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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2012-0177; FRL-9387-3]

Cyproconazole; Pesticide Tolerances

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes tolerances for residues of cyproconazole in or on peanut and peanut, hay. 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-2012-0177, 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), EPA West 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: Shaunta Hill, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (703) 347-8961; email address: *hill.shaunta@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 Printing Office's eCFR site at *http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl*. To

access the OCSPP test guidelines referenced in this document electronically, please go to *http://www.epa.gov/ocspp* and select "Test Methods and Guidelines."

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-2012-0177 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-2012-0177, 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.htm*.

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 May 23, 2012 (77 FR 30481) (FRL-9347-8), 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 1F7956) by Syngenta Crop Protection, LLC., P.O. Box 18300, Greensboro, NC 24719. The petition requested that 40 CFR 180.485 be amended by establishing tolerances for residues of the fungicide cyproconazole, in or on peanut, hay at 6.0 parts per million (ppm), and peanut, nutmeat; peanut, meal; peanut, butter; and peanut, refined oil at 0.03 ppm. That document referenced a summary of the petition prepared by Syngenta Crop Protection, the registrant, which is available in the docket, *http://www.regulations.gov*. There were no substantive comments received in response to the notice of filing.

Based upon review of the data supporting the petition, EPA has modified the requested tolerance levels and crops for which tolerances were needed. The reasons for these changes are explained in Unit IV.C.

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 cyproconazole including exposure resulting from the tolerances established by this action. EPA's assessment of exposures and risks associated with cyproconazole 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 acute studies demonstrate that cyproconazole is moderately toxic by the oral, dermal, and inhalation routes. It is neither an eye nor dermal irritant. Cyproconazole did not cause dermal sensitization. Consistent with similar anti-fungal pesticide active ingredients in this class (e.g., tetraconazole), the critical toxicological effects for cyproconazole in mammals appear to be indicative of hepatotoxicity. These effects include elevated levels of the liver enzymes lactate dehydrogenase (LDH) and aspartate aminotransferase, increased liver weight (relative and absolute), vacuolization, fatty changes, hepatocytomegaly, hypertrophy, and single-cell necrosis. For both subchronic and chronic durations, hepatotoxicity was observed in rats, mice and dogs, and all of these species appeared to be equally sensitive to cyproconazole toxicity with regards to the range of the doses tested (~0.5 to 130 milligrams/kilogram/day (mg/kg/day)). Other notable effects seen in rat subchronic oral feeding studies included increased macrophages in the lung, increased white blood cell counts and globulins, decreased spleen weights, histocytosis of the spleen, and spleen micropathology.

There are two dermal toxicity studies submitted for cyproconazole, both showing effects similar to the oral studies. In the 21-day study, dermal exposure to cyproconazole resulted in decreased body-weight gain and food consumption (males), increased aspartate aminotransferase (males), increased creatinine (females), and increased cholesterol in both sexes at the highest dose tested (1,250 mg/kg/day). In the 28-day study, toxicity occurred at the mid-dose (100 mg/kg/day). These effects included increased plasma globulin, protein and cholesterol, and hemosiderin deposition in the

spleen in females (1,000 mg/kg/day in males), hypertrophy of the thyroid follicular epithelium in both males and females, and increased incidences of centrilobular hepatocellular hypertrophy in males (1,000 mg/kg/day in females).

The developmental studies indicate that cyproconazole causes developmental toxicity. There are two developmental toxicity studies in rabbits, which were more sensitive for developmental effects than the rat. In the older study using chinchilla rabbits, the pups showed increased susceptibility with toxicity occurring at the lowest dose tested (2 mg/kg/day, the developmental no observed adverse effect level (NOAEL) was not established). These effects included increased incidences of hydrocephalus internus (abnormal accumulation of cerebral spinal fluid in the ventricles of the brain). The maternal lowest observed adverse effect level (LOAEL) was 10 mg/kg/day. This developmental toxicity study was classified unacceptable and does not satisfy the guideline requirement for a developmental toxicity study (OPPTS Guideline 870.3700; OECD 414) in the rabbit because the concentrations of test material were not within the acceptable range (±15% of nominal concentration) for the mid- and high-dose suspensions immediately after preparation. In the most recent study using New Zealand white rabbits, cyproconazole produced increased incidences of malformed fetuses and litters with malformed fetuses (hydrocephalus and kidney agenesis) at doses lower than the doses that produced maternal toxicity (50 mg/kg/day for dams and 10 mg/kg/day for fetuses). In rats, cyproconazole increased the incidences of supernumerary ribs at the same doses at which maternal adverse effects (decreased body-weight gain) were observed (12 mg/kg/day). There was no evidence of reproductive toxicity in the 2-generation reproduction toxicity study. The parental toxicity in the 2-generation

reproduction study was manifested as increased lipid storage and relative liver weights in males and increased relative liver weights in females (8.29 mg/kg/day). No offspring toxicity was observed at any of the doses tested.

