BILLING CODE 6560-50-P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2011-0144; FRL-9944-48]

Aminocyclopyrachlor; Pesticide Tolerances

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes tolerances for residues of aminocyclopyrachlor in or on milk and livestock commodities imported into the United States, which are identified and discussed later in this document. E.I. du Pont de Nemours and Company 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-2011-0144, 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: Susan Lewis, 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 Printing Office's e-CFR 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/test-guidelines-pesticides-and-toxic-substances.*

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-2011-0144 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-2011-0144, 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 Tuesday, March 29, 2011 (76 FR 17376) (FRL-8867-4), 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 0F7817) by E.I. du Pont de Nemours and Company, 1007 Market Street, Wilmington, DE 19898. The petition requested that 40 CFR part 180 be amended by establishing tolerances for residues of the herbicide aminocyclopyrachlor, 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid, and aminocyclopyrachlor methyl ester, methyl 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylate, expressed as aminocyclopyrachlor, in or on grass, forage at 65 parts per million (ppm); grass, hay at 125 ppm; fat (of cattle, goat, horse, and sheep) at 0.07 ppm; meat (of cattle, goat, horse, and sheep) at 0.02 ppm; meat byproducts, excluding liver (of cattle, goat, horse, and sheep) at 0.4 ppm; liver (of cattle, goat, horse, and sheep) at 0.06 ppm; and milk at 0.035 ppm. That document referenced a summary of the petition prepared by E.I. du Pont de Nemours and Company, the registrant, which is available in the docket, *http://www.regulations.gov*. There were no comments received in response to the notice of filing.

After issuance of the notice of filing, the registrant revised the petition by rescinding the proposed grass commodities and amending the purpose of establishing tolerances from domestic to import use (i.e. import tolerances).

Based upon review of the data supporting the petition, EPA has lowered the proposed tolerances for milk, meat (of cattle, goat, horse, and sheep), and fat (of cattle, goat, horse, and sheep) and changed the proposed tolerances from liver and meat byproducts, except liver (of cattle, goat, horse, and sheep) to meat byproducts (of cattle, goat, horse, and sheep). 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 aminocyclopyrachlor including exposure resulting from the tolerances established by this action. EPA's assessment of exposures and risks associated with aminocyclopyrachlor 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.

Aminocyclopyrachlor

Aminocyclopyrachlor (parent acid) has low acute toxicity by all routes of exposure (oral, dermal, inhalation), does not cause skin irritation or skin sensitization, but causes mild eye

irritation. There are no target organs of toxicity for aminocyclopyrachlor. In the subchronic oral toxicity studies in rats, mild systemic toxicity effects of decreased body weights, body weight gains, food consumption, and food efficiency in both sexes were observed with repeated exposures at very high (limit) doses. There was no appreciable increase in the severity of these effects with time. The most sensitive species is the rat. Subchronic and chronic dietary studies in dogs and mice showed no adverse effects at all treatment doses including the limit dose. The subchronic dermal toxicity study in rat showed no evidence of toxicity at the limit dose. Subchronic inhalation toxicity studies are not available; however, based on the results of the acute inhalation studies showing low toxicity at twice the limit concentration, the likelihood of subchronic toxicity via inhalation route is expected to be low.

In the prenatal developmental toxicity study, there were no adverse effects of aminocyclopyrachlor on prenatal development or maternal health in rats at all treatment doses including the limit dose. In the rabbit study, administration at the limit dose resulted in one treatment-related death and two abortions which were considered secondary effects to maternal weight losses which occurred over a period of 5 to 7 days. No developmental effects were observed in the offspring. There were no adverse effects of aminocyclopyrachlor on reproduction and fertility in rats at the limit dose. Toxicity in parental rats and offspring was limited to decreases in body weights at the limit dose.

