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**ENVIRONMENTAL PROTECTION AGENCY**

**40 CFR Part 180**

**[EPA-HQ-OPP-2018-0718 and EPA-HQ-OPP-2019-0076; FRL-10002-06]**

# Difenoconazole; Pesticide Tolerances

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

**ACTION**: Final rule.

**SUMMARY**: This regulation establishes tolerances for residues of difenoconazole in or on vegetable, root, subgroup 1A, except ginseng; vegetable, leaves of root and tuber, group 2; and tea, dried. In addition, this regulation amends the tolerances for residues of difenoconazole in or ginseng; cattle, liver; goat, liver; horse, liver; and sheep, liver. 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-2018-0718 and EPA-HQ-OPP-2019-0076, 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 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*.

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

Under FFDCA section 408(g), 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2018-0718 and EPA-HQ-OPP-2019-0076 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-2018-0718 and EPA-HQ-OPP-2019-0076, 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 June 7, 2019 (84 FR 26630) (FRL-9993-93) and in the **Federal Register** of May 9, 2019 (84 FR 20320) (FRL-9992-36), EPA issued documents pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of pesticide petitions (PP 8F8695 and 8E8728, respectively) by Syngenta Crop Protection, LLC, P.O. Box 18300, Greensboro, NC 27419. Pesticide petition 8F8695 requested that 40 CFR 180.475 be amended by establishing tolerances for residues of the fungicide difenoconazole in or on root vegetable crop subgroup 1A at 0.60 parts per million (ppm) and leaves of root and tuber vegetables crop group 2 at 8.0 ppm; PP 8E8728 requested the establishment of a tolerance for residues of difenoconazole in or on tea at 30 ppm. Those documents referenced summaries of the petitions prepared by Syngenta Crop Protection, LLC, the registrant, which are available in their respective dockets, *http://www.regulations.gov*. One comment was received on EPA's May 9, 2019 notice of filing in docket number EPA-HQ-OPP-2019-0076. EPA's response to this comment is discussed in Unit IV.C.

Based upon review of the data supporting the petition, EPA is establishing tolerances that vary from what the petitioner requested as permitted by FFDCA section 408(d)(4)(A)(i). These differences are explained in Unit IV.D.

## III. Aggregate Risk Assessment and Determination of Safety

Section 408(b)(2)(A)(i) of FFDCA 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 difenoconazole including exposure resulting from the tolerances established by this action. EPA's assessment of exposures and risks associated with difenoconazole 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.

Subchronic and chronic toxicity studies with difenoconazole in mice and rats showed decreased body weights and effects on the liver (e.g., hepatocellular hypertrophy, liver necrosis, fatty changes in the liver). No systemic toxicity was observed at the limit dose in a rat dermal toxicity study. Difenoconazole exhibits low acute toxicity by the oral, dermal and inhalation routes of exposure. It is not an eye or skin irritant and is not a sensitizer.

Acute and subchronic neurotoxicity studies showed evidence of mild neurotoxic effects. However, the selected endpoints of toxicity for risk assessment are protective of any potential neurotoxicity.

The available toxicity studies indicated no increased susceptibility of rats or rabbits from in utero or postnatal exposure to difenoconazole. In prenatal developmental toxicity studies in rats and rabbits and in the 2-generation reproduction study in rats, fetal and offspring toxicity, when observed, occurred at equivalent or higher doses than in the maternal and parental animals. In a rat developmental toxicity study, developmental effects were observed at doses higher than those which caused maternal toxicity. Developmental effects in the rat included increased incidence of ossification of the thoracic vertebrae and thyroid, decreased number of sternal centers of ossification, increased number of ribs and thoracic vertebrae, and decreased number of lumbar vertebrae. In the rabbit study, developmental effects (increases in post-implantation loss and resorptions and decreases in fetal body weight) were also seen at maternally toxic (decreased body weight gain and food consumption) doses. Since the developmental effects are more severe than the maternal effects, qualitative susceptibility is indicated in the rabbit developmental study; however, the selected POD is protective of this effect. In the 2-generation reproduction study in rats, toxicity to the fetuses and offspring, when observed, occurred at equivalent or higher doses than in the maternal and parental animals.

