UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM

Date: 18-April-2012

SUBJECT: Aminocyclopyrachlor. Petition for Tolerances in Support of New Uses on Grasses (PP#0F7817). Summary of Analytical Chemistry and Residue Data.

PC Code: 288008
Decision No.: 443546
Petition No.: 0F7817

DP Barcode: D387442
Registration Nos.: 352-787, 352-786, 352-785
Regulatory Action: Amended Section 3 Registration

Risk Assessment Type: N/A
TXR No.: N/A
MRID No.: See MRID Summary Table

Case No.: NA
CAS No.: 858956-08-8
40 CFR: §180.###

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Note: This document was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted 5/25/11). The document has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

MRID Summary Table		
MRID No.	**Study Type**	**Comments**
48333617	860.1300 Grass	New DER; 48333617.DER See also: 48333620.DER (radiovalidation)
48333618	860.1300 Goat	New DER; 48333618.DER
48333620	860.1340 Grass forage and hay	New DER; 48333620.DER
48333621	860.1340 Grass forage and hay	
48333625	860.1340 ILV Grass hay	
48333626	860.1340 ILV Grass hay	
48333622	860.1340 Cattle commodities	New DER; 48333622.DER
48333623	860.1340 Livestock commodities	
48333627	860.1340 ILV Cattle commodities	
48333624	860.1360 Multiresidue Methods	New DER; 48333624.DER
48333628	860.1380 Grass	New DER 48333628.DER
48333629		
48363401	860.1380 Milk, eggs, and bovine tissue	New DER; 48363401.DE2
	860.1480 Cattle commodities	New DER; 48363401.DE1
48333630	860.1500 Grass forage and hay	New DER; 48333630.DER
48333619	860.1850 Confined rotational crops	New DER; 48333619.DER

Executive Summary

Aminocyclopyrachlor [6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid] is a new herbicide belonging to the pyrimidine carboxylic acid chemical class. The mode of action is dysregulation of gene products involved in auxin receptor activity, which interferes with normal shoot and root development to stop the growth of weeds. Aminocyclopyrachlor is currently registered for non-crop use for general control of broadleaf weeds and woody species on private, public, and military lands. Three forms of aminocyclopyrachlor are currently registered: the parent acid aminocyclopyrachlor (DPX-MAT28; PC code 288008), the potassium salt (PC Code 288010), and the methyl ester (DPX-KJM44; aminocyclopyrachlor-methyl; PC code 288009). This petition (PP#0F7817) is the first food/feed use request for aminocyclopyrachlor.

Under PP#0F7817, DuPont Crop Protection has requested the establishment of tolerances for the herbicide aminocyclopyrachlor, to be determined by measuring only the sum of aminocyclopyrachlor and aminocyclopyrachlor methyl ester, methyl 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylate, calculated as the stoichiometric equivalent of aminocyclopyrachlor in/on the following commodities:

Cattle, fat	0.07 ppm
Cattle, liver	0.06 ppm
Cattle, meat	0.02 ppm
Cattle, meat byproducts, except liver	0.4 ppm
Goat, fat	0.07 ppm
Goat, liver	0.06 ppm
Goat, meat	0.02 ppm
Goat, meat byproducts, except liver	0.4 ppm
Grass, forage	65 ppm
Grass, hay	125 ppm
Horse, fat	0.07 ppm
Horse, liver	0.06 ppm
Horse, meat	0.02 ppm
Horse, meat byproducts, except liver	0.4 ppm
Milk	0.03 ppm
Sheep, fat	0.07 ppm
Sheep, liver	0.06 ppm
Sheep, meat	0.02 ppm
Sheep, meat byproducts, except liver	0.4 ppm

In conjunction with the proposed tolerances, DuPont has submitted a request for amended registration of the 50% dry flowable (i.e., water dispersible granule; WG) formulation of aminocyclopyrachlor (EPA Reg. No. 352-787), the 2 lb a.i./gal soluble liquid (SL) formulation of the potassium salt (K salt; EPA Reg. No. 352-786, equivalent to 2 lb ae/gal aminocyclopyrachlor), and the 80% WG formulation of aminocyclopyrachlor-methyl (EPA Reg. No. 352-785, equivalent to 75% ae aminocyclopyrachlor) for use on pasture and rangeland grasses. Aminocyclopyrachlor is proposed for up to two foliar applications to pasture and

rangeland grasses at 0.038-0.172 lb ai/A/application for a maximum seasonal rate of 0.281 lb ai/A, with a 0-day preharvest interval (PHI) for grass forage and hay.

The nature of the residue in grasses is adequately based on an acceptable grass metabolism study reflecting application of aminocyclopyrachlor-methyl. Aminocyclopyrachlor and aminocyclopyrachlor-methyl were the major identified residues in grass. The data indicate that aminocyclopyrachlor-methyl is rapidly metabolized (demethylated) in grass to form the free acid aminocyclopyrachlor, which is subsequently decarboxylated to form the metabolite IN-LXT69. Photo-induced simultaneous elimination of hydrogen chloride and pyrimidine ring contraction (occurring as a minor pathway) yields the imidazole-nitrile metabolite, IN-QGC48, which undergoes demethylation to form IN-QFH57; IN-QFH57 may also be formed through photolysis of aminocyclopyrachlor. An additional minor pathway involves pyrimidine ring opening proceeding through the postulated intermediate IN-YY905, with subsequent oxidations to form the amide and carboxylic acid compounds, IN-Q3007 and IN-V0977, respectively. HED has concluded that the residues of concern for tolerance enforcement and risk assessment in grass are aminocyclopyrachlor and aminocyclopyrachlor-methyl. Additional metabolism studies may be needed to support future uses on additional crops.

The nature of the residue in ruminants is adequately understood based on an acceptable goat metabolism study reflecting dosing with aminocyclopyrachlor-methyl. Aminocyclopyrachlor was the only identified residue in goat milk and tissues. The data indicate that aminocyclopyrachlor-methyl is rapidly metabolized in the goat and is eliminated as aminocyclopyrachlor primarily in the excreta. HED has concluded that the residues of concern for tolerance enforcement and risk assessment in livestock are aminocyclopyrachlor and aminocyclopyrachlor-methyl. Because grass is not a significant feed stuff for poultry, a hen metabolism study is not required at this time; however, a hen metabolism study may be needed to support future uses on additional crops.

The petitioner has proposed high performance liquid chromatography methods with tandem mass spectrometry detection (HPLC/MS/MS) for enforcement of tolerances for aminocyclopyrachlor on grass commodities, DuPont-22582 SU1 RV2, and livestock commodities, DuPont-27162, Revision No. 1. The methods adequately determine residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl as well as the metabolites IN-LXT69 and INQFH57 and IN-QGC48 (grass commodities only), in/on grass forage and hay, milk, eggs, and bovine tissues. The validated limit of quantitation (LOQ) is 0.01 ppm for each analyte. HED has concluded that the plant and livestock method are adequate for enforcement purposes.HED has determined that laboratory tolerance method validation (TMVs) are not needed for the proposed enforcement methods for plant and livestock commodities. The proposed enforcement methods or earlier versions of the methods were used for data collection in the submitted storage stability, cattle feeding, and grass crop field trial studies.

Acceptable multiresidue methods test data have been submitted for aminocyclopyrachlor and aminocyclopyrachlor-methyl. The data indicate that multiresidue methods may be appropriate for determination of aminocyclopyrachlor-methyl but are not suitable for determination of aminocyclopyrachlor or for determination of the two analytes together. The submitted data will be forwarded to the U.S. Food and Drug Administration (FDA) for further evaluation.

Adequate storage stability data have been submitted for residues of aminocyclopyrachlor, aminocyclopyrachlor-methyl and metabolite IN-LXT69 in grass and livestock commodities and for metabolites INQFH57 and IN-QGC48 in grass commodities. No additional storage stability data are required to support the submitted grass crop field trial study or the cattle feeding study.

An acceptable cattle feeding study has been submitted reflecting dosing of lactating dairy cows with aminocyclopyrachlor-methyl at 73.3, 160, 455, and 1595 ppm in the diet. Samples of milk, skim milk, cream, and tissues were analyzed for residues of aminocyclopyrachlor, aminocyclopyrachlor-methyl, and metabolite IN-LXT69. The data indicate that tolerances are needed for milk and ruminant commodities. The data will support the following tolerances for combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl (expressed in parent equivalents): of 0.02 ppm for milk, and 0.30 ppm for the meat byproducts, 0.05 ppm for the fat, and 0.02 ppm for the muscle of cattle, goat, horse, and sheep.

Adequate field trial data have been submitted reflecting application of products containing aminocyclopyrachlor-methyl and aminocyclopyrachlor to grasses. Samples of grass forage and hay were analyzed for residues of aminocyclopyrachlor, aminocyclopyrachlor-methyl, and metabolites IN-LXT69, INQFH57, and IN-QGC48. The data indicate that the proposed tolerances are too low. Based on these data and the OECD tolerance calculator, HED concludes that the following tolerances for combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl (expressed in parent equivalents) are appropriate: 80 ppm for grass forage and 200 ppm for grass hay.

An adequate confined rotational crop study has been submitted. The data indicate that the metabolism of aminocyclopyrachlor in rotated crops is similar to that in primary crops. HED has concluded that the residues of concern for the tolerance expression in rotational crops are aminocyclopyrachlor and aminocyclopyrachlor-methyl. Aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 were identified in rotational crop commodities. Because residues of aminocyclopyrachlor accumulated above 0.01 ppm in turnip tops and corn forage, stover, and grain at a 300-day plantback interval (PBI), limited field rotational crop data are now required to support the proposed use on grasses. Pending submission of the required limited field rotational crop trials, the labels must be revised to prohibit rotation to any crop other than grasses following application of aminocyclopyrachlor or aminocyclopyrachlor-methyl.

There are no established or proposed Codex or Canadian maximum residue limits (MRLs) for aminocyclopyrachlor in or on any food or feed crops; therefore, there are no harmonization issues.

Regulatory Recommendations and Residue Chemistry Deficiencies

HED has examined the residue chemistry database for aminocyclopyrachlor. Pending submission of a revised Section B and a revised Section F (see requirements below), there are no residue chemistry issues that would preclude granting conditional registration for the requested uses of aminocyclopyrachlor on pasture and rangeland grasses or establishment of tolerances for residues of aminocyclopyrachlor in/on the following commodities as follow:

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.

Cattle, fat	0.05 ppm
Cattle, meat byproducts	0.30 ppm
Cattle, meat	0.02 ppm
Goat, fat	0.05 ppm
Goat, meat byproducts	0.30 ppm
Goat, meat	0.02 ppm
Grass, forage	80 ppm
Grass, hay	200 ppm
Horse, fat	0.05 ppm
Horse, meat byproducts	0.30 ppm
Horse, meat	0.02 ppm
Milk	0.02 ppm
Sheep, fat	0.05 ppm
Sheep, meat byproducts	0.30 ppm
Sheep, meat	0.02 ppm

A human health risk assessment is forthcoming.

860.1200 Directions for Use

- Pending submission and review of the required limited field rotational crop trials, the labels must be revised to prohibit rotation to any crop other than grasses following application of aminocyclopyrachlor or aminocyclopyrachlor-methyl.

860.1550 Proposed Tolerances

- The proposed tolerances for grass forage and hay must be increased to 80 and 200 ppm, respectively.
- The proposed tolerance for milk must be reduced to 0.02 ppm.
- The proposed tolerances for liver and the meat byproducts, except liver, for cattle, horse, goat, and sheep must be replaced with the recommended tolerances for meat byproducts, as specified in Table 9.

860.1650 Submittal of Analytical Reference Standards

- An analytical reference standard for aminocyclopyrachlor-methyl must be supplied and supplies replenished as requested by the Repository.

HED recommends that conversion to unconditional registration for the requested uses may be considered when the following minor deficiencies have been resolved.

860.1900 Field Accumulation in Rotational Crops

- A limited field accumulation in rotational crops study needs to be submitted.

Background

The chemical structure and nomenclature of aminocyclopyrachlor, aminocyclopyrachlor-methyl, and the potassium salt are summarized in Tables 1.1-1.3, and the physicochemical properties of aminocyclopyrachlor and its methyl ester are summarized in Table 2. The chemical names and structures of the residues of concern are presented in Appendix I.