Aminocyclopyrachlor is classified as “Not Likely to be Carcinogenic to Humans.” This classification is based on no treatment-related tumors seen in male or female rats or mice at doses that were adequate to assess carcinogenicity, and no evidence of mutagenicity from a full battery of *in vitro* and *in vivo* genotoxicity studies. There was no evidence of neurotoxicity or immunotoxicity observed in the rodent studies up to the limit dose.

Aminocyclopyrachlor-Methyl

The toxicity database for aminocyclopyrachlor-methyl (ester) via the oral route of exposure is bridged with aminocyclopyrachlor (parent acid) based on evidence from metabolism studies, acute toxicity studies, and repeat-dose toxicity studies with common endpoints. The rat metabolism studies showed that aminocyclopyrachlor-methyl rapidly metabolizes (within 30 minutes) to aminocyclopyrachlor. A full suite of acute toxicity studies conducted with aminocyclopyrachlor and aminocyclopyrachlor-methyl resulted in the same toxicity category classifications. The subchronic oral toxicity study and the modified one-generation reproduction toxicity study in rats conducted with aminocyclopyrachlor-methyl showed effects of decreased body weights and body weight gains at the limit dose similar to those observed in the aminocyclopyrachlor studies. This one-generation reproduction study showed no evidence of reproductive, developmental, or neurotoxicity at the limit dose. There was no evidence of mutagenicity in the *in vitro* bacterial genotoxicity test conducted with aminocyclopyrachlor-methyl. The results of these studies show that aminocyclopyrachlor-methyl causes effects similar to aminocyclopyrachlor at the same dose levels. Therefore, studies conducted with aminocyclopyrachlor can be used to support aminocyclopyrachlor-methyl.

Cyclopropane Carboxylic Acid

Cyclopropane carboxylic acid (CPCA), also known as IN-V0977, is an environmental photolytic degradate of aminocyclopyrachlor present only in surface water. CPCA has a different mode of toxic action than aminocyclopyrachlor and aminocyclopyrachlor-methyl. Based on extensive pre-clinical studies of the anxiolytic drug candidate panadiplon, which metabolizes to CPCA after oral administration, the target organ is the liver, causing impairment of mitochondrial function by inhibiting the beta oxidation of fatty acids, resulting in microvesicular steatosis (accumulation of small fat droplets in cells) that is often accompanied by liver necrosis and inflammation, decreased hepatic glycogen, and decreased blood glucose levels. These

effects were observed with acute (1 to 3 days) and repeated (up to 14 days) exposures. The most sensitive species is the rabbit. Hepatic microvesicular steatosis in the rabbit follows a different dose-response than body-weight decreases observed with aminocyclopyrachlor and aminocyclopyrachlor-methyl in rats, with a 100-fold lower adverse-effect level.

There are no chronic dietary toxicity studies available to assess the carcinogenic potential of CPCA. However, structural-activity relationship (SAR) analyses on CPCA and panadiplon indicated no structural alerts for genotoxicity or carcinogenicity. Also, there were no reports of tumorigenic responses to CPCA or panadiplon in the open scientific literature.

Specific information on the studies received and the nature of the adverse effects caused by aminocyclopyrachlor, aminocyclopyrachlor-methyl, and cyclopropane carboxylic acid, 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 *Aminocyclopyrachlor: Human Health Risk Assessment for Section 3, Food Use on Rangeland/Pastures/CRP Acres* at pages 15-26 in docket ID number EPA-HQ-OPP-2011-0144.

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-science-and-assessing-pesticide-risks/assessing-human-health-risk-pesticides.*

Summaries of the toxicological endpoints for aminocyclopyrachlor and cyclopropane carboxylic acid used for human health risk assessment are shown in Tables 1 and 2 of this unit.

