket ID number EPA-HQ-OPP-2018-0088.

#### *B. Toxicological Points of Departure/Levels of Concern*

Once a pesticide’s toxicological profile is determined, EPA identifies toxicological points of departure (POD) and levels of concern to use in evaluating the risk posed by human exposure to the pesticide. For hazards that have a threshold below

which there is no appreciable risk, the toxicological POD is used as the basis for derivation of reference values for risk assessment. PODs are developed based on a careful analysis of the doses in each toxicological study to determine the dose at which no adverse effects are observed (the NOAEL) and the lowest dose at which adverse effects of concern are identified (the LOAEL). Uncertainty/safety factors are used in conjunction with the POD to calculate a safe exposure level - generally referred to as a population-adjusted dose (PAD) or a reference dose (RfD) - and a safe margin of exposure (MOE). For non-threshold risks, the Agency assumes that any amount of exposure will lead to some degree of risk. Thus, the Agency estimates risk in terms of the probability of an occurrence of the adverse effect expected in a lifetime. For more information on the general principles EPA uses in risk characterization and a complete description of the risk assessment process, see <http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/assessing-human-health-risk-pesticides>.

A summary of the toxicological endpoints for emamectin used for human risk assessment is shown in Table 1 of this unit.

**Table 1.-Summary of Toxicological Doses and Endpoints for Emamectin for Use in Human Health Risk Assessment**

Exposure/Scenario	Point of Departure and Uncertainty/Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
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Dietary, all durations (General population including infants and children)	NOAEL = 0.25 mg/kg/day UF <sub>A</sub> = 10x UF <sub>H</sub> = 10x FQPA SF = 1x	Acute RfD = 0.0025 mg/kg/day aPAD = 0.0025 mg/kg/day Chronic RfD = 0.0025 mg/kg/day cPAD = 0.0025 mg/kg/day	Subchronic and chronic oral toxicity studies in dogs  Subchronic LOAEL = 0.5 mg/kg/day based skeletal muscle atrophy and white matter multifocal degeneration in the brains of both sexes and white matter multifocal degeneration in the spinal cords of males.  Chronic LOAEL=0.5 mg/kg/day based on axonal degeneration in the pons, medulla, and peripheral nerves (sciatic, sural, and tibial); whole body tremors; stiffness of the hind legs, spinal cord axonal degeneration, and muscle fiber degeneration
Cancer (Oral, dermal, inhalation)	Classification: Not Likely to be carcinogenic to humans based on the absence of significant increase in tumor incidence in two adequate rodent carcinogenicity studies		

FQPA SF = Food Quality Protection Act Safety Factor. LOAEL = lowest-observed-adverse-effect-level. LOC = level of concern. mg/kg/day = milligram/kilo gram/day. MOE = margin of exposure. NOAEL = no-observed-adverse-effect-level. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. UF = uncertainty factor. UF<sub>A</sub> = extrapolation from animal to human (interspecies). UF<sub>H</sub> = potential variation in sensitivity among members of the human population (intraspecies).

### *C. Exposure Assessment*

1. *Dietary exposure from food and feed uses.* In evaluating dietary exposure to emamectin, EPA considered exposure under the petitioned-for tolerances as well as all existing emamectin tolerances in 40 CFR 180.505. EPA assessed dietary exposures from emamectin in food as follows:

i. *Acute exposure.* Quantitative acute dietary exposure and risk assessments are performed for a food-use pesticide, if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1-day or single exposure.