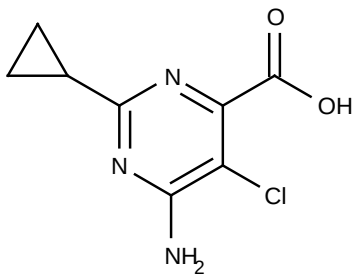
Table 1.1. Test Compound Nomenclature-Aminocyclopyrachlor	
Chemical Structure	
Common Name	Aminocyclopyrachlor (parent acid)
Company Experimental Name	DPX-MAT28
IUPAC Name	6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid
CAS Name	6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid
CAS Registry Number	858956-08-8
End-use product (EP)	50% WG (DuPont Method™ 50 SG; EPA Reg. No. 352-787)

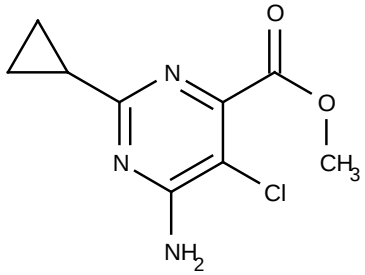
Table 1.2 Test Compound Nomenclature-Aminocyclopyrachlor-methyl (methyl ester)	
Chemical Structure	
Common Name	Aminocyclopyrachlor-methyl
Company experimental Name	DPX-KJM44

Table 1.2 Test Compound Nomenclature-Aminocyclopyrachlor-methyl (methyl ester)	
IUPAC Name	methyl 6-amino-5-chloro-2-cyclopropylpyrimidine-4-carboxylate
CAS Name	methyl 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylate
CAS Registry Number	858954-83-3
End-use product (EP)	80% WG (DuPont DPX-KJM44 80XP; EPA Reg. No. 352-785; equivalent to 75% ae aminocyclopyrachlor)

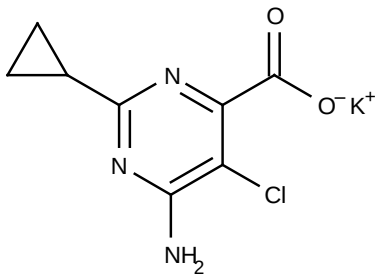
Table 1.3. Test Compound Nomenclature-Aminocyclopyrachlor (potassium salt)	
Chemical Structure	
Empirical Formula	$C_8H_7ClKN_3O_2$
Common Name	Aminocyclopyrachlor potassium salt
Company Experimental Name	DPX-MAT28 potassium salt
IUPAC Name	potassium 6-amino-5-chloro-2-cyclopropylpyrimidine-4-carboxylate
CAS Name	potassium 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylate
CAS Registry Number	858956-35-1
End-use product (EP)	2 lb/gal SL (DuPont Method™ 240 SL; EPA Reg. No. 352-786; equivalent to 2 lb ae/gal aminocyclopyrachlor)

Table 2. Physiochemical Properties of Aminocyclopyrachlor		
Parameter	Value	Reference
Aminocyclopyrachlor (DPX-MAT28)		
Melting point	140.8ºC	DP# 369057, J. Ryman et al., 3/17/10
pH (20.1°C)	3.34	
Density (20°C)	1.34 g/mL	
Water solubility (20°C)	3.13 g/L (pH 4) 4.20 g/L (pH 7) 3.87 g/L (pH 9)	
Vapor pressure	6.92 x10^{-6} Pa (20°C) 4.91 x10^{-6} Pa (25°C)	

Table 2. Physiochemical Properties of Aminocyclopyrachlor		
Parameter	Value	Reference
Dissociation constant (20°C)	4.65	
Octanol/water partition coefficient (log_{10}) at 20°C	-1.01 (pH 4) -2.48 (pH 7) 1.07 (mili-Q water)	
UV/visible absorption spectrum	pH/nm 1.8/220 7.0/285, 240, 210 10.5/280, 240, 210	
Aminocyclopyrachlor-methyl (DPX-KJM44)		
Melting point	148.9ºC	DP# 369057, J. Ryman et al., 3/17/10
pH (20.1°C)	6.16	
Density (20°C)	1.44 g/mL	
Water solubility (20°C)	0.354 g/L	
Vapor pressure	4.19 $x10^{-4}$ Pa (20°C) 4.45 $x10^{-4}$ Pa (25°C)	
Dissociation constant (20°C)	Not applicable	
Octanol/water partition coefficient (log_{10}) at 20°C	1.87	
UV/visible absorption spectrum	pH/nm 1.8/300, 220 7.0/300, 235, 205 10.5/285, 235	

860.1200 Directions for Use

DuPont has submitted draft amended labels for the 50% WG formulation (EPA Reg. No. 352-787), the 2 lb/gal SL formulation (EPA Reg. No. 352-786) of the K salt, and the 80% WG formulation (EPA Reg. No. 352-786) of aminocyclopyrachlor-methyl. A summary of the proposed use pattern is presented in Table 3.

Table 3. Summary of Directions for Use of Aminocyclopyrachlor.

Applic. Timing, Type, and Equip.[1]	Formulation [EPA Reg. No.]	Applic. Rate[2] (lb ai/A)	Max. No. Applic. per Season[2]	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Pasture (including grass grown for hay) and Rangeland Grasses						
Foliar, Broadcast, Ground (min. 10 gal/A) or aerial (min. 2 gal/A)	50% WG [352-787] 2 lb/gal SL of the K salt[3] [352-786] 80% WG of aminocyclopyrachlor-methyl[4] [352-785]	0.038-0.172	2	0.281	0 (forage and hay)	Apply to new plantings when the majority of grasses are in the 3- to 4-leaf stage or to perennial native grasses and pasture grasses established for at least one growing season. A 30-day treatment interval is specified. Use of a spray adjuvant (nonionic surfactant or crop oil concentrate) is specified. Minimum spray volume of 10 gal/A for ground applications and 2 gal/A for aerial applications.

[1] Do not apply through any type of irrigation system; a 12-hour reentry interval is specified.
[2] Rates expressed in terms of the aminocyclopyrachlor ai. Based on calculations, individual maximum application rates are 0.166 lb ai/A for the 50% WG, 0.172 lb ai/A for the 2 lb/gal K SL, and 0.164 lb ai/A for the 80% WG formulation.
[3] Equivalent to 2 lb ae/gal aminocyclopyrachlor.
[4] Equivalent to 75% ae/gal aminocyclopyrachlor.

The labels state that a nonionic surfactant (NIS) is the preferred adjuvant, to be included at 0.06-0.50% v/v; crop oil concentrates (COCs), including petroleum or modified seed oil (MSO) may be used at up to 0.5% v/v for MSOs or at 1-2% v/v for all others.

The products may be tank mixed with other herbicides, insecticides, and fungicides that are registered for the same use sites, methods of application, and timings. When tank mixing, the most restrictive label limitations of the products being used are to be followed; use of a spray adjuvant is specified for postemergence applications.

The following rotational crop restrictions are specified: a 4-month PBI is specified for grasses (over-seeding or renovation); and a 1-year PBI is specified for all other crops. Forage legumes may be seeded after a soil bioassay has been conducted verifying that the level of aminocyclopyrachlor in the soil will not adversely effect the new crop.

Conclusions. The submitted use directions are sufficient to allow for evaluation of the available residue data relative to the proposed use. The submitted field trial data for grass reflect the maximum proposed use rate and the minimum PHI and support the use of spray adjuvants for applications to grasses.

The results of the confined rotational crop study indicate that limited rotational crop studies are required to establish PBIs and/or tolerances for rotated crops. Pending submission of the required limited field rotational crop trials, the labels must be revised to prohibit rotation to any

crop other than grasses following application of aminocyclopyrachlor or aminocyclopyrachlor-methyl.

860.1300 Nature of the Residue - Plants

DER Reference: 48333617.DER

E. I. du Pont de Nemours and Company has submitted a study investigating the metabolism of [2-pyrimidinyl-^{14}C]aminocyclopyrachlor-methyl (specific activity 1.64 MBq/mg) following a single foliar application to grass. Aminocyclopyrachlor-methyl (DPX-KJM44) is the methyl ester of aminocyclopyrachlor (DPX-MAT28). The radiolabeled test substance was formulated as a 25% wettable powder (WP) and applied at a nominal rate of 0.333 lb ai/A (373 g ai/ha), equivalent to 0.312 lb ae/A (350 g ae/ha) aminocyclopyrachlor. The application rate corresponds to 1.1x the maximum seasonal application rate for grass. Grass foliage samples were harvested immediately following application (0 days), and 3, 7, 14, 30, and 60 days after application (DAA), and were subjected to an acetonitrile (ACN) surface wash prior to storage. The in-life and analytical phases of the study were conducted by Charles River Laboratories (Tranent, Edinburgh, UK).

Total radioactive residues (TRR) in grass were determined by summing radioactivity in surface washes, extracts, and nonextractable residues. TRR were 15.6, 15.4, 12.0, 5.94, 4.08, and 2.45 ppm in grass foliage harvested 0, 3, 7, 14, 30, and 60 DAA.

The TRR removed by the ACN surface wash declined from 13% TRR (2.03 ppm) at 0 DAA to 1.2% TRR (0.030 ppm) at 60 DAA. Extraction with ACN:formic acid (8:2, v:v) released the majority of radioactivity from all but the 60-DAA grass samples: extractable residues decreased from 76.6% TRR (12.0 ppm) at 0 DAA to 35.4% TRR (0.866 ppm) at 60 DAA. Subsequent extraction with ACN:formic acid (1:1, v:v) removed 8.3-12.0% TRR (1.28- 0.715 ppm).

Nonextractable residues remaining following extraction increased with harvest interval, from 1.8% TRR (0.280 ppm) at 0 DAA to 51.7% TRR (1.27 ppm) at 60 DAA. The 0, 7, and 60 DAA nonextractable residues were subjected to enzyme, base, and acid hydrolysis. Enzyme hydrolysis with α-amylase (50 ^{o}C for 72 hours) followed by a mixture of amyloglucosidase and cellulase (50 ^{o}C for 48 hours) released, respectively, 0.7% and 0.3% TRR from the 0-DAA sample, 1.5% and 1.0% TRR from the 7-DAA sample, and 14.0% and 6.3% TRR from the 60-DAA sample. Base (0.1 N NaOH; 60 ^{o}C for 6 hours) and acid (1 M HCl; 60 ^{o}C for 6 hours) hydrolysis each released 0.1% TRR from the 0-DAA sample and 0.4% TRR from the 7-DAA sample, and released 4.8% and 3.4% TRR, respectively, from 60-DAA sample. The nonextractable residues remaining following extraction and hydrolysis accounted for 0.6% TRR (0.102 ppm) in 0-DAA, 4.7% TRR (0.553 ppm) in 7-DAA, and 23.4% TRR (0.572 ppm) in 60-DAA samples.

These procedures adequately extracted the majority of residues from grass collected at all harvest intervals with the exception of 60 DAA. With respect to the 60-DAA sample, HED notes that 20% TRR was attributed to loss during analysis associated primarily with solid-phase extraction (SPE) cleanup; therefore, further characterization procedures (e.g., strong acid or base hydrolysis) are unlikely to yield further elucidation of the metabolite profile. Extraction results

were normalized; therefore, accountabilities were 100%. Residues were initially identified and quantitated by high performance liquid chromatography (HPLC); identification of aminocyclopyrachlor-methyl and major metabolites was confirmed by liquid chromatography/mass spectroscopy (LC/MS).

Samples were stored frozen for up to 4.5 months prior to completion of initial analysis. A 60-DAA sample was re-extracted and analyzed at the end of the study following storage at -20 °C for 13 months to confirm the stability of the metabolite profile.

Aminocyclopyrachlor-methyl was identified in grass from all harvest intervals; residues declined from 24.7% TRR (3.86 ppm) at 0 DAA to 8.6% TRR (0.211 ppm) at 60 DAA. aminocyclopyrachlor was the major identified residue in grass samples at all harvest intervals, accounting for 32.9-67.7% TRR (0.805-10.5 ppm). Several minor metabolites were identified, including IN-LXT69, IN-QFH57, IN-QGC48, IN-Q3007, and IN-V0977. IN-LXT69 was identified at all sampling intervals, accounting for 4.2-6.1% TRR (0.138- 0.769 ppm); the remaining metabolites were each present at ≤ 4.1% TRR.

Radiovalidation data were submitted for the extraction procedure of the proposed residue analytical enforcement method, DuPont-22582 and are discussed under 860.1340 Residue Analytical Methods.