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

Exposure/Scenario	Point of Departure and Uncertainty/Safety Factors	RfD and PAD for Risk Assessment	Study and Toxicological Effects
Acute dietary (All populations)	No hazard attributable to a single-exposure was identified.		
Chronic dietary (All populations)	NOAEL= 279 mg/kg/day UF_A = 10x UF_H = 10x FQPA SF = 1x	Chronic RfD = 2.79 mg/kg/day cPAD = 2.79 mg/kg/day	Combined Chronic Toxicity/Carcinogenicity Rat Study LOAEL = 892 (males)/957 (females) mg/kg/day based on mild decreases in body weight/body weight gain

Table 2.--Summary of Toxicological Doses and Endpoints for Cyclopropane Carboxylic Acid for Use in Human Health Risk Assessment

Exposure/Scenario	Point of Departure and Uncertainty/Safety Factors	RfD and PAD for Risk Assessment	Study and Toxicological Effects
Acute dietary (All populations)	LOAEL= 2.55 mg/kg/day CPCA UF_A = 10x UF_H = 10x FQPA SF (UF_{DB}, UF_L) = 10x	Acute RfD = 0.026 mg/kg/day aPAD = 0.0026 mg/kg/day	Panadiplon Subchronic Oral Rabbit Study LOAEL = 10 mg/kg/day panadiplon (calculated to 2.55 mg/kg/day CPCA) based on hepatic steatosis
Chronic dietary (All populations)	LOAEL= 2.55 mg/kg/day CPCA UF_A = 10x UF_H = 10x FQPA SF (UF_{DB}, UF_L, UF_S) = 30x	Chronic RfD = 0.0087 mg/kg/day cPAD = 0.00087 mg/kg/day	Panadiplon Subchronic Oral Rabbit Study LOAEL = 10 mg/kg/day panadiplon (calculated to 2.55 mg/kg/day CPCA) based on hepatic steatosis

FQPA SF = Food Quality Protection Act Safety Factor. LOAEL = lowest-observed-adverse-effect-level. mg/kg/day = milligram/kilogram/day. 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_{DB} = to account for the absence of data or other data deficiency. UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. UF_S = use of a short-term study for long-term risk assessment.

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* In evaluating dietary exposure to aminocyclopyrachlor, EPA considered exposure under the petitioned-for tolerances only, as there are no registered food/feed uses. CPCA is an environmental photodegradate of aminocyclopyrachlor present only in surface water; therefore, any dietary exposure would be from drinking water only and is not expected through food or feed. EPA assessed dietary exposures from aminocyclopyrachlor 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. No such effects were identified in the toxicological studies for aminocyclopyrachlor; therefore, a quantitative acute dietary exposure assessment was not conducted.

ii. *Chronic exposure*. In conducting the chronic dietary exposure assessment for aminocyclopyrachlor, EPA used food consumption information from the United States Department of Agriculture (USDA) 2003-2008 National Health and Nutrition Examination Survey, What We Eat in America (NHANES/WWEIA).

iii. *Cancer*. Based on the data summarized in Unit III.A., EPA has concluded that aminocyclopyrachlor and CPCA do not pose cancer risks to humans. Therefore, 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 aminocyclopyrachlor. Tolerance-level residues and 100 PCT were assumed for all petitioned-for 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 aminocyclopyrachlor and CPCA in drinking water. These simulation models take into account data on the physical, chemical, and fate/transport characteristics. Further information regarding EPA drinking water models used in pesticide exposure assessment can be found at *http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/ about-water-exposure-models-used-pesticide*.

The importation of milk and livestock commodities containing potential residues of aminocyclopyrachlor will not increase pesticide exposure in U.S. drinking water. Therefore, the

drinking water estimates are based on pesticide exposure from the existing non-food/non-feed uses of aminocyclopyrachlor.