Although there was evidence of carcinogenicity found in a mouse study, EPA has determined that cyproconazole is "not likely to be carcinogenic to humans" at doses that do not cause a mitogenic response in the liver (Ref. 1). In contrast to rodent cells, there are some limited data to suggest that constitutive androstane receptor (CAR) activation does not stimulate cell proliferation or inhibit apoptosis in human cells. However, the literature does not yet support the conclusion that CAR activation is not biologically plausible in humans. This conclusion is based on the weight of evidence that supports a non-genotoxic mitogenic mode of action for cyproconazole. The activation of the CAR receptor, the required initiating event, leads to a cascade of key events resulting in liver tumor development in mice. The data did not support: (1) Peroxisome proliferation, (2) mutagenesis, or (3) cytotoxicity followed by sustained regenerative proliferation as alternative modes of action. The quantification of carcinogenic potential is not required. The current reference dose (RfD) of 0.01 mg/kg/day is based on a 1-year dog study in which hepatotoxicity and organ weight changes were seen at 3.2 mg/kg/day and no adverse effects were observed at 1 mg/kg/day (NOAEL). This RfD would be protective of any liver effects caused by cyproconazole in the mouse toxicity studies or mode of action studies at higher doses.

There is no evidence of targeted neurotoxicity in the toxicity database. There were no central nervous system (CNS) malformations present in the developmental toxicity studies in rats and rabbits. In a 2-generation reproduction study in rats, there

were no findings in pups that were suggestive of changes in neurological development. Additionally, there was no evidence of neurotoxicity in other studies.

Finally, there is no evidence that cyproconazole is an immunotoxicant. Although there is no immunotoxicity study currently available for cyproconazole, the available data indicate that cyproconazole does not have immunotoxic effects. This is consistent with the fact that the target organ is the liver, which is similar to the other triazole fungicides, which do not have immunotoxic effects.

Specific information on the studies received and the nature of the adverse effects caused by cyproconazole as well as the NOAEL and the LOAEL from the toxicity studies can be found at *http://www.regulations.gov* in document "Cyproconazole. Tolerance Petition for Residues in/on Peanuts, Human-Health Risk Assessment" in docket ID number EPA-HQ-OPP-2012-0177.

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://www.epa.gov/pesticides/factsheets/riskassess.htm*.

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

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

Exposure Scenario	POD	Uncertainty/ FQPA SF	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General population, including infants and children)	N/A	N/A	N/A	A dose and endpoint attributable to a single dose were not identified in the database including the developmental toxicity studies.
Acute Dietary (Females 13-49 years of age)	NOAEL = 2 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	aPAD = aRfD = 0.02 mg/kg/day	**Prenatal Developmental toxicity Study – New Zealand white rabbits** Developmental LOAEL = 10 mg/kg/day based on increased incidence of malformed fetuses and litters with malformed fetuses
Chronic Dietary (All populations)	NOAEL = 1.0 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	cPAD = cRfD = 0.01 mg/kg/day	**Chronic oral toxicity study - dog** LOAEL = 3.2 mg/kg/day based on liver effects (P450 induction in females and histopathology, laminar eosinophilic intrahepatocytic bodies in males)
Short (1-30 days)- and Intermediate (1-6 months)- Term Dermal	NOAEL = 10 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	Residential LOC for MOE = 100	**28-Day Dermal Study – rat** LOAEL = 100 mg/kg/day, based on increased plasma globulin, protein and cholesterol, and hemosiderin deposition in the spleen in females, and hypertrophy of the thyroid follicular epithelium in

Exposure Scenario	POD	Uncertainty/ FQPA SF	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
				both males and females
Cancer (oral, dermal, inhalation)	EPA has classified cyproconazole as "not likely to be carcinogenic to humans", according to EPA *Proposed Guidelines for Carcinogen Risk Assessment* (April 10, 1996).			