Such effects were identified for emamectin. In estimating acute dietary exposure, EPA used 2003-2008 food consumption information from the U.S. Department of Agriculture's National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). As to residue levels in food, a refined acute assessment was conducted. The assessment relied upon percent crop treated (PCT) data, and a combination of monitoring data from the Pesticide Data Program (PDP) and field trial data. For hog meat, a tolerance level residue was assumed. For all other livestock commodities, anticipated residue values were used.

ii. *Chronic exposure.* In conducting the chronic dietary exposure assessment EPA used 2003-2008 food consumption data from the USDA's NHANES/WWEIA. As to residue levels in food, a refined chronic assessment was conducted. The assessment relied upon the same data as above, except for using mean field trial data for cottonseed, tree nuts, globe artichoke, cherry subgroup 12-12A, and herb subgroup 19A.

iii. *Cancer*. Based on the data summarized in Unit III.A., EPA has concluded that emamectin does not pose a cancer risk to humans. Therefore, a dietary exposure assessment for the purpose of assessing cancer risk is unnecessary.

iv. *Anticipated residue and percent crop treated (PCT) information*. Section 408(b)(2)(E) of FFDCA authorizes EPA to use available data and information on the anticipated residue levels of pesticide residues in food and the actual levels of pesticide residues that have been measured in food. If EPA relies on such information, EPA must require pursuant to FFDCA section 408(f)(1) that data be provided 5 years after the tolerance is established, modified, or left in effect, demonstrating that the levels in food are not above the levels anticipated. For the present action, EPA will issue such data calls as are required by FFDCA section 408(b)(2)(E) and authorized under FFDCA section 408(f)(1). Data will be required to be submitted no later than 5 years from the date of issuance of these tolerances.

Section 408(b)(2)(F) of FFDCA states that the Agency may use data on the actual percent of food treated for assessing chronic dietary risk only if:

- Condition a: The data used are reliable and provide a valid basis to show what percentage of the food derived from such crop is likely to contain the pesticide residue.
- Condition b: The exposure estimate does not underestimate exposure for any significant subpopulation group.
- Condition c: Data are available on pesticide use and food consumption in a particular area, and the exposure estimate does not understate exposure for the population in such area.

In addition, the Agency must provide for periodic evaluation of any estimates used. To provide for the periodic evaluation of the estimate of PCT as required by FFDC section 408(b)(2)(F), EPA may require registrants to submit data on PCT.

The Agency estimated the PCT for existing uses as follows:

Specific values used in the acute assessment for percent crop treated are: 10% almonds, 20% apples, 20% broccoli, 40% brussels sprouts, 25% cabbage, 20% cauliflower, 40% celery, 10% chicory, 2.5% cotton, 20% lettuce, 20% pears, 15% peppers, 2.5% pistachios, 10% spinach, 20% tomatoes, and 2.5% walnuts.

Specific values used in the chronic assessment for percent crop treated are: 2.5% almonds, 10% apples, 5% broccoli, 20% brussels sprouts, 10% cabbage, 5% cauliflower, 20% celery, 5% chicory, 10% lettuce, 5% pears, 5% peppers, 2.5% pistachios, 5% spinach, 15% tomatoes, and 2.5% walnuts.

In most cases, EPA uses available data from United States Department of Agriculture/National Agricultural Statistics Service (USDA/NASS), proprietary market surveys, and California Department of Pesticide Regulation (CalDPR) Pesticide Use Reporting (PUR) for the chemical/crop combination for the most recent 10 years. EPA uses an average PCT for chronic dietary risk analysis and a maximum PCT for acute dietary risk analysis. The average PCT figures for each existing use is derived by combining available public and private market survey data for that use, averaging across all observations, and rounding up to the nearest 5%, except for those situations in which the average PCT is less than 1% or less than 2.5%. In those cases, the Agency would use less than 1% or less than 2.5% as the average PCT value, respectively. The maximum PCT figure is the highest observed maximum value reported within the most recent 10

years of available public and private market survey data for the existing use and rounded up to the nearest multiple of 5%, except where the maximum PCT is less than 2.5%, in which case, the Agency uses less than 2.5% as the maximum PCT.

2. *Dietary exposure from drinking water.* The Agency used screening level water exposure models in the dietary exposure analysis and risk assessment for emamectin in drinking water. These simulation models take into account data on the physical, chemical, and fate/transport characteristics of emamectin. Further information regarding EPA drinking water models used in pesticide exposure assessment can be found at <http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/about-water-exposure-models-used-pesticide>.