Based on the First Index Reservoir Screening Tool (FIRST) and Pesticide Root Zone Model Ground Water (PRZM-GW) models, the estimated drinking water concentrations (EDWCs) of aminocyclopyrachlor for chronic exposures for non-cancer assessments are estimated to be 18.3 parts per billion (ppb) for surface water, and 78.0 ppb for ground water. The EDWCs of CPCA from surface water are estimated to be 1.7 ppb for acute exposure, and 1.2 ppb for chronic exposures for non-cancer assessments. Ground water EDWCs for CPCA were not calculated since CPCA is a photodegradate of aminocyclopyrachlor and is not anticipated to be present in ground water due to the absence of sunlight.

Modeled estimates of drinking water concentrations were directly entered into the dietary exposure model. For chronic dietary risk assessment to aminocyclopyrachlor, the water concentration value of 78.0 ppb was used to assess the contribution to drinking water. For acute dietary risk assessment to CPCA, the water concentration value of 1.7 ppb was used to assess the contribution to drinking water. For chronic dietary risk assessment to CPCA, the water concentration value of 1.2 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). Aminocyclopyrachlor is not currently registered for any specific use patterns that would result in residential exposure. In the risk assessment, EPA had assessed residential exposure based on previously-registered uses on lawn and turf, including golf courses; however, those residential use patterns are no longer registered, and therefore non-dietary residential exposure does not occur.

4. *Cumulative effects from substances with a common mechanism of toxicity*. Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA has not found aminocyclopyrachlor to share a common mechanism of toxicity with any other substances, and aminocyclopyrachlor does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that aminocyclopyrachlor does not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see EPA's website at *http://www.epa.gov/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*. As discussed in Unit III.A., there was no evidence of prenatal toxicity resulting from exposure to aminocyclopyrachlor. There was no evidence of

increased susceptibility following *in utero* exposure in the rat and rabbit developmental toxicity studies. An increase in abortions in maternal rabbits was observed at the limit dose, but the abortions were considered secondary effects due to severe maternal body weight loss. There was also no evidence of increased susceptibility of offspring in the rat reproduction and fertility studies, with only body weight decreases observed in both maternal rats and offspring at the limit dose.

For CPCA, there were no information available investigating developmental or offspring effects. However, there is indirect evidence in the open literature that the young may be more sensitive to the metabolic effects of CPCA, and this evidence does not allow this potential sensitivity to be ruled out. This evidence is provided by inherited conditions, specifically inborn errors of metabolism that results in compromised metabolism of fatty acids that is qualitatively similar to that of CPCA's effect of inhibition of beta oxidation of fatty acids. These inborn metabolism errors result in energy deficiencies during periods of fasting, and it is known that developing/young children are more sensitive to these effects than pregnant women or adults. The magnitude of this effect would be much more severe in the inherited case than for CPCA. This is because fatty acid oxidation is almost completely compromised in the inherited case and other cellular processes are also impacted, whereas only beta oxidation of fatty acids would be impacted for CPCA, and the magnitude of this impact is anticipated to be negligible for the estimated (low-level) dietary exposures.

3. *Conclusion*. For aminocyclopyrachlor, 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.

For the degradate cyclopropane carboxylic acid, the FQPA SF is retained at 10X for acute dietary exposures, to account for the extrapolation of data from a LOAEL to a NOAEL for hepatic steatosis/necrosis in rabbits, and to account for any potential uncertainties regarding

developmental toxicity effects based on the available data. This SF is considered protective because hepatic steatosis/necrosis and any developmental toxicity effects would be caused by the same cellular mechanism. Therefore, protecting for these liver effects would protect any potential developmental toxicity resulting from very low dietary exposures to CPCA.

For chronic dietary exposures, the FQPA SF is increased from 10X to 30X to account for the use of a short-term (acute) study to assess long-term (chronic) exposure. The additional 3X SF is considered protective since the duration of the acute study was 14 days with the dose administered as a bolus (via gavage). Because the exposure in this study was repeated and a bolus dose was used that would overestimate dietary exposure, the severity of the liver effects are not expected to vary substantially with time.