FQPA SF = Food Quality Protection Act Safety Factor. LOAEL = lowest-observed-adverse-effect-level. LOC = level of concern. mg/kg/day = milligrams/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 cyproconazole, EPA considered exposure under the petitioned-for tolerances as well as all existing cyproconazole tolerances in 40 CFR 180.485. EPA assessed dietary exposures from cyproconazole 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. In conducting the acute dietary exposure assessment, EPA used the food consumption data from the U.S. Department of Agriculture's (USDA) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). This dietary survey was conducted from 2003 to 2008. As to residue levels in food, an unrefined acute dietary exposure and risk analysis was performed assuming tolerance-level residues, 100% crop treated, DEEM (ver. 7.81) default processing factors.

ii. *Chronic exposure*. In conducting the chronic dietary exposure assessment, EPA used the food consumption data from the USDA's NHANES/WWEIA. This dietary survey was conducted from 2003 to 2008. An unrefined chronic dietary exposure and

risk analysis was performed assuming tolerance-level residues, 100% crop treated, DEEM (ver. 7.81) default processing factors.

iii. *Cancer*. Based on the data summarized in Unit III.A., EPA has concluded that cyproconazole 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*. EPA did not use anticipated residue and/or PCT information in the dietary assessment for cyproconazole. Tolerance-level residues and 100% crop treated was assumed for all food commodities.

2. *Dietary exposure from drinking water*. The Agency used screening-level water exposure models in the dietary exposure analysis and risk assessment for cyproconazole in drinking water. These simulation models take into account data on the physical, chemical, and fate/transport characteristics of cyproconazole. Further information regarding EPA drinking water models used in pesticide exposure assessment can be found at *http://www.epa.gov/oppefed1/models/water/index.htm*.

Based on the First Index Reservoir Screening Tool (FIRST) and Screening Concentration in Ground Water (SCI-GROW) models, the estimated drinking water concentrations (EDWCs) of cyproconazole for acute exposures are estimated to be 113 parts per billion (ppb) for surface water and 1.52 ppb for ground water. For chronic exposures for non-cancer assessments are estimated to be 43 ppb for surface water and 1.52 ppb for ground water.

Modeled estimates of drinking water concentrations were directly entered into the dietary exposure model. Since the EDWC estimates from surface water were higher than

those from ground water, EDWC estimates in surface water were used in both acute and chronic dietary risk assessments.

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). Cyproconazole is not registered for any specific use patterns that would result in residential handler exposure. Cyproconazole is proposed for use on golf course turf, which may result in post-application dermal exposure to golfers (both adults and children). No chemical-specific data were available to assess potential short-term dermal post-application exposures to adult and youth golfers. Therefore, a series of assumptions and exposure factors served as the basis for completing the residential post-application risk assessment. Each assumption and factor is detailed in the 2012 Residential SOPs (*http://www.epa.gov/pesticides/science/residential-exposure-sop.html*). Post-application oral and inhalation exposures, as well as residential handler exposures, are not expected based on the current use patterns for cyproconazole. Further information regarding EPA standard assumptions and generic inputs for residential exposures may be found at *http://www.epa.gov/pesticides/trac/science/trac6a05.pdf*.

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."

Cyproconazole is a member of the triazole-containing class of pesticides. Although conazoles act similarly in plants by inhibiting ergosterol biosynthesis, there is not necessarily a relationship between their pesticidal activity and their mechanism of toxicity in mammals. Structural similarities do not constitute a common mechanism of toxicity. Evidence is needed to establish that the chemicals operate by the same, or essentially the same, sequence of major biochemical events (Ref. 2). In conazoles, however, a variable pattern of toxicological responses is found; some are hepatotoxic and hepatocarcinogenic in mice. Some induce thyroid tumors in rats. Some induce developmental, reproductive, and neurological effects in rodents. Furthermore, the conazoles produce a diverse range of biochemical events including altered cholesterol levels, stress responses, and altered DNA methylation. It is not clearly understood whether these biochemical events are directly connected to their toxicological outcomes. Thus, there is currently no evidence to indicate that conazoles share common mechanisms of toxicity and EPA is not following a cumulative risk approach based on a common mechanism of toxicity for the conazoles. For information regarding EPA's procedures for cumulating effects from substances found to have a common mechanism of toxicity, see EPA's website at *http://www.epa.gov/pesticides/cumulative*.

Cyproconazole is a triazole-derived pesticide. This class of compounds can form the common metabolite 1,2,4-triazole and two triazole conjugates (triazolylalanine and triazolylacetic acid). To support existing tolerances and to establish new tolerances for triazole-derivative pesticides, including cyproconazole, EPA conducted a human health risk assessment for exposure to 1,2,4-triazole, triazolylalanine, and triazolylacetic acid resulting from the use of all current and pending uses of any triazole-derived fungicide.