Although there is some evidence that difenoconazole affects antibody levels at doses that cause systemic toxicity, there are no indications in the available studies that organs associated with immune function, such as the thymus and spleen, are affected by difenoconazole. Difenoconazole is not mutagenic or genotoxic, and no evidence of carcinogenicity was seen in rats. Evidence for carcinogenicity was seen in mice as induction of liver tumors at doses which

were considered to be excessively high for carcinogenicity testing. Difenoconazole has been classified as "Suggestive Evidence of Carcinogenic Potential" based on liver tumors observed in mice. EPA has concluded that the chronic point of departure (POD) for assessing chronic risk will be protective of any cancer effects for the following reasons: (1) Tumors were seen in only one species; (2) carcinoma tumors were observed only at the two highest doses in the mouse carcinogenicity study; (3) benign tumors and necrosis were observed at the mid-dose; (4) the absence of tumors at the study's lower doses; (5) the absence of genotoxic or mutagenic effects. The cRfD is well below the no-observed- adverse-effect-level (NOAEL) of the mouse carcinogenicity study, at which no effects on the biological endpoints relevant to tumor development (i.e., hepatocellular hypertrophy, liver necrosis, fatty changes in the liver and bile stasis) were seen. As a result, EPA has concluded that a nonlinear RfD approach is appropriate for assessing cancer risk to difenoconazole and a separate quantitative cancer exposure assessment is unnecessary.

Specific information on the studies received and the nature of the adverse effects caused by difenoconazole 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 document "Difenoconazole. Human Health Risk Assessment for Proposed New Foliar Uses on All Members of Vegetable, Root, Subgroup 1A and Vegetable, Leaves of Root and Tuber, Group 2 and Establishment of a Tolerance with No U.S. Registration in/on Imported Tea" in docket ID number EPA-HQ-OPP-2018-0718.

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

Once a pesticide's toxicological profile is determined, EPA identifies toxicological 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 NOAEL and 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 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 difenoconazole used for human risk assessment is shown in Table 1 of this unit.

**Table 1. Summary of Toxicological Doses and Endpoints for Difenoconazole 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** |
|---|---|---|---|
| Acute dietary (All populations) | NOAEL = 25 mg/kg/day<br>$UF_A$ = 10x<br>$UF_H$ = 10x<br>FQPA SF = 1x | Acute RfD = 0.25 mg/kg/day<br><br>aPAD = 0.25 mg/kg/day | Acute Neurotoxicity Study in Rats<br>LOAEL = 200 mg/kg/day in males based on reduced fore-limb grip strength in males on Day 1 and increased motor activity on Day 1 |
| Chronic dietary (All populations) | NOAEL= 0.96 mg/kg/day<br>$UF_A$ = 10x<br>$UF_H$ = 10x<br>FQPA SF = 1x | Chronic RfD = 0.01 mg/kg/day<br><br>cPAD = 0.01 mg/kg/day | Combined Chronic Toxicity/Carcinogenicity (rat, dietary)<br>LOAEL = 24.1/32.8 mg/kg/day (male/female) based on cumulative decreases in body-weight gains |

