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OFFICE OF PREVENTION, PESTICIDE
AND TOXIC SUBSTANCES

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

Date: 10/22/2009

SUBJECT: Aminopyralid and Aminopyralid Triisopropanolammonium (TIPA) Salt. Request to Add Uses on Field Corn to Milestone® (EPA Reg. No. 62719-519). Summary of Analytical Chemistry and Residue Data.

PC Codes: 005100 (Aminopyralid) and 005209 (Aminopyralid TIPA Salt)	**DP Barcode:** D360100
Decision No.: 401475	**Registration No.:** 62719-519
Petition No.: PP#8F7455	**Regulatory Action:** Section 3 Registration
Risk Assessment Type: NA	**Case No.:** NA
TXR No.: NA	**CAS No.:** 150114-71-9 (Aminopyralid) and 566191-89-7 (Aminopyralid TIPA Salt)
MRID No.: 46661301, 46729001, 46729601-03, 47572601, 47572603-04	**40 CFR:** 180.610

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This document was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850). The document has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

Executive Summary

Aminopyralid is a systemic postemergence herbicide which belongs to the pyridine carboxylic acid class of herbicides. It is currently registered for use on rangeland, permanent grass pastures, and wheat. In addition, it is registered for use on wildlife habitat and industrial vegetation management areas, including right-of-way for roads, railroads, and utility lines.

Under PP#8F7455, Dow AgroSciences is proposing the establishment of permanent tolerances for aminopyralid (2-pyridine carboxylic acid, 4-amino-3,6-dichloro-), expressed as total parent, free and conjugated, in or on the following raw agricultural commodities:

Corn, forage	0.30 ppm
Corn, grain	0.20 ppm
Corn, stover	0.20 ppm

In conjunction with the submitted petition, Dow AgroSciences is requesting an amended Section 3 registration to add uses on field corn to Milestone® (EPA Reg. No. 62719-519), a liquid soluble concentrate (SL) formulation in which aminopyralid is formulated as the triisopropanolammonium (TIPA) salt. The product contains 40.6% aminopyralid TIPA salt at an acid equivalent (ae) of 21.1% or 2 lb ae/gal. The product is proposed for postemergence foliar broadcast or spot applications to field corn up to the V6 growth stage at a maximum seasonal rate of 0.027 lb ae/A. Preharvest intervals (PHIs) of 0 days for grain and 8 days for forage or silage are proposed.

Tolerances for aminopyralid are currently established under 40 CFR §180.610. Tolerances for residues in/on crop commodities are established under 180.610(a)(1) and are expressed in terms of free and conjugated residues of aminopyralid, calculated as aminopyralid. Tolerances have been established for aspirated grain fractions, grass forage and hay, and wheat bran, forage, grain, hay, and straw. Tolerances for residues in livestock commodities are established under 180.610(a)(2) and are expressed in terms of aminopyralid. Tolerances have been established for milk and the fat, kidney, meat, and meat byproducts of cattle, goat, horse, and sheep.

The qualitative nature of aminopyralid residues in field corn is adequately understood for the purposes of this petition based on previously submitted metabolism studies with grass and wheat. In metabolism studies reflecting foliar applications to grass and wheat, aminopyralid was found to be metabolized to a multi-component mixture of water-soluble complexes that consist mostly of isomeric mixtures of acid- and base-labile N-glucosides and glucose ester conjugates of aminopyralid. HED concluded that the residues of concern in grass and cereal grain commodities are free and conjugated aminopyralid.

Previously submitted metabolism studies with lactating goats and laying hens show that most of the administered dose is rapidly excreted (~80% for hens and ~95% for goat). Residues in all poultry commodities, including eggs, were too low to allow identification of residues (residues were less than 0.004 ppm aminopyralid-equivalents across all commodities). In the goat, residues were less than 0.008 ppm aminopyralid-equivalents in all commodities except kidney.

In kidney, 80% of the residues (0.07 ppm) were identified as parent aminopyralid. Although residues in other tissues were too low to permit identification, the weight of the evidence is that the limited amount of aminopyralid that is not excreted remains as the parent compound. Therefore, the residue of concern in livestock is aminopyralid.

Adequate high performance liquid chromatography (LC) methods with tandem mass spectroscopy detection (MS/MS) have been submitted for tolerance enforcement for crop and livestock commodities. The validated limit of quantitation (LOQ) is 0.01 ppm in each matrix. Samples from the submitted field corn crop field trial and processing studies were analyzed using the crop commodity tolerance enforcement method. Samples of grass and wheat commodities from the submitted storage stability study were analyzed using a previous version of the crop commodity enforcement method.