Based on the Pesticide in Water Calculator (PWC), the estimated drinking water concentrations (EDWCs) of emamectin for acute exposures are estimated to be 1.5 parts per billion (ppb) for surface water and EDWCs for chronic exposures are estimated to be 1.15 ppb for surface water. No groundwater concentrations are predicted for emamectin, as the model (PRZM-GW; pesticide root zone model - groundwater) indicates emamectin will not break through into groundwater over the 100-year course of the modeled scenario.

Modeled estimates of drinking water concentrations were directly entered into the dietary exposure model. For the acute dietary risk assessment, the water concentration value of 1.5 ppb was used to assess the contribution to drinking water and for the chronic dietary risk assessment, the water concentration of value 1.15 ppb was used to assess the contribution to drinking water.

3. *From non-dietary exposure.* The term “residential exposure” is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets).

Residential exposures are not anticipated from the proposed uses of emamectin, nor are they anticipated from existing uses of emamectin since they are agricultural uses, restricted use products (i.e., restricted to use by certified applicators only), or are limited to non-residential areas (i.e., commercial and industrial areas) with the exception of a gel bait product. The ready-to-use (RTU) gel bait product is registered for use in multiple locations, including in residential areas. As the RTU product requires no mixing/loading, the only potential for residential handler exposure is via application. When applying this product according to use directions, bait points and bait beads are intended to be placed in cracks and crevices where direct contact by adults is anticipated to be negligible. Post-application exposures for adults and children are also unlikely due to the nature of the application method, and the location of the bait placement. Therefore, a residential exposure assessment has not been conducted and there are no residential risk estimates recommended for use in the aggregate risk assessment for emamectin.

4. *Cumulative effects from substances with a common mechanism of toxicity.* The Agency is required to consider the cumulative risks of chemicals sharing a common mechanism of toxicity. In 2016, EPA’s Office of Pesticide Programs released a guidance document entitled *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* (<https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework>). This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach

beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. This framework supplements the existing guidance documents for establishing common mechanism groups (CMGs) and conducting cumulative risk assessments (CRA).

The Agency has utilized this framework for abamectin and determined that abamectin along with emamectin form a candidate CMG of the avermectin macrocyclic lactones. This group of pesticides is considered a candidate CMG because they share characteristics to support a testable hypothesis for a common mechanism of action and while there are sufficient toxicological data to suggest a common pathway, there are not adequate data to establish those key events in a pathway as described in the mode of action/adverse outcome pathway (MOA/AOP) framework (*e.g.*, lack of dose or temporal concordance of proposed key events).

In 2017, the Agency conducted a screening-level cumulative exposure analysis consistent with the guidance described in the cumulative screening framework. The screening-level cumulative assessment for the avermectin macrocyclic lactones, abamectin and emamectin, indicated that cumulative aggregate dietary and residential exposures for abamectin and emamectin were below the Agency's levels of concern.

Based upon updated use information (*i.e.*, new uses), the Agency has updated its screening-level cumulative exposure analysis for the avermectin macrocyclic lactones, including abamectin and emamectin. This updated screening-level cumulative exposure assessment for the avermectin macrocyclic lactones, abamectin and emamectin, indicated that that cumulative aggregate dietary and residential exposures for abamectin and emamectin were below the Agency's levels of concern. The screening memo, titled

*“Avermectin Macrocyclic Lactones, Abamectin and Emamectin. Cumulative Screening Risk Assessment”* can be found in docket ID number EPA-HQ-OPP-2018-0088 at <http://www.regulations.gov>.

#### *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.

2. *Prenatal and postnatal sensitivity.* Emamectin did not elicit increased fetal sensitivity in developmental toxicity studies in rats and rabbits. In the reproductive toxicity study, emamectin produced neuronal degeneration in the brain and spinal cord in parental and offspring animals at a similar dose level (1.8 mg/kg/day), and no increase in quantitative sensitivity was found in the pup with respect to the neurotoxicity. However, in the developmental neurotoxicity study in rats, there was an increase in both quantitative and qualitative sensitivity in the pups as no adverse effect was seen at the highest dose tested (3.6/2.5 mg/kg/day) in parental animals, while at 0.6 mg/kg/day, the pups showed a dose-related decrease in open field motor activity at post-natal day 17. Body tremors, hind-limb extension, and auditory startle were also observed in the high dose pups (3.6/2.5 mg/kg/day).