The risk assessment is a highly conservative, screening-level evaluation in terms of hazards associated with common metabolites (e.g., use of a maximum combination of uncertainty factors) and potential dietary and non-dietary exposures (i.e., high end estimates of both dietary and non-dietary exposures). In addition, the Agency retained the additional 10X FQPA Safety Factor for the protection of infants and children. The assessment includes evaluations of risks for various subgroups, including those comprised of infants and children. The Agency's complete risk assessment is found in the propiconazole reregistration docket at *http://www.regulations.gov*, docket identification (ID) number EPA-HQ-OPP-2005-0497.

An updated dietary exposure and risk analysis for the common triazole metabolites 1,2,4-triazole (T), triazolylalanine (TA), triazolylacetic acid (TAA), and triazolylpyruvic acid (TP) was conducted and completed in August 2012, in association with a registration request for the triazole fungicide, propiconazole. Residue data demonstrated that there was no increase in exposure to the common triazole metabolites with the proposed use. The tolerances for cyproconazole in/on peanuts covered by this action are not expected to change the risk of exposure to the triazoles determined in that risk analysis. The document, titled "*Common Triazole Metabolites: Updated Aggregate Human Health Risk Assessment to Address the Amended Propiconazole Section 3 Registration to Add Use on Sugarcane*" may be found in docket ID number EPA-HQ-OPP-2012-0427.

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*. There are no residual uncertainties with regard to prenatal and postnatal toxicity, and the database is complete for purposes of assessing prenatal and postnatal toxicity. There is evidence that cyproconazole is a developmental toxicant; however, the LOC is low since: (1) The effects in fetuses are well-characterized with a clear NOAEL and (2) the developmental toxicity study where increased susceptibility was observed is being used for the acute dietary endpoint (females 13-49 years), which will be protective of effects in infants and children. There is no evidence of reproductive toxicity or neurotoxicity in the cyproconazole database.

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 cyproconazole is complete, except for an immunotoxicity study. As noted in Unit III.A., the concern for the lack of this study is low because there is no evidence that cyproconazole causes immunotoxic effects. EPA does not believe that an immunotoxicity study will result in a lower point of departure (POD) than that which is currently in use for overall risk assessment. As such, a database uncertainty factor is not necessary to account for the lack of an immunotoxicity study.

ii. There is no indication that cyproconazole is a neurotoxic chemical and there is no need for a developmental neurotoxicity study or additional UFs to account for neurotoxicity.

iii. While there is evidence that exposure to cyproconazole results in increased susceptibility in *in utero* rabbits, EPA does not believe that the FQPA safety factor of 10X is necessary to protect infants and children for the reasons stated in Unit III.D.2. above.

iv. There are no residual uncertainties identified in the exposure databases. EPA made conservative (protective) assumptions in the ground water and surface water modeling used to assess exposure to cyproconazole in drinking water. These assessments will not underestimate the exposure and risks posed by cyproconazole.

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 cyproconazole will occupy 32% of the aPAD for females 13-49 years old. The acute dietary exposure and risk analysis was conducted only for females 13-49 years old since an endpoint of concern attributable to a single dose for the general population was not identified.

2. *Chronic risk*. Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that chronic exposure to cyproconazole from food and water will utilize 28% of the cPAD for infants (<1 years old), the population group receiving the greatest exposure. There are no residential uses for cyproconazole.

3. *Short-term risk*. Short-term aggregate exposure is calculated by aggregating short-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). A short-term adverse effect was identified; however, cyproconazole is not currently registered for any use patterns that would result in short-term residential exposure. In consideration of a pending turf use for cyproconazole, a short-term aggregate assessment was completed. The pending golf course use is the only use that may result in residential exposure. The golfer exposure (dermal) represents the highest residential exposure of all potential adult exposure scenarios. Therefore, the short-term assessment is protective of all potential exposures resulting from the pending golf course use. For the short-term aggregate assessment, the short-term oral NOAEL of 1.5 mg/kg/day (from the 90-day oral rat study) is compared to the total (dietary + residential) exposure to calculate risk. Since the aggregate MOEs are greater than 100, the calculated risks do not exceed the Agency's LOCs.

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). There are no residential scenarios that result in intermediate-term exposure; therefore, an intermediate-term aggregate exposure and risk assessment is not required.

5. *Aggregate cancer risk for U.S. population*. Although there was evidence of carcinogenicity found in a mouse study, EPA has determined that cyproconazole is "not likely to be carcinogenic to humans" at doses that do not cause a mitogenic response in the liver (Ref. 1). As a result, an aggregate cancer exposure and risk assessment is not required, as cyproconazole 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 cyproconazole residues.