Those decisions are based on the following findings:

i. The toxicity database for aminocyclopyrachlor is adequate for assessing the sensitivity of infants and children under FQPA and for selecting endpoints for risk assessment.

The database for CPCA is also adequate, as there is a substantial amount of toxicological information available in the open literature that identifies the target organ of toxicity, the mechanism of toxicity, and the most sensitive species. The FQPA SFs account for any residual uncertainties in the toxicity database for CPCA.

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

Based on the mechanism of toxicity for CPCA that has been identified in the open scientific literature, the nervous system is not expected to be more sensitive than the liver. Although there are no studies available that directly investigate the effects of CPCA on the nervous system, there is indirect evidence that the endpoint on which the Agency is regulating CPCA (hepatic steatosis/necrosis) is protective of the nervous system. First, the molecular

mechanism underlying hepatic steatosis has been identified as inhibition of the metabolic pathway of beta oxidation of fatty acids in the mitochondria. This is a major, energy producing pathway in liver but not in the brain. Since the ketone bodies generated by this process in the liver are metabolized by the brain for energy, any brain effects from inhibition of this pathway would be secondary to liver effects. Second, CPCA is a metabolite of panadiplon, a drug that was developed to target the nervous system as an anxiolytic. Panadiplon failed in preclinical development not as a result of neurotoxicity, but as a result of liver toxicity that was caused by CPCA. This further supports that adverse effects on the liver is more sensitive than the brain. Since the endpoint chosen for risk assessment is protective for liver effects, it is therefore also protective for any primary or secondary neurotoxicity that may result from CPCA exposure.

iii. There is no evidence that aminocyclopyrachlor results in increased susceptibility in *in utero* rats or rabbits in the prenatal developmental studies or in young rats in the 2-generation reproduction study. In the rabbit prenatal developmental study, an increase in abortions was observed at the limit dose, which were considered secondary effects to severe decreases in maternal body weight.

As discussed in Unit III.D.2., there is no information available that directly investigates the developmental effects of CPCA. However, based on the known information, the magnitude of the potential impact of CPCA exposure on the inhibition of beta oxidation of fatty acids is anticipated to be negligible for the estimated dietary exposure, and less than the non-CPCA-related effects resulting from inborn metabolic errors which compromises the metabolism of fatty acids and other cellular processes.

iv. There are no residual uncertainties identified in the exposure databases. The dietary food exposure assessments were performed based on 100 PCT and tolerance-level residues. EPA made conservative (protective) assumptions in the ground and surface water modeling used to

assess exposure to aminocyclopyrachlor and CPCA in drinking water. These assessments will not underestimate the exposure and risks posed by aminocyclopyrachlor and CPCA.

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.* An acute aggregate risk assessment takes into account acute exposure estimates from dietary consumption of food and drinking water. For aminocyclopyrachlor, no adverse effect resulting from a single oral exposure was identified and no acute dietary endpoint was selected. Therefore, aminocyclopyrachlor is not expected to pose an acute risk.

For CPCA, using the exposure assumptions discussed in this unit for acute exposure, the acute dietary exposure from drinking water only will occupy 11% of the aPAD for all infants less than 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 will utilize <1% of the cPAD for aminocyclopyrachlor (from food and water) and 7.4% of the cPAD for CPCA (from water only) for all infants less than 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 aminocyclopyrachlor and CPCA is not expected.

3. *Short- and Intermediate-term risks.* Short- and intermediate-term aggregate exposures take into account short- and intermediate-term residential exposures plus chronic exposure to food and water (considered to be a background exposure level).

Short- and intermediate-term adverse effects were identified; however, aminocyclopyrachlor is no longer registered for any use patterns that would result in residential exposure. Short- and intermediate-term risks are assessed based on short-term/intermediate-term residential exposure plus chronic dietary exposure. Because there is no 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-/intermediate-term risk), no further assessment of short- and intermediate-term risks are necessary, and EPA relies on the chronic dietary risk assessments for evaluating short- and intermediate-term risks for aminocyclopyrachlor and CPCA.