3. *Conclusion.* EPA has determined that reliable data show the safety of infants and children would be adequately protected if the FQPA SF were reduced to 1x. That decision is based on the following findings:

i. The toxicity database for emamectin is complete.

ii. The proposed MOA is interaction with GABA receptors leading to neurotoxicity. The clinical signs observed in the emamectin database are consistent with the proposed MOA. Following emamectin exposure, neurotoxicity has been seen across multiple studies and species of test animals. Neurotoxic effects seen in various studies are consistent with the MOA of emamectin, and the selected toxicity endpoints and POD is protective of the neurotoxic effects in the data.

iii. As discussed above, the developmental neurotoxicity study showed an increase in both quantitative and qualitative sensitivity in the pups as indicated by a dose-related decrease in open field motor activity at post-natal day 17 at 0.6 mg/kg/day. Body tremors, hind-limb extension, and auditory startle were also observed in the high dose pups (2.5 mg/kg/day), while no adverse effects were seen in the parental animals at the highest tested dose (3.6 mg/kg/day). However, the toxicity endpoint and POD (0.25 mg/kg/day) selected for risk assessment are protective of the effects seen in the pups.

iv. There are no residual uncertainties for emamectin with respect to the exposure databases. Although the dietary exposure estimates are partially refined, anticipated residue estimates for most commodities were derived from field trials which are still considered conservative since field trials are conducted under maximum use conditions (maximum allowed application rate and number of applications, minimum pre-harvest interval, etc.). Monitoring data were used for apples in the acute assessment since apple

juice had a significant impact on exposure. EPA made conservative (protective) assumptions in the ground and surface water modeling used to assess exposure to emamectin in drinking water. There are no anticipated exposures to residential handlers, or for post-application exposure of adults and children. These assessments will not underestimate the exposure and risks posed by emamectin.

#### *E. Aggregate Risks and Determination of Safety*

EPA determines whether acute and chronic dietary pesticide exposures are safe by comparing aggregate exposure estimates to the acute PAD (aPAD) and chronic PAD (cPAD). For linear cancer risks, EPA calculates the lifetime probability of acquiring cancer given the estimated aggregate exposure. Short-, intermediate-, and chronic-term risks are evaluated by comparing the estimated aggregate food, water, and residential exposure to the appropriate PODs to ensure that an adequate MOE exists.

1. *Acute risk.* Using the exposure assumptions discussed in this unit for acute exposure, the acute dietary exposure from food and water to emamectin will occupy 26% of the aPAD for children 1 to 2 years old, the population group receiving the greatest exposure.

2. *Chronic risk:* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that chronic exposure to emamectin from food and water will utilize 3.4% of the cPAD for children 1 to 2 years old, the population group receiving the greatest exposure. Based on the explanation in Unit III.C.3., regarding residential use patterns, chronic residential exposure to residues of emamectin is not expected.

3. *Short-term risk.* A short-term adverse effect was identified; however, emamectin is not registered for any use patterns that would result in short-term residential exposure. Short-term risk is assessed based on short-term residential exposure plus chronic dietary exposure. Because there is no short-term residential exposure and chronic dietary exposure has already been assessed under the appropriately protective cPAD (which is at least as protective as the POD used to assess short-term risk), no further assessment of short-term risk is necessary, and EPA relies on the chronic dietary risk assessment for evaluating short-term risk for emamectin.

4. *Intermediate-term risk.* An intermediate-term adverse effect was identified; however, emamectin is not registered for any use patterns that would result in intermediate-term residential exposure. Intermediate-term risk is assessed based on intermediate-term residential exposure plus chronic dietary exposure. Because there is no intermediate-term residential exposure and chronic dietary exposure has already been assessed under the appropriately protective cPAD (which is at least as protective as the POD used to assess intermediate-term risk), no further assessment of intermediate-term risk is necessary, and EPA relies on the chronic dietary risk assessment for evaluating intermediate-term risk for emamectin.