| | | | |
|---|---|---|---|
| Oral short-term (1 to 30 days) | NOAEL= 1.25 mg/kg/day<br>$UF_A$ = 10x<br>$UF_H$ = 10x<br>FQPA SF = 1x | Residential LOC for MOE = <100 | Reproduction and Fertility Study (rat dietary)<br>Parental/Offspring LOAEL = 12.5 mg/kg/day based on decreased pup weight in in males on Day 21 and reduction in body weight gain of $F_0$ females prior to mating, gestation and lactation |
| Dermal short-term (1 to 30 days) and intermediate-term (1 to 6 months) | NOAEL = 1.25 mg/kg/day (dermal absorption factor = 6%)<br>$UF_A$ = 10x<br>$UF_H$ = 10x<br>FQPA SF = 1x | LOC for MOE = <100 | Reproduction and Fertility Study (rat, dietary)<br>Parental/Offspring LOAEL = 12.5 mg/kg/day based on decreased pup weight in males on Day 21 and reduction in body weight gain of $F_0$ females prior to mating, gestation and lactation |
| Inhalation short-term (1 to 30 days) and intermediate-term (1 to 6 months)<br>*Inhalation and oral absorption assumed equivalent | NOAEL= 1.25 mg/kg/day<br>$UF_A$ = 10x<br>$UF_H$ = 10x<br>FQPA SF = 1x | LOC for MOE = <100 | Reproduction and Fertility Study (rat, dietary)<br>Parental/Offspring LOAEL = 12.5 mg/kg/day based on decreased pup weight in males on Day 21 and reduction in body weight gain of $F_0$ females prior to mating, gestation and lactation |
| Cancer (Oral, dermal, inhalation) | Difenoconazole is classified "Suggestive Evidence of Carcinogenic Potential". Quantification of cancer risk is not required. The RfD would address the concern for chronic toxicity, including carcinogenicity, likely to result from exposure to difenoconazole. | | |

FQPA SF = Food Quality Protection Act Safety Factor. LOAEL = lowest-observed-adverse-effect-level. LOC = level of concern. mg/kg/day = milligram/kilogram/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. $UF_A$ = extrapolation from animal to human (interspecies). $UF_H$ = 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 difenoconazole, EPA considered exposure under the petitioned-for tolerances as well as all existing difenoconazole tolerances in 40 CFR 180.475. EPA assessed dietary exposures from

difenoconazole 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 difenoconazole. In estimating acute dietary exposure, EPA used food consumption information from the United States Department of Agriculture (USDA) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA) 2003 to 2008. As to residue levels in food, EPA assumed tolerance-level residues, 100 percent crop treated (PCT), and available empirical or default processing factors.

ii. *Chronic exposure*. In conducting the chronic dietary exposure assessment EPA used the food consumption data from the USDA NHANES/WWEIA 2003 to 2008. As to residue levels in food, EPA used tolerance-level residues for some commodities, average field trial residues and USDA Pesticide Data Program monitoring samples for the remaining commodities, available empirical or default processing factors, and average PCT assumptions for some commodities.

iii. *Cancer*. Based on the data summarized in Unit III.A., EPA has concluded that a nonlinear RfD approach is appropriate for assessing cancer risk due to difenoconazole. Cancer risk was assessed using the same exposure estimates as discussed in Unit III.C.1.ii., *chronic exposure*.

iv. *Anticipated residue and 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 call-ins 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, 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 FFDCA section 408(b)(2)(F), EPA may require registrants to submit data on PCT.

The Agency estimated the PCT for existing uses as follows: almond 15%, apples 25%, apricot 10%, artichoke 15%, blueberry 10%, broccoli 2.5%, cabbage 10%, cantaloupe 2.5%, carrot 2.5%, cauliflower 2.5%, cherry 2.5%, cucumbers 5%, garlic 10%, grapefruit 10%, grape (raisin) 10%, grape (table) 25%, grape (wine) 15%, hazelnut 2.5%, lemon 5%, onions 10%, orange 5%, peach 10%, pear 10%, pecan 5%, peppers 15%, pistachio 10%, plum/prune 10%, potato 20%, pumpkin 5%, soybean 2.5%, squash 10%, strawberry 2.5%, sugar beets 20%, sweet corn 5%, tangerine 5%, tomato 35%, walnut 5%, watermelon 15%, and wheat 15%.

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. 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.