Based on the results of the study, the petitioner concluded that aminocyclopyrachlor-methyl is rapidly metabolized (demethylated) in grass to form the free acid aminocyclopyrachlor, which is subsequently decarboxylated to form IN-LXT69. Photo-induced simultaneous elimination of hydrogen chloride and pyrimidine ring contraction (occurring as a minor pathway) yields the imidazole-nitrile metabolite, IN-QGC48, which undergoes demethylation to form IN-QFH57; IN-QFH57 may also be formed through photolysis of aminocyclopyrachlor. An additional minor pathway involves pyrimidine ring opening proceeding through the postulated intermediate IN-YY905, with subsequent oxidations to form the amide and carboxylic acid compounds, IN-Q3007 and IN-V0977, respectively. Chemical structures are shown in Appendix 1.

Conclusions. The submitted grass metabolism study is adequate to satisfy data requirements. Based on the submitted data, HED concludes that the nature of the residue in grass is adequately understood for purposes of this petition. The residues of concern for tolerance enforcement and risk assessment are aminocyclopyrachlor and aminocyclopyrachlor-methyl (expressed in parent equivalents). Additional metabolism studies may be needed to support future uses on additional crops.

860.1300 Nature of the Residue - Livestock

DER Reference: 48333618.DER

Ruminants

E. I. du Pont de Nemours and Company has submitted a study investigating the metabolism of [2-pyrimidinyl-^{14}C]aminocyclopyrachlor-methyl (DPX-KJM44) in the lactating goat (specific activity 1.64 Bq/mg). The test substance was administered orally twice daily via gelatin capsule to one goat at a nominal 75 ppm in the diet for 5 consecutive days. Based on feed consumption, actual mean dose level was 91ppm (parent acid equivalents) (1x the dietary burden to cattle). Milk was collected twice daily throughout the study, before each dosing; tissues, including muscle (composite of loin, hind, and fore quarter), fat (omental, renal, and subcutaneous), liver, and kidney were collected at sacrifice, approximately 6 hours after the final dose. The in-life and analytical phases of the study were conducted by Charles River Laboratories (Edinburgh, UK).

Following oral dosing at 97.3 ppm for 5 consecutive days, TRR were 0.015-0.031 ppm in milk, 0.299 ppm in liver, 1.673 ppm in kidney, 0.042 ppm in muscle, 0.01 ppm in omental fat, 0.016 ppm in renal fat, and 0.026 ppm in subcutaneous fat. Centrifugation of milk into skim milk and cream demonstrated that the majority of radioactive residues were present in the cream fraction. Radioactive concentrations in cream and skim milk were 0.118 and 0.016 ppm, respectively. Radioactivity was highest in kidney and lowest in fat. Radioactivity in milk appeared to plateau by Day 3. Most of the administered dose was excreted (~77%), with 20.02% in the feces, 54.07% in urine, and 3.14% in cage wash.

Extraction with 0.1% formic acid in ACN/water (tissues) or acetone (milk) released the majority of the radioactivity from all goat matrices, except omental fat: 86.7% TRR from liver, 98.3% TRR from kidney, 87.5% TRR from muscle, 80.5% TRR from milk, 83.8% TRR from renal fat, and 80.7% TRR from subcutaneous fat. Only 47.5% TRR was released in omental fat. Initial extraction of cream with hexane and acetone released 11.36% TRR in the acetone fraction and 84.96% TRR in the hexane fraction. The liver and kidney samples required SPE clean-up prior to HPLC analysis to provide reproducible chromatographic profiles. Efforts to improve low recoveries resulting from SPE clean-up impaired the quality of the chromatography, resulting in a significant loss of radioactive residues in the extracts; residues in the extracts after SPE cleanup were 57.40% TRR in liver and 55.26% TRR in kidney. Nonextractable residues were not investigated further in muscle, milk, renal fat, subcutaneous fat, or omental fat; remaining nonextractable residues were 12.5% TRR (0.005 ppm), 19.5% TRR (0.004 ppm), 16.2% TRR (0.003 ppm), 19.3% TRR (0.005 ppm), and 52.6% TRR (0.005 ppm), respectively. Nonextractable residues of liver and kidney were subjected to sequential pepsin and protease enzyme hydrolysis which released 10.1% TRR and 1.5% TRR in liver, respectively, and 0.9% TRR and 0.12% TRR in kidney, respectively. Nonextractable residues remaining were 1.7% TRR (0.006 ppm) in liver and 0.68% TRR (0.011 ppm) in kidney. These procedures adequately extracted the majority of the residues from goat matrices. Results were normalized, thus accountabilities were 100% in all goat matrices.

Residues were initially identified and quantitated by HPLC. Identification of the parent acid, aminocyclopyrachlor, was confirmed in liver and kidney extracts prior to SPE clean-up by TLC

co-chromatography and in kidney extracts after SPE clean-up by LC/MS/MS. Liver, kidney, muscle, and fat (renal and subcutaneous) were stored frozen for a maximum of 3.3 months prior to HPLC analysis. Omental fat and milk samples were initially extracted within 2.1 months of sample collection and analyzed within 8.4 months of sample collection; milk was subsequently re-extracted and analyzed within 10.7 months of sample collection. The petitioner demonstrated that the metabolic profile in liver and kidney is relatively stable for 11 months. No additional storage stability data are required for omental fat because the TRR level was below the threshold concentration requiring metabolite identification. Storage stability data for liver will be translated to milk.

Aminocyclopyrachlor-methyl was not detected in excreta, milk, or any tissue. The parent acid, aminocyclopyrachlor, was the only compound identified and was found in all matrices. It was the single radiolabeled component detected in liver (65.7% TRR; 0.197 ppm), kidney (55.3% TRR; 0.925 ppm), omental fat (47.5% TRR; 0.005 ppm), renal fat (83.8% TRR; 0.013 ppm), and subcutaneous fat (80.7% TRR; 0.021 ppm). Aminocyclopyrachlor was detected in muscle at 43.3% TRR (0.018 ppm) along with two unknowns (14.4-18.3% TRR; 0.006- 0.008 ppm), and in milk at 15.9% TRR (0.004 ppm) along with three unknowns (7.4-29.5% TRR; 0.002-0.007 ppm). TLC analysis of liver and kidney extracts prior to SPE clean-up (86.7% TRR and 98.3% TRR, respectively) confirmed that aminocyclopyrachlor was the only compound present in these samples.

Based on the study results, the petitioner concluded that aminocyclopyrachlor-methyl is rapidly metabolized in the goat and is eliminated as aminocyclopyrachlor primarily in the excreta. Chemical structures are shown in Appendix 1.

Conclusions. The submitted goat metabolism study is adequate to satisfy data requirements. Based on the submitted data, HED concludes that the nature of the residue in livestock is adequately understood for purposes of this petition. The residues of concern for tolerance enforcement and risk assessment are aminocyclopyrachlor and aminocyclopyrachlor-methyl (expressed in parent equivalents).

Because grass is not a significant feed stuff for poultry, a hen metabolism study is not required at this time; however, a hen metabolism study may be needed to support future uses on additional crops.

860.1340 Residue Analytical Methods

DER References: 48333620.DER (Plant method; includes review of MRIDs 48333617, 48333621, 48333625, and 48333626)
48333622.DER (Livestock method; includes review of MRIDs 48333623 and 48333627)

Plant Method

Enforcement method: DuPont has submitted an LC/MS/MS method, DuPont-22582 and revision DuPont-22582 SU1 RV2, for the determination of aminocyclopyrachlor (DPX-MAT28), aminocyclopyrachlor-methyl (DPX-KJM44), and metabolites IN-LXT69, QFH57, and IN-QGC48 in/on grass forage and hay. DuPont is proposing the revised method as an enforcement method, and has submitted method descriptions, method validation data, radiovalidation data, and ILVs of the method. The LC/MS/MS methods were used for data collection in the storage stability and crop field trial studies reviewed under PP#0F7817 (this petition).

The method submissions include: (1) a description and validation data for the original method (DuPont-22582; MRID 48333620), which determines residues of aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 only; (2) a description and validation data for the revised version of the method (Supplement No. 1, Revision Nos. 1 and 2; DuPont-22582 SU1 RV2; MRID 48333621) which includes analysis for metabolites IN-QFH57 and IN-QGC48 and incorporates changes to the method resulting from the ILV studies; (3) two ILV studies (MRIDs 48333625 and 48333626); and (4) radiovalidation conducted in conjunction with the grass metabolism study (MRID 48333617). Except as noted, the method addressed and described hereafter is DuPont-22582 SU1 RV2.

Briefly, samples are soaked in 0.15 M ammonium acetate, then extracted with ACN and centrifuged. The supernatant is reserved, and the sample is extracted with ACN:0.15 M ammonium acetate (70:30, v:v) and centrifuged. The supernatants are combined, 0.1 N HCl is added, and the extract is diluted with water. For analysis of aminocyclopyrachlor, aminocyclopyrachlor-methyl, IN-LXT69, and IN-QGC48, the extract is concentrated, then diluted with 0.5% formic acid and purified through a strong anion exchange (SAX) SPE cartridge after which it is transferred to a mixed-mode (cation exchange and reverse-phase; MCX) SPE cartridge. Residues are eluted with 75 mM ammonium hydroxide in methanol, and the eluate is combined with 0.2% formic acid, concentrated, and diluted with 0.01% formic acid, then filtered for analysis by LC/MS/MS. For analysis of IN-QFH57, the extract is concentrated, then diluted with 0.01% formic acid and purified through a SAX SPE cartridge. Residues are eluted with 1% formic acid in methanol, and the eluate is combined with 0.01% formic acid, concentrated, and diluted with 0.01% formic acid, then filtered for analysis by LC/MS/MS. Two transition ions are monitored for each analyte. An HPLC using a Phenomenex Phenyl-Hexyl analytical column and a gradient mobile phase of 0.1% formic acid in water and methanol; and an Applied Biosystems API-5000 Triple Quadrupole with electrospray interface (ESI) positive (negative for IN-QHF57) mode Multiple Reaction Monitoring (MRM).

The transition ions monitored are:
Aminocyclopyrachlor-methyl: 228→68 m/z and 228→168 m/z
Aminocyclopyrachlor: 214→68 m/z and 214→101 m/z
IN-LXT69: 170→76 m/z and 170→103 m/z
IN-QFH57: 176→132 m/z and 176→105 m/z
IN-QGC48: 192→178 m/z and 192→132 m/z

Based on the lowest level of method validation, the LOQ is 0.01 ppm for all analytes in all matrices. The reported limits of detection (LODs) (based on 3X the baseline noise in a control extract) are 0.002 ppm for aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-QGC48, 0.003 ppm for IN-QFH57, and 0.0003 ppm for IN-LXT69 in/on grass forage; and 0.002 ppm for aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-QGC48, 0.003 ppm for IN-QFH57, and 0.0005 ppm for IN-LXT69 in/on grass hay.

Acceptable method validation recoveries for DuPont-22582 and DuPont-22582 SU1 RV2 were obtained for all analytes from samples of grass forage and hay fortified at 0.01 and 0.10 ppm. Mean recoveries and coefficients of variation (CVs) were 73-95% (0-8.9%) for DuPont-22582 and 71-93% (1.0-17%) for DuPont-22582 SU1 RV2. The validation data include results of an analytical laboratory method tryout (MTO) conducted by ABC Laboratories. Acceptable method validation recoveries were obtained for all analytes from samples of grass forage and hay. The fortification levels used in method validation, in conjunction with concurrent method validation, are adequate to bracket expected residue levels in/on grass forage and hay.

Two ILV studies were also conducted using samples of grass hay fortified at 0.010 and 0.10 ppm for all analytes. The first ILV study was conducted on DuPont-22582 Supplement 1 by MPI Research, Inc. (State College, PA), and the second ILV study was conducted on DuPont-22582 Supplement 1 (Revision 1) by ABC Laboratories (Columbia, MO). The first ILV study was unsuccessful for aminocyclopyrachlor, aminocyclopyrachlor-methyl, IN-LXT69, and IN-QGC48; only IN-QFH57 was successfully recovered in the second of three trials, with mean recoveries of 97-111%. The second ILV, which reflected an alternative simplified purification procedure that used SAX SPE only, was successful for recovery of aminocyclopyrachlor-methyl, aminocyclopyrachlor, IN-LXT69, and IN-QGC48. The petitioner indicated that additional results from the second ILV reflecting the SPE/MCX purification procedures described above will be reported separately (in Study No. 65869a/D-30574, Supplement 1).