The submitted storage stability data are adequate to support the crop field trial study and the field corn processing study.

Acceptable field corn crop field trial studies have been submitted. The proposed use on field corn must be amended to remove the proposed PHIs of 0 and 8 days for grain and forage, as the submitted data do not support these low PHIs. The data support application to field corn up to the V6 growth stage, with harvest of forage occurring at the dent growth stage or later. The data support the proposed tolerances of 0.30 ppm for field corn forage and 0.20 ppm for field corn grain and stover.

The submitted field corn processing study is adequate and indicates that tolerances are not needed for field corn processed commodities, and that no change in the existing tolerance for aspirated grain fractions is needed as a result of the proposed uses on field corn.

The nature of the residue in rotational crops is adequately understood based on a previously submitted study with lettuce, turnip, and sorghum. No field rotational crop data have been submitted for aminopyralid. Although the proposed uses reflect an increased maximum seasonal rate, a limited field rotational crop study with aminopyralid does not need to be submitted. The only crops which are likely to have quantifiable residues at the requested plantback intervals (PBIs) are wheat, grasses, and corn, all of which will be treated as primary crops and have tolerances to cover the resulting residues. HED considers the rotation intervals listed on the supplemental label for field corn to be adequate.

No changes to the existing tolerances for livestock commodities are needed as a result of the proposed uses on field corn.

Codex and Canadian MRLs have been established for residues of aminopyralid; however, no MRLs have been established for the requested crop commodities. No Mexican MRLs have been established for aminopyralid.

Regulatory Recommendations and Residue Chemistry Deficiencies

HED has examined the residue chemistry database for aminopyralid. Pending submission of a revised Section B (see requirements under Directions for Use) and a revised Section F (see requirements under Proposed Tolerances), there are no residue chemistry issues that would preclude granting Section 3 registration for the requested uses of aminopyralid, or establishment of tolerances for residues of aminopyralid, as follows:

Corn, field, forage	0.30 ppm
Corn, field, grain	0.20 ppm
Corn, field, stover	0.20 ppm

HED recommends that 40CFR §180.610(a)(1) be amended by replacing the tolerance expression with the following: "Tolerances are established for residues of aminopyalid (4-amino-3,6-dichloro-2-pyridinecarboxylic acid), 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 free and conjugated aminopyralid." HED further recommends that 40CFR §180.610(a)(2) be amended by replacing the tolerance expression with the following: "Tolerances are established for residues of aminopyralid, 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 aminopyralid."

With the review of the interference study and the final report of the grass and wheat storage stability study in this document, all the data requirements that were identified as conditions of registration in the previous aminopyralid petition (PP#4F6827; D305665, M. Doherty, 7/12/05) have now been satisfied.

860.1200 Directions for Use

- The proposed label must be modified to specify that spray or spot applications may not be made after the V6 growth stage (BBCH 16) and that forage may not be harvested prior to the dent stage of growth. If the petitioner wishes to support a shorter PHI for field corn forage (or harvest of forage at an earlier growth stage), then adequate crop field trial data reflecting the shorter PHI and/or earlier forage harvest must be submitted.

860.1550 Proposed Tolerances

- The proposed tolerances should be revised to reflect the correct commodity definitions as specified above and in Table 8.

Background

Aminopyralid is a systemic postemergence herbicide that belongs to the pyridine carboxylic acid class of herbicides. The chemical structure and nomenclature of aminopyralid and aminopyralid TIPA salt are presented in Table 1. The physiochemical properties of the technical grade of aminopyralid are presented in Table 2.