IV. Other Considerations

A. Analytical Enforcement Methodology

Adequate enforcement methodology (gas chromatograph/nitrogen-phosphorus detection) is available to enforce the tolerance expression. 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. The Codex has not established a MRL for cyproconazole.

C. *Revisions to Petitioned-For Tolerances*

The Agency is correcting the commodity terminology for peanut by establishing a tolerance for peanut, rather than peanut, nutmeat. In addition, the Agency has modified the levels for which tolerances are being established for peanut (0.03 to 0.01 ppm). Based on an analysis of the residue data using the OECD tolerance calculation procedures, the tolerance for peanut is based on the limit of quantitation (0.01 ppm). Following exaggerated-rate applications of cyproconazole, average residues of cyproconazole were below the limit of quantitation in/on peanut, meal, refined oil, and butter; therefore, processing factors could not be calculated. Accordingly, separate tolerances for residues of cyproconazole are not required for peanut, meal, refined oil, and peanut butter.

Also, EPA has revised the tolerance expression for cyproconazole 40 CFR 180.485 to clarify:

1. That as provided in FFDCA section 408(a)(3), the tolerance covers metabolites and degradates of cyproconazole.

2. That compliance with the specified tolerance levels is to be determined by measuring only the specific compounds mentioned in the tolerance expression.

V. Conclusion

Therefore, tolerances are established for residues of cyproconazole, in or on peanut and peanut, hay at 0.01 and 6.0 ppm, respectively.

VI. References

The following is a listing of the documents that are specifically referenced in this rule.

1. J. Kidwell, *et al.*, December 4, 2007. Cyproconazole: Fourth Report of the Cancer Assessment Review Committee PC Code: 128993.

2. Environmental Protection Agency. January 14, 2002. Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity.

VII. Statutory and Executive Order Reviews

This final rule 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 final rule has been exempted from review under Executive Order 12866, this final rule is not subject to Executive Order 13211, entitled "Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use" (66 FR 28355, May 22, 2001) or Executive Order 13045, entitled "Protection of Children from Environmental Health Risks and Safety Risks" (62 FR 19885, April 23, 1997). This final rule 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 final rule 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 final rule. In addition, this final rule does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act of 1995 (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 of 1995 (NTTAA) (15 U.S.C. 272 note).

VIII. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq.*), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This action is not a "major rule" as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: June 11, 2013.

Lois Rossi,

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. Section 180.485 is amended as follows:

a. Revise paragraph (a)(1) introductory text.

b. Add alphabetically the entries "peanut" and "peanut, hay" to the table in paragraph (a)(1).

c. Revise paragraph (a)(2) introductory text.

d. Revise paragraph (a)(3) introductory text.

The amendments read as follows:

§ 180.485 Cyproconazole; tolerances for residues.

(a) * * * (1) Tolerances are established for residues of the free and conjugated forms of the fungicide cyproconazole, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the proposed tolerance levels specified below is to be determined by measuring only cyproconazole (α-(4-chlorophenyl)-α-(1-cyclopropylethyl)-1*H*-1,2,4-triazole-1-ethanol) in or on the following commodities:

Commodity	Parts per million
* *	* * * * *
Peanut	0.01
Peanut, hay	6.0
* *	* * * * *

* * * * *

(2) A tolerance is established for the combined residues of the free and conjugated forms of the fungicide cyproconazole, including its metabolites and degradates, in or on the commodity in the table below. Compliance with the tolerance level specified below is to be determined by measuring only the sum of cyproconazole (α-(4-chlorophenyl)-α-(1-cyclopropylethyl)-1*H*-1,2,4-triazole-1-ethanol) and its metabolite δ-(4-chlorophenyl)-β,δ-dihydroxy-γ-methyl-1*H*-1,2,4-triazole-1-hexenoic acid, calculated as the stoichiometric equivalent of cyproconazole, in or on the following commodity:

* * * * *

(3) Tolerances are established for the combined residues of the free and conjugated forms of the fungicide cyproconazole, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance level specified below is to be determined by measuring only the sum of cyproconazole (α-(4-chlorophenyl)-α-(1-cyclopropylethyl)-1*H*-1,2,4-triazole-1-ethanol) and its metabolite 2-(4-chlorophenyl)-3-cyclopropyl-1-[1,2,4]triazol-1-yl-butane-2,3-diol, calculated as the stoichiometric equivalent of cyproconazole, in or on the following commodities:

* * * * *

[FR Doc. 2013-14914 Filed 06/20/2013 at 8:45 am; Publication Date: 06/21/2013]