For the second ILV study to be acceptable, the petitioner must confirm that the laboratory personnel involved in the ILV were unfamiliar with the method. OPPTS 860.1340 requires that the personnel chosen to conduct the ILV trials must be unfamiliar with the method, both in its development and in its subsequent use in analyzing field samples. Because ABC Laboratories was the analytical laboratory for the storage stability and crop field trials reviewed under PP#0F7817, performed an analytical laboratory MTO on DuPont-22582, and was responsible for the development of the alternative SAX SPE cleanup procedure that was validated in the second ILV study, it appears there may be a potential conflict with the guideline requirements for ILV. The registrant has since submitted information stating the personnel involved in the ILV were not involved in method development (XXXXXXXX) therefore, this deficiency is resolved.

DuPont submitted radiovalidation data with the grass metabolism study to evaluate the efficiency of the extraction methodology presented in DuPont-22582 for extracting aminocyclopyrachlor and IN-QFH57 from field-grown grass. Aminocyclopyrachlor-methyl, IN-LXT69, and IN-QGC48 were also evaluated; however, resolution using the residue analytical method was inadequate to allow individual quantification using HPLC methodology. The extraction efficiencies were determined to be 108%, 126%, and 73%, respectively, for aminocyclopyrachlor, IN-QFH57, and components with a similar retention time to IN-LXT69, IN-QGC48, and aminocyclopyrachlor–methyl in ^{14}C-labeled grass.

A confirmatory method was not included; however none is required because the LC/MS/MS method monitors two transition ions for each analyte.

Data collection methods: The proposed enforcement method, DuPont-22582 SU1 RV2, and earlier versions of the method, including DuPont-22582 and DuPont-22582, Supplement No. 1, were used for data collection in the storage stability and crop field trial studies reviewed under PP#0F7817. Original method DuPont-22582 included analysis for aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69, and DuPont-22582, Supplement No. 1 added analysis for metabolites IN-QFH57 and IN-QGC48. The methods were adequately validated concurrently with the storage stability and crop field trial studies.

Livestock Method

DuPont has submitted an LC/MS/MS method, DuPont-25836 and a revised version of the method, DuPont-27162, Revision No. 1, for the determination of aminocyclopyrachlor (DPX-MAT28), aminocyclopyrachlor-methyl (DPX-KJM44), and metabolite IN-LXT69 in bovine muscle, liver, kidney, fat, milk, and feces. DuPont is proposing the revised method as an enforcement method, and has submitted method descriptions, method validation data, and ILV of the method. The LC/MS/MS method was used for data collection in the cattle feeding study reviewed under PP#0F7817.

The method submissions include: (1) a description and validation data for the original method (DuPont-25836; MRID 48333623); (2) a description and validation data for the revised version of the method (DuPont-27162, Revision No. 1; MRID 48333622) which includes minor modifications to the method and incorporates changes to the method resulting from the ILV study; and (3) an ILV (MRIDs 48333627) conducted on DuPont-27162. Except as noted, the method addressed and described hereafter is DuPont-27162, Revision No. 1. We note that, although the procedures of methods DuPont-25836 and DuPont-27162 are essentially identical, the method description for DuPont-27162 establishes separate sections for analysis of milk (Method No. 1474A), bovine muscle and feces (Method No. 1474B), and bovine liver, kidney, and fat (Method No. 1474C). In addition, the original method provides instructions for analysis of skim milk, cream, whole eggs, and fish, while the revised method does not include these matrices.

Briefly, milk samples are extracted twice with ACN:0.1% formic acid (90:10, v:v) and centrifuged. The combined extracts are diluted with extraction solvent, then adjusted to volume with 0.01% formic acid for analysis by LC/MS/MS. Liver, kidney, fat, muscle, and feces

samples are extracted sequentially with ACN:0.1% aqueous formic acid (at 90:10, v:v; 70:30, v/v; and 50:50, v/v) and centrifuged. The combined extracts are diluted with 0.1% formic acid and concentrated. An aliquot of the concentrated extract of liver, kidney, and fat is diluted with 0.01% formic acid for analysis by LC/MS/MS. An aliquot of the extract of muscles and feces is diluted with 0.2% aqueous formic acid and purified on an MCX SPE cartridge. Residues are eluted with 75 mM ammonium hydroxide in methanol, and the eluate is combined with 0.2% formic acid, concentrated, and combined with 0.01% formic acid for analysis by LC/MS/MS. Two ion transitions are monitored for each analyte. An HPLC using a Phenomenex Luna Phenyl-Hexyl analytical column and a gradient mobile phase of 0.01 M aqueous formic acid and methanol; and an Applied Biosystems API-4000 Triple Quadrupole with turbo ion spray interface in positive mode Multiple Reaction Monitoring (MRM) was used. The method notes that if background levels of AMINOCYCLOPYRACHLOR-METHYL are found, this analyte may also be analyzed with an isocratic mobile phase of 0.01 M formic acid:methanol at 40:60 (v:v).

The transition ions monitored are:
Aminocyclopyrachlor-methyl: 228.1→68.2 m/z and 228.1→100.9 m/z
Aminocyclopyrachlor: 214.2→68.1 m/z and 214.2→101.1 m/z
IN-LXT69: 170.1→76.1 m/z and 170.1→103.1 m/z

Based on the LLMV, the LOQ is 0.01 ppm for all analytes in all matrices. The reported LODs (based on 3X the baseline noise in a control extract) for aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69, respectively, are 0.0065, 0.0021, and 0.0022 ppm in muscle; 0.0074, 0.00044, and 0.0010 ppm in liver; 0.0056, 0.0016, and 0.0014 ppm in kidney; 0.0056, 0.00059, and 0.0010 ppm in fat; 0.0055, 0.00091, and 0.0028 ppm in milk; and 0.0039, 0.0012, and 0.0015 ppm in feces.

Acceptable method validation recoveries for method DuPont-25836 were obtained for all analytes from samples of bovine muscle, liver, kidney, fat, skim milk, whole milk, heavy cream, whole eggs, and fish fortified at 0.01 and 0.10 ppm. The mean recoveries were 81-103% for aminocyclopyrachlor, 79-106% for aminocyclopyrachlor-methyl, and 74-102% for IN-LXT69, with CVs <20% for each matrix tested. Acceptable method validation recoveries for method DuPont-27162, Revision No. 1 were obtained for all analytes from samples of bovine muscle, liver, kidney, fat, milk, and feces fortified at 0.01 and 0.10 ppm. The mean recoveries were 75-111% for aminocyclopyrachlor, 77-104% for aminocyclopyrachlor-methyl, and 73-103% for IN-LXT69, with CVs <20% for each matrix tested. The fortification levels used in method validation in conjunction with concurrent method validation are adequate to bracket expected residue levels in livestock tissues and milk.

An ILV study was also conducted on DuPont-27162 using samples of bovine liver, milk, and eggs fortified with aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 at 0.010 and 0.10 ppm. The first trial was successful for all analytes in milk and eggs, with acceptable mean recoveries ranging from 92%-110% (CVs <20%). The first trial was also successful for IN-LXT69 in bovine liver (mean recoveries 102-106%) but was unsuccessful for aminocyclopyrachlor and aminocyclopyrachlor-methyl. Low recoveries for aminocyclopyrachlor –methyl and high recoveries for aminocyclopyrachlor indicated that

aminocyclopyrachlor –methyl was converting to aminocyclopyrachlor during the analysis. The second trial for liver was successful for aminocyclopyrachlor and aminocyclopyrachlor –methyl (mean recoveries 80-97%) when the performance validation set was separated into four smaller sub-sets to minimize the observed degradation of aminocyclopyrachlor-methyl.

No radiovalidation data were submitted to support the submitted livestock analytical method; however, no data are required because the extraction solvents used in the goat metabolism study are the same as those used in the residue analytical method. Acceptable extraction efficiencies were indicated in the metabolism study; therefore, no additional data are required.

A confirmatory method was not included; however none is required because the LC/MS/MS method monitors two ion transitions for each analyte.

Data collection methods: An earlier version of the proposed enforcement method, DuPont-27162, was used for data collection in the storage stability and cattle feeding studies reviewed under PP#0F7817. The method included analysis for aminocyclopyrachlor, aminocyclopyrachlor, and IN-LXT69 in milk and bovine tissues. The method was adequately validated concurrently with the storage stability and crop field trial studies.

Conclusions. The submitted residue analytical methods data are adequate to satisfy data requirements for the subject petition. HED has concluded that the livestock method is adequate for enforcement purposes, and that the grass method is adequate for enforcement purposes. The Agency has considered the submitted data and has reviewed the analytical methods against the TMV (Tolerance Method Validation) checklist contained in ACB (Analytical Chemistry Branch/BEAD)'s SOP No. 019, Revision 1.0. HED has determined that TMVs are not needed for the proposed enforcement methods for plant and livestock commodities.

The analytical methods submitted under the subject action do not provide for conversion of residues of aminocyclopyrachlor-methyl to stoichiometric equivalents of aminocyclopyrachlor and the residue data presented herein do not reflect correction to stoichiometric equivalents. The conversion factor, based on molecular weights (MWs) of 213.6 for aminocyclopyrachlor and 227.6 for aminocyclopyrachlor-methyl is 0.93849.

860.1360 Multiresidue Methods

DER References: 48333624.DER

DuPont has submitted multiresidue methods testing data for aminocyclopyrachlor (DPX-MAT28) and aminocyclopyrachlor-methyl (DPX-KJM44). The test substances were screened through multiresidue methods described in the U.S. FDA Pesticide Analytical Manual Volume I (PAM Vol. I). The study was conducted by Pyxant Labs Inc. (Colorado Springs, CO).

AMINOCYCLOPYRACHLOR was tested through Protocols A, B, and C; based on the results of these tests, it was not further tested through Protocols D, E, or F. Aminocyclopyrachlor-methyl was tested through Protocols A, B (via methylation of aminocyclopyrachlor), C, D, E and F. Neither aminocyclopyrachlor nor aminocyclopyrachlor-methyl was tested under Protocol G because the compounds are not substituted ureas.

The test substances were not found to be naturally fluorescent; therefore, further testing under Protocol A was not required.

Protocol B testing was conducted on aminocyclopyrachlor because it has an acid structure; methylation in Protocol B testing yielded the methyl ester, aminocyclopyrachlor-methyl. Both test substances were found to be chromatographable in Protocol C testing; therefore, aminocyclopyrachlor was methylated according to Protocol B with observed conversion of 37.2% to the methyl ester (DPX-KJM44). Acceptable recovery was obtained through Florisil (93%), but recovery through gel permeation chromatography (GPC) was unacceptable (14.2%); therefore, no further testing was conducted under Protocol B.

In Protocol C testing aminocyclopyrachlor was chromatographable in Section 302, Level II testing, using module DG-5 with nitrogen-phosphorus detection (NPD). Aminocyclopyrachlor-methyl was chromatographable in Section 302, Level I testing, using module DG-5 (NPD). The results of Protocol C testing indicated that further testing of aminocyclopyrachlor-methyl under Protocols D-F was required.

Based on the results of Protocol C testing, aminocyclopyrachlor-methyl was tested through Protocol D without cleanup. Testing under Protocol D, Section 302, E1, yielded complete recovery (109%) of aminocyclopyrachlor-methyl in skim milk fortified at 0.1 ppm and partial recovery (53%) in skim milk fortified at 0.5 ppm.

Testing of aminocyclopyrachlor-methyl through Protocols E and F was suspended because recovery through Florisil was unacceptable.

These data indicate that Protocol D described in FDA PAM Vol. I may be applicable for determination of aminocyclopyrachlor-methyl; however, the FDA multiresidue methods are not appropriate for determining residues of aminocyclopyrachlor, or for the two compounds (aminocyclopyrachlor-methyl and aminocyclopyrachlor) together.

Conclusions. The submitted multiresidue methods test data for aminocyclopyrachlor and DPX-KLM44 are acceptable. The data indicate that multiresidue methods are not suitable for determination of aminocyclopyrachlor or for determination of the two analytes together. The submitted data will be forwarded to the U.S. FDA for further evaluation.