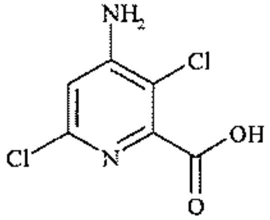
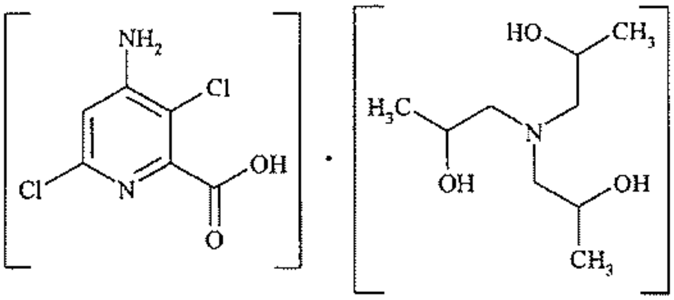
Table 1. Aminopyralid Nomenclature.	
Chemical structure	
Common name	Aminopyralid
Company experimental name	XDE-750
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid
CAS name	4-amino-3,6-dichloro-2-pyridinecarboxylic acid
CAS registry number	150114-71-9
Chemical structure	
Common name	Aminopyralid, triisopropanolammonium (TIPA) salt
PC Code	005209
Company experimental name	XDE-750 TIPA salt
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid - (2RS,2'RS,2"RS)-1,1',1"-nitrilotripropan-2-ol (1:1)
CAS name	4-amino-3,6-dichloropyridine-2-carboxylic acid compound with 1,1',1"-nitrilotris[2-propanol] (1:1)
CAS registry number	566191-89-7
End-use product (EP)	Milestone® (2 lb ae/gal SL; EPA Reg. No. 62719-519)

TABLE 2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value	Reference
Melting point/range	163.5°C	MRID 46235703
pH	2.31 at 23.4°C (1% solution in water)	MRID 46235703
Density	1.72 at 20°C	MRID 46235703
Water solubility	2.48 g/L unbuffered water at 18°C 212 g/L pH 5 buffer at 20°C 205 g/L pH 7 buffer at 20°C 203 g/L pH 9 buffer at 20°C	MRID 46235703
Solvent solubility at 20°C	methanol 52.2 g/L acetone 29.2 g/L n-octanol 3.9 g/L ethyl acetate 3.9 g/L 1,2-dichloroethane 0.2 g/L xylene 0.04 g/L heptane <10 µg/mL	MRID 46235703
Vapor pressure	2.59×10^{-8} Pa at 25°C; 9.52×10^{-9} Pa at 20°C	MRID 46235703
Dissociation constant, pK_a	2.56	MRID 46235703
Octanol/water partition coefficient, Log(K_{OW})	0.201 unbuffered water at 19°C -1.76 at pH 5 -2.87 at pH 7 -2.96 at pH 9	MRID 46235703
UV/visible absorption spectrum	Solution / Wavelength λ max, nm / Extinction coefficient L/(mol*cm) Neutral 217 29100 Basic (pH 12.6) 220 26100 Basic (pH 12.6) 245 10150 Acidic (pH 1.4) 217 22800 Acidic (pH 1.4) 270 9140	MRID 46235703

860.1200 Directions for Use

The petitioner submitted a proposed supplemental label (pin punched with date 10/15/08) for the 2 lb ae/gal SL product (Milestone®; EPA Reg. No. 62719-519) for use on field corn. The proposed use directions are presented in Table 3. The supplemental label states that use is subject to all use precautions and limitations imposed by the label on the parent product.

Table 3. Summary of Directions for Use of Aminopyralid.

Applic. Timing, Type, and Equip.	Formulation (EPA Reg. No.)	Applic. Rate (lb ae/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Field Corn and Field Corn grown for Ensilage						
Postemergence, Broadcast, Ground	2 lb ae/gal SL (62719-519)	0.0089-0.027	Not specified	0.027	0 (grain); 8 (forage or silage)	Application is to be made to actively growing corn before it reaches 20 inches in height or V6 growth stage. Spot treatments are to be made at rates equivalent to broadcast application, in a minimum spray volume of 0.5 gal/1,000 ft^2.
Postemergence, Spot treatment, Ground		0.00021-0.00063 lb ae/1,000 ft^2				

The label specifies that aerial applications are not to be made unless permitted by EPA-approved supplemental labeling. Under the mixing instructions, the master label specifies that a non-ionic surfactant at 0.25-0.5% v/v (1-2 quarts per 100 gallons spray) is recommended to enhance herbicide activity under adverse environmental conditions.

The following rotational crop restrictions are specified: 0-month plantback interval for wheat; 4-month plantback interval for grasses and field corn; 12-month plantback interval for barley, canola (rapeseed), flax, grain sorghum, mustard, oats, sweet corn, and popcorn; and a 24-month plantback interval for crops not listed. The label also specifies that a field bioassay should be conducted prior to planting any broadleaf crops not listed within 18 months of application.