5. *Aggregate cancer risk for U.S. population.* Based on the lack of evidence of carcinogenicity in two adequate rodent carcinogenicity studies, emamectin is not expected to pose a cancer risk to humans.

6. *Determination of safety.* Based on these risk assessments, EPA concludes that there is a reasonable certainty that no harm will result to the general population, or to infants and children from aggregate exposure to emamectin residues.

## **IV. Other Considerations**

### *A. Analytical Enforcement Methodology*

Adequate methods (Method 244-92-3 and Method 244-92-3, Revision 1) are available for the enforcement of tolerances on plants. The methods determine residues of emamectin and its regulated isomers and degradates/metabolites using high performance liquid chromatography with fluorescence detection (HPLC/FLD).

The method may be requested from: Chief, Analytical Chemistry Branch, Environmental Science Center, 701 Mapes Rd., Ft. Meade, MD 20755-5350; telephone number: (410) 305-2905; email address: *residuemethods@epa.gov*.

### *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 FFDC section 408(b)(4). The Codex Alimentarius 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, FFDC section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level.

The Codex has established MRLs for emamectin on various commodities that are different than the tolerances established for emamectin in the United States.

The U.S. and Codex residue definitions are not harmonized. The U.S. residue definition for emamectin includes the sum of emamectin and its metabolites (8,9-isomer) for plants and livestock. The Codex residue definition includes only emamectin for plants and livestock commodities.

Codex has MRLs for residues of emamectin on tomato, tomatillo, bell pepper, and non-bell pepper, the representative commodities of the fruiting vegetable group 8-10 at 0.02 ppm each. The U.S. tolerance at 0.02 ppm for residues on crop group 8-10 is being harmonized with these Codex MRLs.

Codex has an MRL for residues of emamectin on mustard greens, the representative commodity for *Brassica* leafy greens subgroup 4-16B at 0.2 ppm. The U.S. tolerance on subgroup 4-16B is being harmonized with Codex mustard greens, the representative commodity, at 0.20 ppm.

Codex has MRLs for residues of emamectin on head lettuce at 1 ppm and leaf lettuce at 0.7 ppm. The current U.S. tolerance is 0.1 ppm for subgroup 4-16A, which has head lettuce, leaf lettuce, and spinach as the representative commodities. EPA is therefore harmonizing the tolerance for subgroup 4-16A with Codex head lettuce at 1 ppm.

Codex has MRLs for apple and pear at 0.02 ppm each. EPA harmonizing the tolerance on pome fruit, group 11-10 with these MRLs at 0.02 ppm.

For tree nut crop group 14-12, the Codex MRLs for residues on the representative commodities of this group is 20x lower than the U.S. tolerances being established in this rulemaking. Lowering the tolerance could cause U.S. growers to have violative residues when following label instructions; therefore, EPA is not harmonizing the tolerance with the Codex MRLs.

For all other commodities, Codex does not have established MRLs.

### *C. Revisions to Petitioned-For Tolerances*

For new uses on globe artichoke, herb subgroup 19A, and cherry subgroup 12-12A, the tolerances differ slightly from those proposed by IR-4 due to differences in calculating parent equivalents of emamectin metabolites from the residue data.

The currently established tolerance on crop group 11 and the proposed tolerance on crop group 11-10 are both at 0.025 ppm. The tolerance for pome fruit crop group 11-10 is being established at 0.02 ppm to harmonize with Codex MRLs on apple and pear.

The tolerance on *Brassica* leafy greens subgroup 4-16B is being set at 0.2 ppm instead of the proposed level at 0.050 ppm and the tolerance on leafy greens subgroup 4-16A is being set at 1 ppm instead of 0.1 ppm to harmonize with Codex.