The Agency believes that the three conditions discussed in Unit III.C.1.iv. have been met. With respect to Condition a, PCT estimates are derived from Federal and private market survey data, which are reliable and have a valid basis. The Agency is reasonably certain that the percentage of the food treated is not likely to be an underestimation. As to Conditions b and c, regional consumption information and consumption information for significant subpopulations is taken into account through EPA's computer-based model for evaluating the exposure of significant subpopulations including several regional groups. Use of this consumption information in EPA's risk assessment process ensures that EPA's exposure estimate does not understate exposure for any significant subpopulation group and allows the Agency to be reasonably certain that no regional population is exposed to residue levels higher than those

estimated by the Agency. Other than the data available through national food consumption surveys, EPA does not have available reliable information on the regional consumption of food to which difenoconazole may be applied in a particular area.

2. *Dietary exposure from drinking water*. The drinking water assessment was performed using a total toxic residue method, which considers both parent difenoconazole and its major metabolite, CGA 205375, or total toxic residues (TTR) from difenoconazole uses, in surface and groundwater. The Agency used screening level water exposure models in the dietary exposure analysis and risk assessment for difenoconazole in drinking water. These simulation models take into account data on the physical, chemical, and fate/transport characteristics of difenoconazole plus CGA 205375. 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 Tier II Pesticide in Water Calculator (PWC v1.52) model and Tier 1 Rice Model, the estimated drinking water concentrations (EDWCs) of TTR of difenoconazole for acute exposures are estimated to be 33.4 parts per billion (ppb) for surface water and 2.0 ppb for ground water. Chronic exposure EDWCs for non-cancer assessments are estimated to be 27.4 ppb for surface water and 0.60 ppb for ground water.

Modeled estimates of drinking water concentrations were directly entered into the dietary exposure model. For acute dietary risk assessment, the water concentration value of 33.4 ppb was used to assess the contribution to drinking water. For chronic dietary risk assessment, the water concentration of value 27.4 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). Difenoconazole is currently registered for the following uses that could result in residential exposures: treatment of ornamental plants in commercial and residential landscapes and interior plantscapes as well as turf applications to golf courses. EPA assessed residential exposure using the following assumptions: For residential handlers, adult short-term dermal and inhalation exposure is expected from mixing, loading, and applying difenoconazole on ornamentals (gardens and trees). For residential post-application exposures, short-term dermal exposure is expected for both adults and children (6 < 11 years old and 11 <16 years old) from post-application activities in treated residential landscapes and on golf courses. There are no residential uses for difenoconazole that would result in incidental oral exposure to children.

The scenarios used in the aggregate assessment were those that resulted in the highest exposures. The highest exposures consist of the short-term dermal exposure to adults from post-application activities in treated gardens and short-term dermal exposure to children 6 to 11 years old from post-application activities in treated gardens. Further information regarding EPA standard assumptions and generic inputs for residential exposures may be found at *http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide*.

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."

Unlike other 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 difenoconazole and any other substances, although EPA has previously concluded that there are no conclusive data that difenoconazole shares a common mechanism of toxicity with other conazole pesticides. Although the conazole fungicides (triazoles) produce 1,2,4 triazole and its acid-conjugated metabolites (triazolylalanine and triazolylacetic acid), 1,2,4 triazole and its acid-conjugated metabolites do not contribute to the toxicity of the parent conazole fungicides (triazoles). A separate aggregate risk assessment was conducted for triazole and the conjugated triazole metabolites (*Common Triazole Metabolites: Updated Aggregate Human Health Risk Assessment to Address New Section 3 Registrations For Use of Difenoconazole and Mefentrifluconazole*; DP451447, dated May 15, 2019) and it can be found at *https://www.regulations.gov* at docket ID number EPA-HQ-OPP-2018-0002. These new uses of difenoconazole considered with existing uses of triazole compounds do not result in a risk of concern for 1,2,4-trizaole and its metabolites. Difenoconazole does not appear to produce any other toxic metabolite produced by other substances. For the purposes of this action, therefore, EPA has not assumed that difenoconazole has 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 *https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/cumulative-assessment-risk-pesticides*.