Conclusions. The submitted label is adequate to allow evaluation of the residue data relative to the proposed use. The submitted crop field trial data represent application at the proposed maximum seasonal rate (with a nonionic surfactant) and at the proposed growth stage. The proposed PHIs of 0 days for grain and 8 days for forage or silage are not supported by the submitted data. The proposed label should be modified to specify that spray or spot applications may not be made after the V6 growth stage (BBCH 16) and that forage may not be harvested prior to the dent stage of growth. If the petitioner wishes to support a shorter PHI for field corn forage (or harvest of forage at an earlier growth stage), then adequate crop field trial data reflecting the shorter PHI and/or earlier forage harvest must be submitted.

860.1300 Nature of the Residue - Plants

Residue Chemistry Memo DP# 305665, 7/12/05, M. Doherty (PP#4F6827)

The nature of the residue in field corn is adequately understood for the purposes of this petition based on previously submitted metabolism studies with grass and wheat. The major residue identified in these studies was the parent aminopyralid (free and conjugated). In the grass metabolism study, there did not appear to be any significant metabolic alterations to the basic structure of the parent compound, with the exception of a minor conjugated metabolite formed by addition of a hydroxyl group to the parent molecule and found to be present at <1% total radioactive residues (TRR). Aminopyralid was rapidly conjugated to yield a multi-component mixture of water-soluble complexes which consisted mostly of isomeric mixtures of acid- and base-labile N-glucosides and glucose ester conjugates of aminopyralid. In the wheat metabolism study, the petitioner concluded that the major metabolic pathway of aminopyralid in wheat proceeded via conjugation of aminopyralid and hydroxylated aminopyralid with glucose. The petitioner further concluded that any metabolites present in wheat which were not identified were believed to be conjugates of glucose or similar endogenous compounds, based on the fact that most of the radioactivity in the wheat samples that was not initially detected as the parent could be hydrolyzed to aminopyralid.

Based on these studies, HED concluded that the residues of concern in grass and cereal grain commodities are free and conjugated aminopyralid. Additional metabolism data will be required to support uses on non-grass or non-grain commodities.

860.1300 Nature of the Residue - Livestock

Residue Chemistry Memo DP# 305665, 7/12/05, M. Doherty (PP#4F6827)

The nature of the residue in livestock is adequately understood based on previously submitted studies with goat and hen. Although the residues in the goat and hen studies were too low to allow adequate characterization/identification of residues, HED concluded that new studies would not be needed. The available metabolism data from the goat, hen, and rat indicate that the majority of the administered aminopyralid is excreted as unchanged parent in all three species, and the small amount which is absorbed remains unchanged. Therefore, the residue of concern in livestock is aminopyralid. This finding is supported by the residues of concern for the related compounds picloram and clopyralid which, in each case, show parent compound to be the major residue.

860.1340 Residue Analytical Methods

Crop commodities

DER References: 46729001.der.doc
47572602.de1.doc
MRID 46729601 (no DER; reviewed herein)
MRID 46729603 (no DER; reviewed herein)
Residue Chemistry Memo DP# 305665, 7/12/05, M. Doherty (PP#4F6827)
Analytical Chemistry Branch Memo DP# 312724, 11/3/05, D. Wright

Enforcement method: Dow AgroSciences had previously proposed an LC/MS/MS method, Method GRM 02.31, for the enforcement of tolerances for aminopyralid residues in grass and wheat commodities. The method was adequately validated in barley grain, forage, and straw; grass forage and hay; sorghum grain, forage, and stover; and wheat grain, forage, and straw.

Adequate ILV data were submitted for the method using grass forage and wheat grain, and adequate radiovalidation data were submitted for the extraction procedures using samples of grass and wheat commodities bearing incurred residues from the metabolism studies.

Method GRM 02.31 was sent to ACB for review. It was concluded that the method was adequate for enforcement purposes and that no laboratory validation at ACB was needed. ACB concluded that the method needed confirmatory procedures. The single ion transition monitored in the method is not considered sufficient for positive confirmation of analyte information. ACB additionally noted two errors in the analyte peak response area and quantitation ratio data reported in one of the representative chromatograms in the independent laboratory validation study (MRID 46235712).

In review of Method GRM 02.31, HED expressed concern that the proposed enforcement method might not be able to differentiate between aminopyralid, picloram, and clopyralid, and requested that the petitioner complete an interference study using these three compounds.