860.1380 Storage Stability

DER References: 48333628.DER (Grass; includes review of MRID 48333629)
48363401.DE2 (Milk, eggs, and bovine tissues)

Grass

DuPont has submitted the results of two storage stability studies with aminocyclopyrachlor (DPX-MAT28), aminocyclopyrachlor-methyl (DPX-KJM44), and the metabolites, IN-LXT69, IN-QFH57, and IN-QGC48 in grass forage and hay. Separate studies were submitted for aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 (MRID 48333628), and for IN-QFH57 and IN-QGC48 (MRID 48333629). Samples of untreated grass forage and hay were fortified with aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 at 0.50 ppm each for forage and 1.0 ppm each for hay, and with IN-QFH57 and IN-QGC48 at 0.30 ppm each for both forage and hay. The fortified samples were stored frozen (-20 °C) and analyzed at target intervals of 0, 7, 14, 30, 60, 90, 150, 210, 300, 360, and 400-500 days. Both studies were conducted by ABC Laboratories, Inc. (Columbia, MO).

Grass forage and hay samples were analyzed for residues of aminocyclopyrachlor, aminocyclopyrachlor-methyl, IN-LXT69, IN-QFH57, and IN-QGC48 by LC/MS/MS using DuPont-22582 (for analysis of aminocyclopyrachlor, aminocyclopyrachlor-methyl, IN-LXT69) and DuPont-22582 Supplement No.1 (for analysis of IN-QFH57 and IN-QGC48). The methods are acceptable for data collection based on adequate method validation data and concurrent method recovery data. The validated LOQ was 0.01 ppm in grass forage and hay.

The study results indicate that residues of aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 are stable in/on grass forage and hay stored frozen (-20 °C) for up to 499-502 days (~16.5 months), and residues of IN-QFH57 and IN-QGC48 are stable in/on grass forage and hay stored frozen for up to 401-402 days (13.2 months).

Sample storage intervals and conditions

The storage durations and conditions of samples from the crop field trials and processing studies submitted to support this petition are presented in Table 4.

Table 4. Summary of Storage Conditions and Durations of Samples from Crop Field Trial Study

Matrix	Analytes	Storage Temperature (°C)	Actual Storage Duration	Interval of Demonstrated Storage Stability
Grass forage	aminocyclopyrachlor, aminocyclopyrachlor-methyl, IN-LXT69, INQFH57, and IN-QGC48	-20	37-400 days (1.2-13.2 months)	499-502 days (~16.5 months) for aminocyclopyrachlor-methyl, aminocyclopyrachlor and IN-LXT69 and 401-402 days (13.2 months) for metabolites IN-QFH57 and IN-QGC48
Grass hay			41-408 days (1.3-13.4 months)	

Conclusions. Acceptable supporting storage stability data have been submitted for grass forage and hay. No additional storage stability data are required to support the submitted grass crop field trials.

Livestock Commodities

DuPont has submitted the results of a storage stability study with aminocyclopyrachlor (DPX-MAT28), aminocyclopyrachlor-methyl (DPX-KJM44), and metabolite IN-LXT69 in milk, eggs, and bovine tissues. The study was conducted concurrently with the cattle feeding study. Samples of homogenized bovine muscle, liver, kidney, fat, milk, and eggs were fortified with aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 at 0.2 ppm. The fortified samples were placed in frozen storage at approximately -20 °C and analyzed at target intervals of 1 and 2 weeks, and 1, 2, 3, and 5 months; kidney was not analyzed at 5 months. In addition, extracts of liver and kidney were stored frozen at ~-20 °C and analyzed after storage intervals of 7 and 14 days. The study was conducted by Charles River Laboratories (Tranent, Edinburgh, Scotland)

Samples of milk, eggs, and tissues were analyzed for residues of aminocyclopyrachlor, aminocyclopyrachlor-methyl, and metabolite IN-LXT69 by an LC/MS/MS method, DuPont-27162. Samples of liver and kidney fortified with aminocyclopyrachlor-methyl were analyzed for residues of both aminocyclopyrachlor-methyl and aminocyclopyrachlor to investigate biotransformation. We note that the method description for DuPont-27162 establishes separate sections for analysis of milk (Method No. 1474A), bovine muscle and feces (Method No. 1474B), and bovine liver, kidney, and fat (Method No. 1474C). This method is acceptable for data collection based on adequate method validation and concurrent recovery data. Based on the LLMV, the LOQ for aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 was 0.01 ppm in milk and tissue samples.

The study results indicate that residues of aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 are stable in milk, eggs, and bovine muscle and fat stored frozen (~-20 °C) for up to 5 months, and that residues of aminocyclopyrachlor and IN-LXT69 are stable in liver and

kidney for up to 5 and 3 months, respectively. aminocyclopyrachlor-methyl was not stable in homogenized liver or kidney stored frozen for ≥1 week; however, the recovery of aminocyclopyrachlor from samples fortified with aminocyclopyrachlor-methyl demonstrated the biotransformation of aminocyclopyrachlor-methyl to aminocyclopyrachlor under frozen storage conditions. When recoveries for aminocyclopyrachlor-methyl in stored samples were adjusted for biotransformation to aminocyclopyrachlor, corrected recoveries at all storage intervals were 92-98% for liver and 91-102% for kidney. All analytes were found to be stable in extracts of liver and kidney stored frozen for up to 14 days.

Sample storage intervals and conditions

The storage durations and conditions of samples from the cattle feeding submitted to support this petition are presented in Table 5.

Table 5. Summary of Storage Conditions and Durations of Samples from the Cattle feeding Study

Matrix	Analyte	Storage Temperature (°C)	Actual Storage Duration	Interval of Demonstrated Storage Stability
Milk, skim milk, and cream	aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69	-20	2-65 days (0.1-2.1 months)	Up to 146 days (4.8 months)
Muscle			12-44 days (0.4-1.5 months)	Up to 138 days (4.5 months)
Fat			11-36 days (0.4-1.2 months)	Up to 147 days (4.8 months)
Kidney			0 and 16-45 days (0 and 0.5-1.5 months)	Up to 88 days (2.9 months) for aminocyclopyrachlor and IN-LXT69. Residues of aminocyclopyrachlor-methyl were unstable; however, biotransformation to aminocyclopyrachlor accounted for nearly all loss on storage.
Liver			0 and 28-29 days	Up to 147 days (4.8 months) for aminocyclopyrachlor and IN-LXT69. Residues of aminocyclopyrachlor-methyl were unstable; however, biotransformation to aminocyclopyrachlor accounted for nearly all loss on storage.

Conclusions. Acceptable supporting storage stability data have been submitted for milk and bovine tissues and hay. No additional storage stability data are required to support the submitted cattle feeding study.

860.1400 Water, Fish, and Irrigated Crops

There are no proposed uses that are relevant to this guideline topic.

860.1460 Food Handling

There are no proposed uses that are relevant to this guideline topic.

860.1480 Meat, Milk, Poultry, and Eggs

DER Reference: 48363401.DE1

The livestock feedstuffs associated with PP#0F7817 are grass forage and hay; these commodities are fed to beef and dairy cattle but are not fed to poultry or swine. The dietary burdens of aminocyclopyrachlor to cattle, based on reasonably balanced diets, are presented in Table 6. The maximum reasonable dietary burden for cattle is 90 ppm.

Table 6. Calculation of Dietary Burdens of Aminocyclopyrachlor Residues to Livestock.

Feedstuff	Type[1]	% Dry Matter[2]	% Diet[2]	Highest Average Field Trial (ppm)[4]	Dietary Contribution (ppm) [3]
Beef Cattle					
Grass hay	R	88	15	117	19.9
CC not registered	CC	--	80	--	--
PC not registered	PC	--	5	--	--
TOTAL BURDEN	--	--	100	--	**19.9**
Dairy Cattle					
Grass forage	R	25	45	50	90
CC not registered	R	--	45	--	--
PC not registered	CC	--	10	--	--
TOTAL BURDEN	--	--	100	--	**90**

[1] R: Roughage; CC: Carbohydrate concentrate; PC: Protein concentrate.
[2] OPPTS 860.1000 Table 1 Feedstuffs (June 2008).
[3] Contribution = ([tolerance /% DM] X % diet) for beef and dairy cattle; contribution = ([tolerance] X % diet) for poultry and swine.
[4] calculated as parent equivalents

DuPont submitted a cattle feeding study with aminocylopyrachlor-methyl (DPX-KJM44). DPX-KJM44 is the methyl ester of aminocyclopyrachlor (DPX-MAT28). In the study, four groups of dairy cows (3 cows/group; Groups 1-4) were dosed orally once a day with gelatin capsules containing aminocyclopyrachlor-methyl (DPX-KJM44) at target doses of 1.8, 3.6, 10.8, and 36 mg/kg bw/day for 28 consecutive days. Based on the average feed consumption, the actual mean daily dose levels were equivalent to 73.3, 160, 455, and 1595 ppm in the diet (dry-weight basis). The dosing levels correspond to ~0.8x, 1.8x, 5.1x, and 17.7x the maximum reasonable dietary burden to cattle based on the proposed use on grass. An additional group of two cows (Group 5) was dosed at 1594 ppm for 28 days, to obtain depuration data. One control cow received capsules containing no aminocyclopyrachlor-methyl (Group 6). The study was conducted by Charles River Laboratories (Tranent, Edinburgh, Scotland)

Cows were milked twice daily. For each cow, milk samples from the afternoon sampling were combined with milk samples from the next morning sampling to produce a daily sample. Samples of milk from Study Days -1, 1, 3, 5, 7, 10, 14, 17, 21, 24, and 28 from all dose groups were analyzed. Milk collected on Days 14 and 21 was used for preparation of skim milk and cream samples. Milk samples were collected from the depuration group (Group 5) on Study Days 24 and 28 during the dosing period and on Depuration Days 1, 3, 5, 10, 14, and 16 post-dosing; only milk from Depuration Days 1, 3, 5, and 7 was analyzed. Skim milk and cream samples were prepared from milk collected on Depuration Days 3 and 10 post-dosing. Control and treated cows except those in the depuration study were sacrificed ~22-24 hours after the final dose on Study Day 28. Samples of liver, kidney, fat (omental, renal, and subcutaneous), and muscle (loin, flank, and hind leg) were collected from each cow.

Milk and tissue samples were analyzed for residues of aminocyclopyrachlor-methyl, aminocyclopyrachlor, and metabolite IN-LXT69 using an acceptable method, and the study is supported by adequate storage stability data. The method LOQ is 0.01 ppm for all analytes in milk and tissues.

All samples were stored frozen (approximately -20 ^{o}C) prior to extraction for analysis, except for samples of liver and kidney, which were generally processed fresh following sacrifice, due to storage stability issues for analysis of aminocyclopyrachlor-methyl. The maximum storage durations from collection to extraction were 65 days for milk, 30 days for skim milk, 59 days for cream, 44 days for muscle, and 36 days for fat. Liver and kidney samples were generally extracted on the day of collection with the exception of selected repeat analysis samples. Adequate storage stability data are available to support the storage conditions and durations of samples from the cattle feeding study.

Residues of aminocyclopyrachlor-methyl and IN-LXT69 were below the LOQ in all samples of milk, skim milk, cream, muscle, liver, kidney, and fat at all dose levels, except that quantifiable residues of 0.014 ppm aminocyclopyrachlor-methyl were observed in liver from one cow at the 73.3-ppm dose level. Quantifiable residues of aminocyclopyrachlor were observed in milk at the 160-, 455-, and 1595-ppm dose levels, although residues at the 160-ppm dose level were generally near or below the LOQ on all sampling days. Quantifiable residues were observed in skim milk and cream beginning at the 160-ppm dose level for skim milk and the 455-ppm dose level for cream. In tissues, quantifiable residues of aminocyclopyrachlor were observed in liver, kidney, and fat at all dose levels and in muscle beginning at the 160- and 1595-ppm dose levels. In tissues, residues were highest in kidney, followed by fat, liver, and muscle.