*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*. The available toxicity studies indicated no increased quantitative susceptibility of rats or rabbits from *in utero* or postnatal exposure to difenoconazole. In prenatal developmental toxicity studies in rats and rabbits and in the 2-generation reproduction study in rats, fetal/offspring toxicity, when observed, occurred at equivalent or higher doses than in the maternal/parental animals. In rabbits there was qualitative susceptibility since the developmental effects were more severe than the maternal effects seen at the same dose; however, the selected POD is protective of this effect. In a rat developmental toxicity study, developmental effects were observed at doses higher than those which caused maternal toxicity. Developmental effects in the rat included increased incidence of ossification of the thoracic vertebrae and hyoid, decreased number of sternal centers of ossification, increased number of ribs and thoracic vertebrae, and decreased number of lumbar vertebrae. In the rabbit study, developmental effects (increases in post-implantation loss and resorptions and decreases in fetal body weight) were also seen at maternally toxic (decreased body weight gain and food consumption) doses. In the two-generation reproduction study in rats, toxicity to the fetuses/offspring (reduction in the body weight of F1 male pups), when observed, occurred at equivalent or higher doses than in the maternal/parental animals (reductions in body weight gain).

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 difenoconazole is sufficient for a full hazard evaluation and is considered adequate to evaluate risks to infants and children.

ii. There are no clear signs indication that difenoconazole is a neurotoxic chemical following acute, subchronic, or chronic dosing in multiple species in the difenoconazole database. The effects observed in acute and subchronic neurotoxicity studies are considered non-adverse as they were transient in nature and were only observed in one sex (males as reduced fore-limb grip strength with no histologic findings) and the selected endpoints of toxicity for risk assessment are protective of any potential neurotoxicity. There is no need for a developmental neurotoxicity study or additional UFs to account for neurotoxicity.

iii. There is no evidence that difenoconazole results in increased quantitative susceptibility in *in utero* rats or rabbits in the prenatal developmental studies or in young rats in the 2-generation reproduction study. However, in the developmental toxicity study in rabbits, developmental effects (increases in post-implantation loss and resorptions and decreases in fetal body weight) were also seen at maternally toxic doses (decreased body weight gain and food consumption). Because these effects are more severe, qualitative susceptibility is evident in the rabbit. The PODs selected to assess dietary exposures are protective of these effects.

iv. There are no residual uncertainties identified in the exposure databases. The dietary food exposure assessments were performed based on tolerance-level residues and 100% CT for the acute assessment while the chronic assessment used USDA Pesticide Data Program (PDP) monitoring data, average field trial residues for some commodities, tolerance level residues for remaining commodities, and average percent crop treated for some commodities. These

assumptions will not underestimate dietary exposure to difenoconazole. EPA made conservative (protective) assumptions in the ground and surface water modeling used to assess exposure to difenoconazole in drinking water. EPA used similarly conservative assumptions to assess post-application exposure of children. These assessments will not underestimate the exposure and risks posed by difenoconazole.

*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 aPAD and 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 difenoconazole will occupy 52% of the aPAD for all infants <1 year 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 difenoconazole from food and water will utilize 53% of the cPAD for all infants <1 year 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 difenoconazole is not expected.

3. *Short-term risk.* Short-term aggregate exposure takes into account short-term residential exposure plus average exposure levels to food and water (considered to be a background exposure level). Difenoconazole is currently registered for uses that could result in

short-term residential exposure, and the Agency has determined that it is appropriate to aggregate chronic exposure through food and water with short-term residential exposures to difenoconazole.