In response, the petitioner submitted a revised version of Method GRM 02.31 in MRID 46729601. The revised method includes instructions for monitoring two additional MS/MS transitions for confirmation of residue identity. In addition, the petitioner submitted MRID 46726903, a revised version of the ILV study, in which the two errors noted by ACB in the representative chromatogram were corrected.

In addition, Dow AgroSciences submitted the requested interference study for the derivatization and LC/MS/MS analysis procedures of Method GRM 02.31. To investigate the potential inference of picloram and clopyralid in the determination of aminopyralid, the petitioner prepared analytical standards of picloram and clopyralid, as well as aminopyralid, and derivatized the standards to form the 1-butyl esters of the compounds using the procedures of Method GRM 02.31. The derivatized compounds were then analyzed by LC/MS/MS.

The analysis of the 1-butyl esters of aminopyralid, clopyralid, and picloram demonstrated that the three compounds have different retention times and that there was no interference in the ion transitions. Therefore, clopyralid and picloram do not interfere in the determination of aminopyralid residues using Method GRM 02.31.

The petitioner noted that, since the original aminopyralid methods were developed, minor changes in the LC conditions and MS/MS parameters have been made to improve the sensitivity and selectivity of the method, including the addition of two ion transitions to monitor for the confirmation of aminopyralid residues. Representative chromatograms from the analysis of a grass forage sample were provided for the quantitation ion transition and the two confirmation ion transitions. The changes in the LC and MS/MS conditions are reflected in the revised methods that were submitted with this tolerance petition: Method GRM 07.07 for crop commodities and Method GRM 07.08 for livestock commodities (see below).

With PP#8F7455, Dow AgroSciences has proposed an LC/MS/MS method, Method GRM 07.07, for the determination of residues of aminopyralid in crop commodities (wet, dry, acidic, and oily crops). The method description indicates that Method GRM 07.07 supersedes Method 02.31. The major differences between the two methods are that Method GRM 02.31 uses a different internal standard ($^{13}C_2{}^{15}N$-aminopyralid) and only includes instructions for the determination of residues in barley, sorghum, wheat, and grass commodities.

Briefly, residues are extracted from homogenized agricultural commodities using 0.1 N NaOH, which hydrolyzes bound residues and base-labile conjugates to yield free aminopyralid. The hydrolysate is acidified with 2 N HCl. Oil samples are extracted with acetone and the extract is evaporated to dryness, redissolved in hexane, and partitioned into water. The aqueous phase is mixed with 0.2 N NaOH to hydrolyze bound residues and base-labile conjugates to yield free aminopyralid, and then acidified with 3 N HCl. For both crop samples and oil samples, the acidified extract is heated at 80°C for 90 minutes, which hydrolyzes acid-labile conjugates to yield free aminopyralid and further solubilizes bound residues. The extract is then purified by anion-exchange solid phase extraction (SPE), using ethyl acetate:trifluoroacetic acid (99:1, v:v) to elute residues. An internal standard ($^{13}C_2{}^{2}H^{15}N$-aminopyralid) is added to the eluate, which is evaporated to dryness, reconstituted in acetonitrile:pyridine:1-butanol (22:2:1, v:v:v; derivatization coupling reagent) and derivatized with butyl chloroformate to form the 1-butyl esters of the analyte and the internal standard. The mixture is diluted with a solution of methanol:water (40:60, v:v) containing 0.05% formic acid and 5 mM ammonium formate for LC/MS/MS analysis. The LOQ and limit of detection (LOD) are 0.01 and 0.003 ppm, respectively, for aminopyralid in each tested matrix.

Method GRM 07.07 was adequately validated using samples of untreated wet crops (broccoli and tomato), dry crops (wheat forage, grain, and straw, corn forage and grain, and grass forage and straw), acidic crops (lemon whole fruit and orange peel, pulp, and whole fruit), and oily crops (palm oil and sunflower seed) fortified with aminopyralid at 0.01 and 2 ppm for all crops other than grass forage and straw, and at 0.01 and 50 ppm for grass forage and straw. The recovery ranges for these matrices were 75-102% for wet crops (average ± standard deviation: 86% ± 6.6%), 70-102% for dry crops (86% ± 8.3%), 72-105% for acidic crops (88% ± 7.4%), and 82-106% for oily crops (93% ± 6.5%).

The fortification levels and samples used in method validation are adequate to bracket expected residue levels. Although field corn stover, aspirated grain fractions, and processed commodities were not included in the validation study, adequate concurrent method recovery data for these commodities were included with the field corn field trial and processing studies submitted with this petition.