For the proposed tolerance on fennel, Florence, the commodity definition was corrected to be Fennel, florence, fresh leaves and stalk.

For the other commodities and crop groups, the tolerances differ from the petitioned-for tolerances due to the use of HED rounding class practice.

The proposed tolerance for emamectin on vegetable, cucurbit, group 9 at 0.03 ppm is not necessary because the available data support the existing tolerance of 0.02 ppm for that crop group.

### **V. Conclusion**

Therefore, tolerances are established for residues of emamectin, including its metabolites and degradates in or on the raw agricultural commodities Artichoke, globe at 0.05 ppm; *Brassica*, leafy greens, subgroup 4-16B at 0.2 ppm; Celtuce at 0.1 ppm; Cherry subgroup 12-12A at 0.09 ppm; Fennel, florence, fresh leaves and stalk at 0.1 ppm;

Fruit, pome, group 11-10 at 0.02 ppm; Herb subgroup 19A at 0.4 ppm; Kohlrabi at 0.05 ppm; Leaf petiole vegetable subgroup 22B at 0.1 ppm; Leafy greens subgroup 4-16A at 1 ppm; Nut, tree, group 14-12 at 0.02 ppm; Vegetable, *brassica*, head and stem, group 5-16 at 0.05 ppm; and Vegetable, fruiting, group 8-10 at 0.02 ppm.

Additionally, the following existing tolerances are removed as unnecessary due to the establishment of the above tolerances: Fruit, pome, group 11 at 0.025; Nut, tree, group 14 at 0.02 ppm; Pistachio at 0.02 ppm; Turnip, greens at 0.050 ppm; Vegetable, *brassica*, leafy, group 5 at 0.050 ppm; Vegetable fruiting, group 8 at 0.020 ppm; and Vegetable, leafy, except *brassica*, group 4 at 0.100 ppm.

## **VI. Statutory and Executive Order Reviews**

This action establishes tolerances 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), nor is it considered a regulatory action under Executive Order 13771, entitled “Reducing Regulations and Controlling Regulatory Costs” (82 FR 9339, February 3, 2017). 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 tolerances 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).

## **VII. 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: August 8, 2019.

**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 § 180.505, amend the table in paragraph (a)(1) as follows:

i. Add alphabetically the entries “Artichoke, globe”; “*Brassica*, leafy greens, subgroup 4-16B”; “Celtuce”; “Cherry subgroup 12-12A”; “Fennel, florence, fresh leaves and stalk”; “Fruit, pome, group 11-10”; “Herb subgroup 19A”; “Kohlrabi”; “Leaf petiole

vegetable subgroup 22B”; “Leafy greens subgroup 4-16A”; “Nut, tree, group 14-12”;  
 “Vegetable, *brassica*, head and stem, group 5-16”; and “Vegetable, fruiting, group 8-10”;

ii. Remove the entries for “Fruit, pome, group 11”; “Nut, tree, group 14”;  
 “Pistachio”; “Turnip, greens”; “Vegetable, *brassica*, leafy, group 5”; “Vegetable fruiting,  
 group 8”; and “Vegetable, leafy, except *brassica*, group 4”.

The additions read as follows:

**§ 180.505 Emamectin; tolerances for residues.**

(a) \* \* \*

(1) \* \* \*

Commodity	Parts per million
* * * *	* * * *
Artichoke, globe	0.05
<i>Brassica</i> , leafy greens, subgroup 4-16B	0.2
Celtuce	0.1
Cherry subgroup 12-12A	0.09
* * * *	* * * *
Fennel, florence, fresh leaves and stalk	0.1
Fruit, pome, group 11-10	0.02
* * * *	* * * *
Herb subgroup 19A	0.4
Kohlrabi	0.05
Leaf petiole vegetable subgroup 22B	0.1
Leafy greens subgroup 4-16A	1
Nut, tree, group 14-12	0.02
* * * *	* * * *
Vegetable, <i>brassica</i> , head and stem, group 5-16	0.05
* * * *	* * * *
Vegetable, fruiting, group 8-10	0.02

\* \* \* \*