Using the exposure assumptions described in this unit for short-term exposures, EPA has concluded the combined short-term food, water, and residential exposures result in aggregate MOEs of 180 for adults and 240 for children 6 to <11 years old. Because EPA's level of concern for difenoconazole is an MOE of 100 or below, these MOEs are not of concern.

4. *Intermediate-term risk*. Intermediate-term aggregate exposure takes into account intermediate-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). An intermediate-term adverse effect was identified; however, difenoconazole 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 difenoconazole.

5. *Aggregate cancer risk for U.S. population.* As discussed in Unit III.A., EPA has determined that use of the chronic reference dose will be protective of the potential for cancer risk. Because the chronic exposure does not exceed the Agency's level of concern, EPA concludes that exposure to difenoconazole would not pose an unacceptable cancer risk.

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 difenoconazole residues.

## IV. Other Considerations

### *A. Analytical Enforcement Methodology*

An adequate tolerance enforcement method, gas chromatography with nitrogen-phosphorus detection (GC/NPD) method AG-575B, is available for the determination of residues of difenoconazole in/on plant commodities. An adequate enforcement method, gas chromatography with mass spectrometry detection (GC/MSD) method AG-676A, is also available for the determination of residues of difenoconazole *per se* in/on canola and barley commodities. A confirmatory method, GC/MSD method AG-676, is also available.

An adequate tolerance enforcement method, Method REM 147.07b, is available for livestock commodities. The method determines residues of difenoconazole and CGA-205375 in livestock commodities by liquid chromatography with tandem mass spectrometry detection (LC-MS/MS). Adequate confirmatory methods, Method AG-544A and Method REM 147.06, are available for the determination of residues of difenoconazole and CGA-205375, respectively, in livestock commodities.

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 FFDCA 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, FFDCA section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level.

Codex has established MRLs for difenoconazole in or on carrot at 0.2 ppm; edible offal at 1.5 ppm; sugar beet at 0.2 ppm; ginseng at 0.08 ppm; ginseng, dried at 0.8 ppm; and ginseng, extracts at 0.6 ppm. Several of these MRLs are different than the tolerances established for difenoconazole in the United States. The U.S. tolerance in/on crop subgroup 1A, except ginseng (0.6 ppm), being established in this rulemaking, is based on radish root data and cannot be harmonized with the Codex MRL for carrot, which is lower than the subgroup tolerance; doing so could result in exceedances of the tolerances even when growers followed label directions. The U.S. tolerance for ginseng has been harmonized with the Codex MRL for ginseng, dried and is inclusive of the lower tolerances for ginseng and ginseng, extracts. The tolerances for cattle, liver; goat, liver; horse, liver; and sheep, liver cannot be harmonized with Codex MRLs due to different dietary burdens.

*C. Response to Comments*

EPA received one comment opposing pesticide residues in food, although no substantive information was provided for EPA to take into consideration in its safety assessment. Although the commenter generally expressed concern about the potential for exposure to difenoconazole to be carcinogenic, EPA has evaluated the available data on carcinogenicity and exposure and determined that aggregate exposure to difenoconazole will not cause a cancer risk. The FFDCA

authorizes EPA to establish tolerances that permit certain levels of pesticide residues in or on food when the Agency can determine that such residues are safe. EPA has made that determination for the tolerances subject to this action; the commenter provided no information relevant to that conclusion.

*D. Revisions to Petitioned-For Tolerances*

The terms "tea;" "root vegetable crop subgroup 1A;" "leaves of root and tuber vegetables crop group 2" requested in the petition are being replaced with "tea, dried;" "vegetable, root, subgroup 1A, except ginseng;" and "vegetable, leaves of root and tuber, group 2", respectively, to reflect the correct commodity definitions. The EPA has modified the tolerance on tea, dried from the requested 30 ppm to 15 ppm to harmonize with Japan's draft MRL. The ginseng tolerance has been removed from the vegetable, root, subgroup 1A and set at 0.8 to harmonize with the highest Codex MRL. Tolerances for cattle, liver; goat, liver; horse, liver; and sheep, liver have been increased from 0.40 to 0.7 ppm based on the re-calculated dairy cattle dietary burden and the available feeding study data for residues of difenoconazole and its metabolite CGA-205375. Trailing zeroes have been removed from tolerances in accordance with current Agency practices.