Residues of aminocyclopyrachlor in milk appeared to reach a plateau by Day 7 for the 455-ppm dose level but continued to increase at the 1595-ppm dose level through study Day 28. We note that OCSPP 860.1480 specifies that dosing should continue until residues plateau in milk if they have not done so in 28 days. Residues of aminocyclopyrachlor in milk (beginning from Day 7) were <0.01, <0.01-0.012, 0.016-0.026, and 0.040-0.10 ppm following dosing at 73.3, 16, 455, and 1595 ppm, and combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl were <0.02, <0.02-<0.022, <0.026-<0.036, and <0.05-<0.11 ppm at the respective dose levels. There was no evidence of preferential transfer of residues to skim milk or cream; in general,

residues of aminocyclopyrachlor were slightly lower in cream at all dose levels with quantifiable residues. Residues in skim milk and cream (Study Days 14 and 21), respectively, were <0.01 (both), <0.01-0.013 and <0.01, 0.015-0.023 and <0.01-0.015, and 0.044-0.098 and 0.017-0.046 ppm at the 73.3-, 16-, 455-, and 1595-ppm dose levels; combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl in skim milk and cream, respectively, were <0.02 (both), <0.02-<0.023 and <0.02, <0.025-<0.033 and <0.02-<0.025, and <0.054 and <0.108 and <0.027-<0.056 ppm at the respective dose levels.

In kidney, residues of aminocyclopyrachlor were 0.092-0.17, 0.23-0.40, 0.20-0.54, and 0.68-1.4 ppm at the 73.3-, 16-, 455-, and 1595-ppm dose levels, and combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl were <0.10-<0.18, <0.24-<0.41, <0.21-<0.55, and <0.69-<1.41 ppm. In fat, residues of aminocyclopyrachlor were <0.01-0.015, <0.01-0.040, 0.029-0.12, and 0.025-0.74 ppm at the 73.3-, 16-, 455-, and 1595-ppm dose levels, and combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl were <0.02-<0.025, <0.02-<0.050, <0.039-<0.13, and <0.035-<0.75 ppm. In liver residues of aminocyclopyrachlor were <0.01-0.082, 0.020-0.064, 0.025-0.075, and 0.088-0.11 ppm at the 73.3-, 16-, 455-, and 1595-ppm dose levels, and combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl were <0.02-<0.092, <0.03-<0.074, <0.035-<0.085, and <0.098-<0.12 ppm. In muscle, residues of aminocyclopyrachlor were <0.01, <0.01-0.012, <0.01, and 0.021-0.10 at the 73.3-, 16-, 455-, and 1595-ppm dose levels, and combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl were <0.02, <0.02-0.022, <0.02, and <0.031-<0.11 ppm at the respective dose levels.

Following cessation of dosing, residues in milk and tissues rapidly declined in the depuration group dosed at 1594 ppm for 28 days. Residues of aminocyclopyrachlor-methyl and IN-LXT69 were not detected above the LOQ (<0.01 ppm) in any milk, skim milk, cream, or tissue samples. Residues of aminocyclopyrachlor were detected above the LOQ in one milk sample (0.017 ppm) on Depuration Day 1 and dropped below the LOQ by Depuration Day 3. Residues of aminocyclopyrachlor were detected above the LOQ in the muscle (0.019 ppm) and fat (0.030 ppm) of the cow sacrificed on Depuration day 15. For the cow sacrificed on Depuration day 17, the aminocyclopyrachlor residues were not detected in the muscle sample and increased to 0.056 ppm in the fat sample.

Conclusions. The submitted cattle feeding study is acceptable for purposes of this petition. Residues in milk did not reach a plateau at the highest dosing level (1595 ppm; 17.7x) in the submitted study; however, because residues plateaued at 7 days at the 455-ppm dose level (5.1x) and were generally near the LOQ at the 160-ppm dose level (1.8x), HED believes the study is adequate to support the proposed use on grass only. Should other uses be proposed which result in an increase in the dietary burden for cattle, additional data may be required.

Samples were analyzed for aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69 using acceptable methods, and the study is supported by adequate storage stability data.

Based on the submitted data, HED has concluded that tolerances are needed for milk and the tissues of cattle, goat, horse, and sheep. Tolerances are not needed for milk fat because residues did not concentrate in cream.

If the residues observed at various dosing levels are adjusted to a 1x feeding level for dairy cattle (see Table 7), maximum expected combined residues would be 0.02 ppm in milk, 0.22 ppm in kidney, 0.04 ppm in fat, 0.10 ppm in liver, and 0.02 ppm in muscle. Based on these data, tolerances are needed for meat byproducts at 0.30 ppm, for fat at 0.05 ppm, and for muscle at 0.02 ppm. The data indicate that a tolerance of 0.02 ppm (equivalent to the combined LOQs for aminocyclopyrachlor and aminocyclopyrachlor-methyl) would be appropriate for milk.

Table 7. Summary of Data from Cattle Feeding Study with Aminocyclopyrachlor-methyl.

Matrix	Maximum combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl at each dosing level[1]				Residues adjusted to 1x feeding level for dairy cattle[2]			
	73.3	160	455	1595	0.8x	1.8x	5.1x	18x
Milk (Days 7-28)	--	<0.022	<0.036	<0.11	--	0.01	0.01	0.01
Skim milk	--	<0.023	<0.033	<0.11	--	0.01	0.01	0.01
Cream	--	--	<0.025	<0.056	--	--	0.01	0.01
Kidney	<0.18	<0.41	<0.55	<1.41	0.23	0.23	0.11	0.08
Fat	<0.025	<0.050	<0.13	<0.75	0.03	0.03	0.03	0.04
Liver	<0.092	<0.074	<0.085	<0.12	0.12	0.04	0.02	0.01
Muscle	--	--	--	<0.11	--	--	--	0.01

[1] The LOQ (0.01 ppm) was used for residues reported as ND or below the LOQ. For purposes of this calculation only, where maximum residues were below the LOQ for both analytes, residues are indicated by --.
[2] The dose rate factors calculated above based on actual dosing levels in calculations.

Because there are no poultry feedstuffs associated with the proposed use on grasses, data requirements for a poultry feeding study are not relevant to this tolerance petition.

860.1500 Crop Field Trials

DER Reference: 48333630.DER

DuPont has submitted field trial data reflecting use of the potassium salt and methyl ester formulations on grass forage and hay in support of the proposed use of aminocyclopyrachlor on pasture and rangeland grasses. The results from these field trials are discussed below and the residue data are summarized in Table 8.

Table 8. Summary of Residue Data from Grass Crop Field Trials with the Methyl Ester and Potassium Salt Formulations of Aminocyclopyrachlor.

Commodity	TRT Plot #[1]	EP[2]	Total Applic. Rate[3], lb ai or ae/A (g ai or ae/ha)	PHI (days)	Residue Levels (ppm)						
					n	Min.	Max.	HAFT[4]	Median	Mean	Std. Dev.
PASTURE AND RANGELAND GRASSES: proposed use = 0.281 lb ai/A total application rate, 0-day PHI											
Aminocyclopyrachlor-methyl											
Grass, forage	1	80% WG	0.274-0.299 (308-335)	0	44	7.7	47	47	22	23	10
	2	2 lb/gal SL	0.275-0.285 (308-319)	0	12	0.014	0.15	0.15	0.031	0.050	0.047
	3	80% WG	0.270-0.280 (303/314)	0	6	9.5	14	14	11	11	1.9
Grass, hay	1	80% WG	0.274-0.299 (308-335)	0	44	13	108	103	35	38	20
	2	2 lb/gal SL	0.275-0.285 (308-319)	0	12	0.061	0.89	0.73	0.15	0.24	0.25
	3	80% WG	0.270-0.280 (303/314)	0	6	19	31	27	22	23	4.5
Aminocyclopyrachlor											
Grass, forage	1	80% WG	0.274-0.299 (308-335)	0	44	0.76	14	13	2.2	3.2	2.7
	2	2 lb/gal SL	0.275-0.285 (308-319)	0	12	12	41	39	20	23	8.9
	3	80% WG	0.270-0.280 (303/314)	0	6	0.43	0.84	0.75	0.65	0.66	0.15
Grass, hay	1	80% WG	0.274-0.299 (308-335)	0	44	2.4	80	79	16	18	16
	2	2 lb/gal SL	0.275-0.285 (308-319)	0	12	29	58	49	41	41	8.3
	3	80% WG	0.270-0.280 (303/314)	0	6	1.1	14	12	2.4	5.2	5.5
Combined residues of aminocyclopyrachlor + aminocyclopyrachlor-methyl											
Grass, forage	1	80% WG	0.274-0.299 (308-335)	0	44	8.7	54	53	25	26	12
	2	2 lb/gal SL	0.275-0.285 (308-319)	0	12	12	41	39	20	23	8.9
	3	80% WG	0.270-0.280 (303/314)	0	6	10	15	14	12	12	1.9
Grass, hay	1	80% WG	0.274-0.299 (308-335)	0	44	28	133	129	50	57	27
	2	2 lb/gal SL	0.275-0.285 (308-319)	0	12	29	59	49	41	41	8.5
	3	80% WG	0.270-0.280 (303/314)	0	6	20	45	39	25	28	9.6

[1] 1= 80% WG formulation of aminocyclopyrachlor-methyl, normal application volume; 2 = 2 lb/gal SL formulation of aminocyclopyrachlor; and 3 = 80% WG formulation of aminocyclopyrachlor-methyl, low application volume.

[2] 80% WG = WG formulation of aminocyclopyrachlor-methyl and 2 lb/gal SL = SL formulation of aminocyclopyrachlor.

[3] Rates reflect lb ae or ai/A aminocyclopyrachlor; refer to the DER for 4833630 for comparison of rates with ai aminocyclopyrachlor-methyl.
[4] HAFT = Highest Average Field Trial result.

DuPont has submitted field trial data for aminocyclopyrachlor (DPX-MAT28), aminocyclopyrachlor-methyl (DPX-KJM44), and metabolites IN-LXT69, IN-QFH57, and IN-QGC48 in/on grass forage and hay from pastures and rangelands in the U.S. and Canada. Twenty-two field trials were conducted in the U.S. and Canada in Zones 1 (PA and PE, 3 trials), 2 (NJ, 1 trial), 5 (IA, MB, MO, NE, and ON, 6 trials), 6 (OK and TX, 3 trials), 7 (ND and SD, 2 trials), 8 (KS, 1 trial), and 14 (AB, MB, and SK, 6 trials) during the 2008 and 2009 growing seasons.

Each field trial included one control plot and one treated plot. Treated plots received a single foliar broadcast application of an 80% WG formulation of DPX-KJM44 (methyl ester) at a target rate of 0.300 lb ai/A (336 g ai/ha), equivalent to 0.281 lb ae/A (315 g ae/ha) aminocyclopyrachlor. Actual application rates were 0.293-0.318 lb ai/A (328-357 g ai/ha), equivalent to 0.274-0.299 lb ae/A (308-335 g ae/ha), with spray volumes of 10-30 gal/A. Additional side-by-side trials were conducted at selected sites as follows. Six trials included a second treated plot which received a single foliar broadcast application of a 2 lb/gal (240 g/L) SL formulation of aminocyclopyrachlor at a target rate of 0.281 lb ai/A (315 g ai/ha). Actual application rates were 0.275-0.285 lb ai/A (308-319 g ai/ha) with spray volumes of 10-30 gal/A. Three trials included a second treated plot which received a single foliar broadcast application of the 80% WG formulation of aminocyclopyrachlor-methyl at a target rate of 0.300 lb ai/A (336 g ai/ha), equivalent to 0.281 lb ae/A (315 g ae/ha) DPX-MAT 28, in a low volume application. Actual application rates were 0.288-0.299 lb ai/A (323-335 g ai/ha), equivalent to 0.270-0.280 lb ae/A (303-314 g ae/ha), in a spray volume of 1 gal/A. The application rates used in the study correspond to ~1-1.1x the maximum seasonal application rate to grasses. An adjuvant (organosilicone, nonionic surfactant, or methylated seed oil) was added to the spray mixture for all of the applications.

Single control and duplicate treated samples of grass forage and hay were harvested from each plot at a PHI of 0 days (approximately 4 hours after application). At two of the trials, four additional sampling intervals were scheduled at PHIs of 3, 7, 14, and 21 days after application to assess residue decline. Samples of hay were allowed to dry in the field for 0-28 days after harvest.