4. *Aggregate cancer risk for U.S. population*. Based on the lack of evidence of carcinogenicity in two adequate rodent carcinogenicity studies, aminocyclopyrachlor is not expected to pose a cancer risk to humans. As discussed in Unit III.A., CPCA is also not expected to pose a cancer risk to humans.

5. *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 aminocyclopyrachlor and CPCA residues.

IV. Other Considerations

A. Analytical Enforcement Methodology

Adequate enforcement methodology ([DuPont-27162, Revision No. 1; high-performance liquid chromatography with tandem mass spectrometry detection (HPLC/MS/MS)) 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). Codex is a joint United Nations Food and Agriculture Organization/World Health Organization food standards program, and it is recognized as an international food safety standards-setting organization in trade agreements to which the United States is a party. EPA may establish a tolerance that is different from a Codex MRL; however, FFDCA section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level.

The Codex has not established any MRLs for aminocyclopyrachlor.

C. Revisions to Petitioned-For Tolerances

Based on the available residue chemistry data and EPA policy on livestock tolerances, the proposed tolerances for liver (0.06 ppm) and meat byproducts except liver (0.40 ppm) of cattle, goat, horse, and sheep are replaced by establishing tolerances for meat byproducts of cattle, goat, horse, and sheep at 0.30 ppm. Also, based on the residue data, EPA is lowering the proposed tolerances for fat of cattle, horse, goat, and sheep from 0.07 ppm to 0.05 ppm. Lastly, EPA is also lowering the proposed tolerances for milk from 0.035 ppm to 0.01 ppm, and meat of

cattle, goat, horse, and sheep from 0.02 ppm to 0.01 ppm to harmonize with established Canadian MRLs.

V. Conclusion

Therefore, tolerances are established for residues of the herbicide aminocyclopyrachlor, 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid, including its metabolites and degradates, in or on cattle, fat at 0.05 ppm; cattle, meat at 0.01 ppm; cattle, meat byproducts at 0.30 ppm; goat, fat at 0.05 ppm; goat, meat at 0.01 ppm; goat, meat byproducts at 0.30 ppm; horse, fat at 0.05 ppm; horse, meat at 0.01 ppm; horse, meat byproducts at 0.30 ppm; milk at 0.01 ppm; sheep, fat at 0.05 ppm; sheep, meat at 0.01 ppm; and sheep, meat byproducts at 0.30 ppm.

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). 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: July 28, 2016.

Jack E. Housenger,
Director, 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. Add § 180.689 to subpart C to read as follows:

§ 180.689 Aminocyclopyrachlor; tolerances for residues.

(a) *General*. Tolerances are established for residues of the herbicide aminocyclopyrachlor, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of aminocyclopyrachlor, 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid, and aminocyclopyrachlor methyl ester, methyl 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylate, calculated as the stoichiometric equivalent of aminocyclopyrachlor.

Commodity	Parts per million
Cattle, fat[1]	0.05
Cattle, meat[1]	0.01
Cattle, meat byproducts[1]	0.30
Goat, fat[1]	0.05
Goat, meat[1]	0.01
Goat, meat byproducts[1]	0.30
Horse, fat[1]	0.05
Horse, meat[1]	0.01
Horse, meat byproducts[1]	0.30
Milk[1]	0.01
Sheep, fat[1]	0.05
Sheep, meat[1]	0.01
Sheep, meat byproducts[1]	0.30

[1]There are no U.S. registrations as of [*insert date of publication in the* **Federal Register**].

(b) *Section 18 emergency exemptions.* [Reserved]

(c) *Tolerances with regional registrations.* [Reserved]

(d) *Indirect or inadvertent residues.* [Reserved]

[FR Doc. 2016-19117 Filed: 8/10/2016 8:45 am; Publication Date: 8/11/2016]