*E. International Trade Considerations*

In this final rule, EPA is reducing the existing tolerance for ginseng from 1.0 ppm to 0.8 ppm in order to harmonize with the Codex MRL. Available residue data demonstrates that the new tolerance is sufficient to cover residues on ginseng.

In accordance with the World Trade Organization's (WTO) Sanitary and Phytosanitary Measures (SPS) Agreement, EPA intends to notify the WTO of this revision in order to satisfy its obligation. In addition, the SPS Agreement requires that Members provide a "reasonable

interval" between the publication of a regulation subject to the Agreement and its entry into force to allow time for producers in exporting Member countries to adapt to the new requirement. At this time, EPA is establishing an expiration date for the existing ginseng tolerance to allow that tolerance to remain in effect for a period of six months after the effective date of this final rule, in order to address this requirement. After the six month period expires, residues of difenoconazole on ginseng cannot exceed the new tolerance of 0.8 ppm.

This reduction in tolerance levels is not discriminatory; the same food safety standard contained in the FFDCA applies equally to domestically produced and imported foods. The new tolerance levels are supported by available residue data.

## V. Conclusion

Therefore, tolerances are established for residues of difenoconazole, difenoconazole, in or on vegetable, root, subgroup 1A, except ginseng at 0.6ppm; vegetable, leaves of root and tuber, group 2 at 8 ppm; and tea, dried at 15 ppm. Tolerances are amended for ginseng from 1.0 to 0.8 ppm; and cattle, liver; goat, liver; horse, liver; and sheep, liver from 0.40 ppm to 0.7 ppm. In addition, the Agency is removing the existing tolerances for beet, sugar; and carrot as they are unnecessary upon the establishment of the tolerance for vegetable, root, subgroup 1A, except ginseng. Finally, the Agency is amending the existing tolerance for ginseng by adding an expiration date.

## VI. Statutory and Executive Order Reviews

This action establishes tolerances 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), 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 tolerance 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: December 19, 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 § 180.475:

a. In the table in paragraph (a)(1):

i. Remove the entries "Beet, sugar" and "Carrot".

ii. Revise the entry for "Ginseng".

iii. Add a second entry for "Ginseng" after the existing entry for "Ginseng" and add alphabetically the entries "Tea, dried"; "Vegetable, leaves of root and tuber, group 2"; and "Vegetable, root, subgroup 1A, except ginseng".

iv. Add footnotes 1 and 2 to the end of the table.

b. Revise the entries "Cattle, liver"; "Goat, liver"; "Horse, liver"; and "Sheep, liver" in the table in paragraph (a)(2).

The additions and revisions read as follows:

**§ 180.475 Difenoconazole; tolerances for residues.**

(a) * * *

(1) * * *

| Commodity | Parts per million |
|---|---|
| * * * * * * * | |
| Ginseng[2] | 1.0 |
| Ginseng | 0.8 |
| * * * * * * * | |
| Tea, dried[1] | 15 |
| * * * * * * * | |
| Vegetable, leaves of root and tuber, group 2 | 8 |
| Vegetable, root, subgroup 1A, except ginseng | 0.6 |
| * * * * * * * | |

[1]There are no U.S. registrations for these commodities.
[2]This tolerance expires on August 14, 2020.

(2) * * *

| Commodity | Parts per million |
|---|---|
| * * * * * * * | |
| Cattle, liver | 0.7 |
| * * * * * * * | |
| Goat, liver | 0.7 |
| * * * * * * * | |
| Horse, liver | 0.7 |
| * * * * * * * | |
| Sheep, liver | 0.7 |
| * * * * * * * | |

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