The results of the grass field trials for residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl are summarized in Table 8. Following a single foliar broadcast application of the 80% WG formulation of aminocyclopyrachlor-methyl WG (at normal or low spray volume) or the 2 lb/gal SL formulation of aminocyclopyrachlor at target rates of ~0.281 ae ai/A and a PHI of 0 days, the major residues found in grass forage and hay were aminocyclopyrachlor-methyl and aminocyclopyrachlor. Quantifiable residues of metabolite IN-LXT69 were observed in/on grass forage and hay at up to 0.035 ppm in/on forage and 0.11 ppm in/on hay; residues of IN-QFH57 or IN-QGC48 were below the LOQ in/on all samples. Comparison of the results for the side-by-side trials reflecting normal and low spray volumes for the 80% WG formulation of aminocyclopyrachlor-methyl indicated that combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl following application in normal spray

volumes were higher in/on grass forage in two of three trials and higher in/on grass hay in all three trials. Comparison of the results for the side-by-side trials reflecting the 80% WG formulation of aminocyclopyrachlor-methyl and the 2 lb/gal SL formulation of aminocyclopyrachlor at a target rate of 0.281 lb ae/A indicated that combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl were generally slightly higher following application of the aminocyclopyrachlor formulation.

In the residue decline trials combined residues of aminocyclopyrachlor-methyl and aminocyclopyrachlor declined with increasing PHI in grass forage and hay. Residues of IN-LXT69 were near or below the LOQ in most trials; where quantifiable residues were observed, residues declined with increasing harvest interval.

Conclusions: The grass field trial data for aminocyclopyrachlor are adequate to fulfill data requirements. The number and locations of field trials are in accordance with the requirements of OCSPP Guideline 860.1500 for grasses, and the use pattern of the field trials adequately reflects the proposed use pattern.

Grass forage and hay samples were analyzed for residues of aminocyclopyrachlor, aminocyclopyrachlor-methyl, and metabolites IN-LXT69, IN-QFH57, and IN-QGC48 by LC/MS/MS using an adequate method, and the study is supported by adequate storage stability data. The method LOQ is 0.01 ppm for all analytes in grass forage and hay.

The available field trial data will support tolerances of 80 ppm for grass forage and 200 ppm for grass hay. The tolerance calculations are presented in Appendix I.

The analytical methods submitted under the subject action do not provide for conversion of residues of aminocyclopyrachlor-methyl to stoichiometric equivalents of aminocyclopyrachlor but the residue data presented herein does reflect correction to stoichiometric equivalents. The conversion factor, based on molecular weights (MWs) of 213.6 for aminocyclopyrachlor and 227.6 for aminocyclopyrachlor-methyl is 0.93849.

As noted above, comparison of the results for the side-by-side trials reflecting application of the 80% WG formulation of aminocyclopyrachlor-methyl and the 2 lb/gal SL formulation of aminocyclopyrachlor indicated that combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl were generally slightly higher following application of the aminocyclopyrachlor formulation. When the trial results for each set of trials are compared in terms of ppm, the results are:

For forage: 5 trials with higher residues following app of the SL (residues 1.2x higher) and 1 trial with higher residues following app of the WG (1.4x):

For hay: 3 trials with higher residues following app of the SL (1.1-1.3x) and 3 trials with higher residues following app of the WG (1.1-1.4x).

HED does not believe these differences are significant enough to warrant additional trials for the SL formulation.

860.1520 Processed Food and Feed

HED does not require residue data for any processed commodities associated with grass. Therefore, data requirements for processed food and feed are not relevant to this tolerance petition.

860.1650 Submittal of Analytical Reference Standards

An analytical standard for aminocyclopyrachlor acid (expiration 2013) is currently available in the EPA National Pesticide Standards Repository (personal communication between T. Cole, ACB, and Versar, 5/4/11); however, a standard for aminocyclopyrachlor-methyl is not currently available. An analytical reference standard for aminocyclopyrachlor-methyl must be supplied and supplies replenished as requested by the Repository. The reference standard should be sent to the Analytical Chemistry Lab, which is located at Fort Meade, to the attention of either Theresa Cole or Thuy Nguyen at the following address:

USEPA
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
701 Mapes Road
Fort George G. Meade, MD 20755-5350

(Note that the mail will be returned if the extended zip code is not used.)

860.1850 Confined Accumulation in Rotational Crops

DER Reference: 48333619.DER

E. I. du Pont de Nemours and Company has submitted a confined rotational crop study with [2-pyrimidinyl-^{14}C]aminocyclopyrachlor-methyl (specific activity 1.64 MBq/mg). The radiolabeled test substance was formulated as a 25% WP and applied to sandy loam soil as a single application at 0.067 lb ai/A (75 g ai/ha), equivalent to 0.063 lb ae/A (70 g ae/ha) aminocyclopyrachlor, or 0.329 lb ai/A (369 g ai/ha), equivalent to 0.309 lb ae/A (346 g ae/ha) aminocyclopyrachlor. The application rates correspond to ~0.2x and ~1.2x the maximum seasonal application rate for grasses. Rotational crops of cabbage, turnip, and field corn were planted at PBIs of 30, 60, 120, and 300 days after soil treatment (DAT) for cabbage and turnips, and 15, 120, and 300 DAT for corn following soil treatment at 0.067 lb ai/A, and at a PBI of 300 DAT for all crops following application at 0.329 lb ai/A. Samples of immature and mature cabbage and turnips (roots and tops), and corn (forage, stover, cobs, and grain) were collected at appropriate harvest intervals. The in-life and analytical phases of the study were conducted by Charles River Laboratories (Tranent, Edinburgh, Scotland).

Following application at 0.067 lb ai/A, TRR accumulated at >0.01 ppm in: 30- and 60-DAT immature and mature cabbage (0.013-0.027 ppm); 30-, 60-, 120-, and 300-DAT immature turnip tops (0.012-0.029 ppm); 60- and 120-DAT mature turnip tops (0.010-0.011 ppm), 30-day immature turnip roots (0.010 ppm); and 15-, 120- and 300-DAT corn forage (0.011-0.091 ppm), stover (0.023-0.149 ppm), and grain (0.012-0.067 ppm); and 15-DAT corn cobs (0.024 ppm). Following application at 0.329 lb ai/A, TRR accumulated at >0.01 ppm in immature and mature

cabbage (0.011-0.012 ppm), immature turnip tops (0.085 ppm), and corn forage, stover, cobs, and grain (0.246, 0.262, 0.012, and 0.085 ppm, respectively), planted 300 DAT. These matrices were subjected to further extraction and characterization procedures.

Approximately 57.3-100% TRR was extracted from rotational crop matrices using ACN:water. Nonextractable residues from the 15-DAT corn forage, stover, and grain and 300-DAT turnip tops and corn stover following application at 0.067 lb ai/A, and from 300-DAT turnip tops, and corn forage, stover, and grain following application at 0.329 lb ai/A were subjected to enzyme hydrolysis with α-amylase (50 ^{o}C for 72 hours) followed by a combination of amyloglucosidase and cellulase (50 ^{o}C for 48 hours) which released an additional 6.9-16.3 % TRR and 3.4-13.9% TRR, respectively. Subsequent hydrolysis with 0.01 N NaOH (60 ^{o}C for 6 hours) and 1 N HCl (60 ^{o}C for 6 hours) released an additional 1.1-3.4% TRR and 0.8-2.4% TRR, respectively. Remaining nonextractable residues following extraction and hydrolysis procedures were ≤0.009 ppm in all matrices. These procedures adequately extracted the majority of the residues from rotational crop matrices. Extraction results were normalized; therefore, accountabilities were 100%.

Because samples were stored frocen for ≤6 months prior to analysis, supporting storage stability data are not required. Extracts were stored for 7-163 days prior to analysis. Extracts of 30-DAT immature cabbage, 60-DAT immature turnip tops, and 15-DAT corn stover were reanalyzed following frozen storage for ~14 months to confirm the stability of the metabolite profile.

Residues were identified and quantitated in the ACN/water extracts and hydrolysates by HPLC. Only three residue components were identified in rotational crops: aminocyclopyrachlor, aminocyclopyrachlor-methyl, and IN-LXT69. aminocyclopyrachlor was the major identified residue and was detected in all crops (40.5-96.0% TRR). Aminocyclopyrachlor-methyl was a major metabolite in 30- and 60-DAT turnip tops (16-18% TRR) and 15-DAT corn forage and stover (9-10% TRR), but was a minor residue component in remaining matrices (≤5.6% TRR). IN-LXT69 was identified at low levels in 15-DAT corn stover and 300-DAT corn forage (≤1.9% TRR).

Aminocyclopyrachlor accounted for accounted for 83.1% and 80.1% TRR (0.014 and 0.021 ppm) in 30- and 60-DAT immature cabbage and for 60.0% and 60.6% TRR (0.014 and 0.008 ppm) in 30- and 60-DAT mature cabbage following application at 0.067 lb ai/A, and for 54.3% TRR (0.006 ppm) and 83.0% TRR (0.010 ppm) in 300-DAT immature and mature cabbage following application at 0.329 lb ai/A. In turnips, aminocyclopyrachlor accounted for 96.0% TRR (0.010 ppm) in 30-DAT immature roots, for 57.3-83.1% TRR (0.010-0.017 ppm) in 30-, 60-, 120-, and 300-DAT immature tops following application at 0.067 lb ai/A, and for 40.5-59.3% TRR (0.004-0.007 ppm) in 60- and 120-DAT mature turnip tops; residues of aminocyclopyrachlor were 85.6% TRR (0.072 ppm) in 300-DAT immature turnip tops following application at 0.329 lb ai/A.

In corn, aminocyclopyrachlor accounted for 62.7-71.4% TRR (0.007-0.176 ppm) in 15-, 120-, and 300-DAT forage following application at 0.067 and/or 0.329 lb ai/A. In stover, aminocyclopyrachlor accounted for 71.9% TRR (0.106 ppm) declining to 45.9% TRR (0.026 ppm) in 15-, 120-, and 300-DAT samples following application at 0.067 lb ai/A, and for 58.0%

TRR (0.151 ppm) in 300-DAT samples following application at 0.329 lb ai/A. Residues of DPX-MAT 28 in cobs accounted for 58.9% and 43.8% TRR (0.014 and 0.005 ppm) in 15-DAT and 300-DAT samples harvested following application at 0.067 and 0.329 lb ai/A, respectively. Residues in grain were 70.9-76.0% TRR (0.009-0.064 ppm) in 15-, 120-, and 300-DAT samples following application at 0.067 and/or 0.329 lb ai/A.

Aminocyclopyrachlor-methyl was identified in immature and mature 30-DAT cabbage, mature 60-DAT cabbage, and immature 300-DAT cabbage following application at 0.329 lb ai/A, and immature turnip roots at 3.3-4.6% TRR. In turnip tops, residues accounted for 15.9-17.8% TRR (0.002-0.003 ppm) in 30- and 60-DAT immature and mature tops, and for 5.6% TRR (0.001 ppm) in 120-DAT immature tops. In 15-DAT corn forage and stover, aminocyclopyrachlor-methyl accounted for 9.1-10.0% TRR (0.009-0.013 ppm); residues were identified at ≤5.4% TRR in 15-DAT grain and cobs, and 300-DAT forage and/or stover and grain following application at 0.067 and/or 0.329 lb ai/A. Remaining residues were characterized as minor unknowns, including an apolar unknown and multicomponent minor unknowns, which accounted for 5.0-6.9% TRR (0.012-0.018 ppm) and 16.3-25.3% TRR (0.038-0.064 ppm), respectively, in 300-DAT corn forage and stover following application at 0.329 ppm, and together accounted for ≤0.014 ppm in all remaining matrices.

Based on the results of the study, the petitioner proposed that metabolism of aminocyclopyrachlor-methyl in rotational crops involves the de-esterification of aminocyclopyrachlor-methyl to form the carboxylic acid, aminocyclopyrachlor. Aminocyclopyrachlor undergoes decarboxylation (to a much lesser extent) to form IN-LXT69. Succeeding crops grown in soils treated with aminocyclopyrachlor-methyl would be exposed primarily to aminocyclopyrachlor, the principal soil degradation product.

Conclusions. The confined rotational crop study is acceptable. HED concludes that the nature of the residue in rotational crops is adequately understood and that metabolism in rotational crops is similar to that in primary crops. The study results indicate that residues of aminocyclopyrachlor may exceed the 0.01-ppm trigger value in turnip tops and corn forage, stover, and grain at a 300-day PBI following application of aminocyclopyrachlor-methyl at ~1x the maximum proposed seasonal application rate to grass. Based on the study results limited rotational crop field trials are required for aminocyclopyrachlor to establish PBIs and/or tolerances for rotational crops.

Pending submission of the required limited field rotational crop trials, the labels must be revised to prohibit rotation to any crop other than grasses following application of aminocyclopyrachlor or aminocyclopyrachlor-methyl.

860.1900 Field Accumulation in Rotational Crops

Based on the results of the confined rotational crop study, limited rotational crop field trials are required for aminocyclopyrachlor to establish PBIs and/or tolerances for rotational crops.

Pending submission of the required limited field rotational crop trials, the labels must be revised to prohibit rotation to any crop other than grasses following application of aminocyclopyrachlor or aminocyclopyrachlor-methyl.

860.1550 Proposed Tolerances

DuPont has proposed that tolerances for aminocyclopyrachlor residues of concern in crop and livestock commodities be expressed in terms of combined residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl. HED has determined that the proposed tolerance expression as stated in Section F of the petition is appropriate:

> 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.

The analytical methods submitted under the subject action do not provide for conversion of residues of aminocyclopyrachlor-methyl to stoichiometric equivalents of aminocyclopyrachlor but the residue data presented herein does reflect correction to stoichiometric equivalents. The conversion factor, based on molecular weights (MWs) of 213.6 for aminocyclopyrachlor and 227.6 for aminocyclopyrachlor-methyl is 0.93849.

Adequate crop field trial data reflecting the proposed use patterns were submitted for purposes of establishing tolerances on grass forage and hay. The OECD MRL Calculator (March 2011 version) was utilized in determining the appropriate tolerance levels. The proposed tolerances of 65 and 125 ppm for grass forage and hay are too low. The tolerances should be established at 80 and 200 ppm, respectively.

An acceptable feeding study has been submitted in support of the proposed use on grasses. The data indicate that tolerances are needed for milk, and the tissues of cattle, goat, horse, and sheep. The proposed tolerance in milk is too high, and the proposed tolerances for liver and meat byproducts, except liver are not consistent with Agency policy. Livestock commodities, individual tolerances in cow, goat, horse, and sheep should be established for meat byproducts at 0.30 ppm, fat at 0.05 ppm, and meat at 0.02 ppm. The tolerance for milk should be established at 0.02 ppm. The tolerances for liver and meat byproducts, except liver should be removed.

There are currently no established Codex, Canadian, or Mexican maximum residue limits (MRLs) for aminocyclopyrachlor; therefore, there are no issues of harmonization. An International Residue Limit Status Sheet (IRLS) follows the references in this document.

The proposed and recommended tolerances for aminocyclopyrachlor as a result of the subject action are presented in Table 9. The proposed tolerances should be revised to reflect the recommended commodities and tolerance levels specified in Table 9.

Table 9. Tolerance Summary for Aminocyclopyrachlor.			
Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
Cattle, fat	0.07	0.05	
Cattle, liver	0.06	Not required	Based on current Agency policy a separate lower tolerance for liver is not appropriate
Cattle, meat	0.02	0.02	
Cattle, meat byproducts, except liver	0.4	Not required	
Cattle, meat byproducts	--	0.30	Based on current Agency policy, the meat byproducts tolerance should be based on the highest residue between liver, kidney, and fat.
Goat, fat	0.07	0.05	
Goat, liver	0.06	Not required	See comment for cattle, liver
Goat, meat	0.02	0.02	
Goat, meat byproducts, except liver	0.4	Not required	
Goat, meat byproducts	--	0.30	See comment for cattle, meat byproducts
Grass, forage	65	80*	
Grass, hay	125	200*	
Horse, fat	0.07	0.05	
Horse, liver	0.06	Not required	See comment for cattle, liver
Horse, meat	0.02	0.02	
Horse, meat byproducts, except liver	0.4	Not required	
Horse, meat byproducts	--	0.30	See comment for cattle, meat byproducts
Milk	0.035	0.02	
Sheep, fat	0.07	0.05	
Sheep, liver	0.06	Not required	See comment for cattle, liver
Sheep, meat	0.02	0.02	
Sheep, meat byproducts, except liver	0.4	Not required	
Sheep, meat byproducts	--	0.30	See comment for cattle, meat byproducts

*Based on OECD MRL Calculator

References

DP Number: 369057
Subject: Aminocyclopyrachlor: Human Health Risk Assessment for Proposed Uses as an Herbicide.
From: J. Ryman, J. Miller, and T. Morton
To: J. Tompkins and M. Ondish
Dated: 3/17/10
MRID(s): None

DP Number: 393619
Subject: Aminocyclopyrachlor. Report of the Residues of Concern Knowledgebase Subcommittee (ROCKS).
From: Ideliz Negrón-Encarnación
To: Aminocyclopyrachlor Risk Assessment Team
Dated: 9/22/11
MRID(s): None

International Residue Limits

Aminocyclopyrachlor (PC Code 288008; 5/05/11)

Summary of US and International Tolerances and Maximum Residue Limits				
Residue Definition:				
US		Canada	Mexico[2]	Codex[3]
40 CFR 180.###: Plant and livestock: 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		None		None
Commodity[1]	*Tolerance (ppm) /Maximum Residue Limit (mg/kg)*			
	US	Canada	Mexico[2]	Codex[3]
Cattle, fat	0.05			
Cattle, meat byproducts	0.30			
Cattle, meat	0.02			
Goat, fat	0.05			
Goat, meat byproducts	0.30			
Goat, meat	0.02			
Grass, forage	80			
Grass, hay	200			
Horse, fat	0.05			
Horse, meat byproducts	0.30			
Horse, meat	0.02			
Milk	0.02			
Sheep, fat	0.05			
Sheep, meat byproducts	0.30			
Sheep, meat	0.02			
Completed: M. Negussie; 05/05/2011				

[1] Includes only commodities of interest for this action. Tolerance values should be the HED recommendations and not those proposed by the applicant.

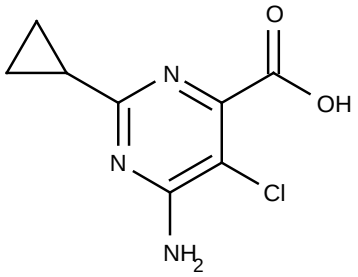
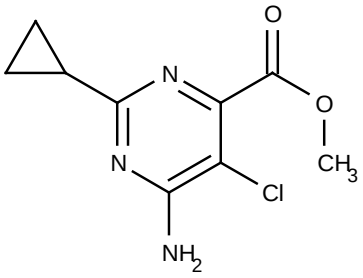
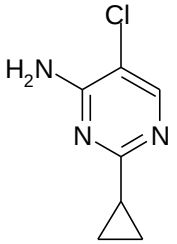
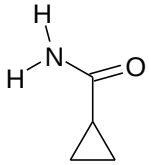
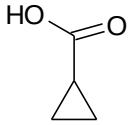
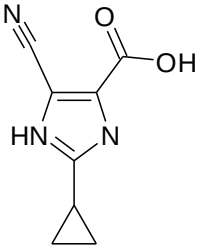
[2] Mexico adopts US tolerances and/or Codex MRLs for its export purposes.

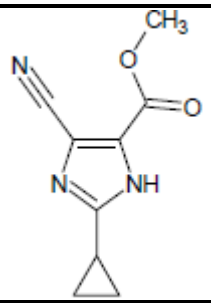
[3] * = absent at the limit of quantitation; Po = postharvest treatment, such as treatment of stored grains. PoP = processed postharvest treated commodity, such as processing of treated stored wheat. (fat) = to be measured on the fat portion of the sample. MRLs indicated as proposed have not been finalized by the CCPR and the CAC.

Attachments:

Appendix I - Chemical Names and Structures of Aminocyclopyrachlor Residues of Concern
Appendix II - Tolerance Assessment Calculations

Appendix I. Chemical Names and Structures of Aminocyclopyrachlor Residues of Concern.

Common name; Company code(s)	Chemical name	Chemical structure
Aminocyclopyrachlor; DPX-MAT28	6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid	
Aminocyclopyrachlor-methyl; DPX-KJM44 (methyl ester)	methyl 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylate	
IN-LXT69	5-chloro-2-cyclopropylpyrimidin-4-ylamine	
IN-Q3007	cyclopropanecarboxamide	
IN-V0977	cyclopropanecarboxylic acid	
IN-QFH57	4-cyano-2-cyclopropyl-1H-imidazole-5- carboxylic acid	

Common name; Company code(s)	Chemical name	Chemical structure
IN-QGC48	methyl-4-cyano-2-cyclopropyl-1H-imidazole-5-carboxylate	

Appendix II. Tolerance Assessment Calculations.

For each of the grass commodities listed below, the OECD MRL calculator (March 2011 version), was used for calculating recommended tolerances. The statistical goal of the OECD MRL calculator is to produce an MRL proposal in the region of the 95th percentile of the underlying residues distribution. The average residue values used to calculate the tolerances are provided in Table I-1. Residue values represent total residues of aminocyclopyrachlor (DPX-MAT28) and aminocyclopyrachlor-methyl (DPX-KJM44) converted to parent acid equivalents.

Table I-1. Residue data used to calculate tolerance for aminocyclopyrachlor in/on grass commodities.		
Regulator:	EPA	
Chemical:	Aminocyclopyrachlor	
Crop:	Grass forage	Grass hay
PHI:	0 Days	0 Days
App. Rate:	0.281 lb ai/A	0.281 lb ai/A
Submitter:	E.I. du Pont de Nemours and Company	E.I. du Pont de Nemours and Company
MRID Citation:	MRID 48333630	MRID 48333630
	Total Aminocyclopyrachlor Residues [Aminocyclopyrachlor + Aminocyclopyrachlor-methyl; ppm]	
	9.25	26.6
	10	28.5
	14.3	32.1
	14.7	35.2
	16.3	35.6
	17.5	36.4
	18.3	36.7
	19.5	41.6
	21.1	42.2
	25.9	43.8
	26.9	47.3
	27.1	48.2
	28.5	48.5
	30.5	49
	31.8	54.5
	32.9	55.9
	33.5	58.7
	40.9	72.5
	47.3	75.8
	50.3	90.2
	14.3	112
	18.3	122

Grass forage

The dataset used to establish a tolerance for aminocyclopyrachlor on grass forage consisted of field trial data representing application rates of 0.274-0.299 lb ai/A aminocyclopyrachlor with a 0-day PHI. The field trial application rates and PHIs are within 25% of the maximum label application rate and minimum label PHI, respectively. The average residues values used to calculate the tolerance are provided in Table I-1. Residue values represent total residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl converted to parent acid equivalents. Residues of both aminocyclopyrachlor and aminocyclopyrachlor-methyl were quantifiable (LOQ = 0.01 ppm) in/on all samples of grass forage.

The aminocyclopyrachlor grass forage dataset was entered into the OECD MRL calculator; the recommended tolerance is 80 ppm for grass forage.

Aminocyclopyrachlor
Grass Forage
US and Canada
1 appl @0.281 lb ai/A 0-day PHI

Total number of data (n)	22
Percentage of censored data	0%
Number of non-censored data	22
Lowest residue	9.250
Highest residue	50.300
Median residue	23.500
Mean	24.961
Standard deviation (SD)	11.334
Correction factor for censoring (CF)	1.000
Proposed MRL estimate	
- Highest residue	50.300
- Mean + 4 SD	70.298
- CF x 3 Mean	74.884
Unrounded MRL	74.884
Rounded MRL	**80**

Grass hay

The dataset used to establish a tolerance for aminocyclopyrachlor on grass hay consisted of field trial data representing application rates of 0.274-0.299 lb ai/A aminocyclopyrachlor with a 0-day PHI. The field trial application rates and PHIs are within 25% of the maximum label application rate and minimum label PHI, respectively. The average residues values used to calculate the tolerance are provided in Table I-1. Residue values represent total residues of aminocyclopyrachlor and aminocyclopyrachlor-methyl. Residues of both aminocyclopyrachlor and aminocyclopyrachlor-methyl were quantifiable (LOQ = 0.01 ppm) in/on all samples of grass forage.

The aminocyclopyrachlor grass hay dataset was entered into the OECD MRL calculator; the recommended tolerance is 200 ppm for grass hay.

Aminocyclopyrachlor
Grass Hay
US and Canada
1 appl @0.281 lb ai/A 0-day PHI

Total number of data (n)	22
Percentage of censored data	0%
Number of non-censored data	22
Lowest residue	26.600
Highest residue	122.000
Median residue	47.750
Mean	54.241
Standard deviation (SD)	25.684
Correction factor for censoring (CF)	1.000
Proposed MRL estimate	
- Highest residue	122.000
- Mean + 4 SD	156.977
- CF x 3 Mean	162.723
Unrounded MRL	162.723
Rounded MRL	**200**