The method includes instructions for monitoring up to three ion transitions for aminopyralid; therefore, confirmatory analysis procedures are not needed.

The method is very similar to the current enforcement method, LC/MS/MS Method GRM 02.31, for which adequate radiovalidation and independent laboratory validation data have been submitted. Because Method GRM 07.07 is considered to be an improvement to Method GRM 02.31, no independent laboratory validation or validation by ACB is needed.

Data collection method: Method GRM 07.07 was used for data collection in samples of corn forage, grain, stover, aspirated grain fractions, and processed commodities from the crop field trial and processing studies submitted with this petition. Overall concurrent method recoveries ranged 69-90% from forage, 75-97% from grain, 72-94% from stover, and 75-98% from corn processed commodities. Samples of grass and wheat commodities from the storage stability study were analyzed using Method GRM 02.31; overall concurrent method recoveries ranged 71-106%.

Conclusions. The submitted crop analytical method data are adequate to satisfy data requirements. Method GRM 07.07 satisfies all requirements for an enforcement method for crop commodities. The method will be forwarded to the FDA for publication in PAM Vol. II.

The submitted interference study satisfies the data requirements for this study identified in PP#4F6827 (Memo, D305665, M. Doherty, 7/12/05).

Livestock commodities

DER References: 47572602.de2.doc
MRID 46729602 (no DER; reviewed herein)
Residue Chemistry Memo: D305665, M. Doherty, 7/12/05 (PP#4F6827)
Analytical Chemistry Branch Memo: D312724, D. Wright, 11/3/05

Enforcement method: Dow AgroSciences had previously proposed an LC/MS/MS method, Method GRM 03.18, for the enforcement of tolerances for aminopyralid residues in ruminant milk and tissues. The method was adequately validated in bovine whole milk, cream, skimmed milk, fat, kidney, liver, and muscle, and adequate ILV data were submitted for the method using bovine milk and kidney. RAB2 concluded that radiovalidation data were not needed for the method because the extraction procedures are very similar to those used in the goat metabolism study. The method was sent to ACB for review. It was concluded that the method was adequate for enforcement purposes and that no laboratory validation at ACB was needed. ACB concluded that the method needed confirmatory procedures. ACB additionally noted that step 9.3.17 of Method GRM 03.18 referred to Section 7.5.1 of the method, which does not exist.

In response, the petitioner submitted a revised version of Method GRM 03.18 in MRID 46729602. The revised method includes instructions for monitoring two additional MS/MS transitions for confirmation of residue identity. In addition, the erroneous reference to Section 7.5.1 was removed.

In review of Method GRM 03.18, HED expressed concern that the proposed enforcement method might not be able to differentiate between aminopyralid, picloram, and clopyralid, and requested that the petitioner complete an interference study using these three compounds. The requested inference study for Method GRM 02.31 has been submitted (see above). Because the derivatization and LC/MS/MS analysis procedures of Method GRM 02.31 are the same as those of Method GRM 03.18, the interference study is sufficient to demonstrate that clopyralid and picloram will not interfere in aminopyralid determination using Method GRM 03.18.

With PP#8F7455, Dow AgroSciences has proposed LC/MS/MS Method GRM 07.08 for the determination of residues of aminopyralid in cattle and poultry tissues, milk, and eggs. The method description indicates that Method GRM 07.08 supersedes Method GRM 03.18. The major differences between the two methods are that Method GRM 03.18 uses a different internal standard ($^{13}C_2{}^{15}N$-aminopyralid) and only includes instructions for the determination of residues in bovine commodities (muscle, fat, liver, kidney, and milk).

Briefly, sodium bicarbonate is added to homogenized livestock commodities and the mixture is extracted using methanol. The extract is purified by anion-exchange SPE, using ethyl acetate:trifluoroacetic acid (99:1, v:v) to elute residues. An internal standard ($^{13}C_2{}^{2}H^{15}N$-aminopyralid) is added to the eluate, which is evaporated to dryness, reconstituted in acetonitrile:pyridine:1-butanol (22:2:1, v:v:v; derivatization coupling reagent) and derivatized with butyl chloroformate to form the 1-butyl esters of the analyte and the internal standard. The mixture is diluted with a solution of methanol:water (40:60, v:v) containing 0.05% formic acid and 5 mM ammonium formate for LC/MS/MS analysis. The LOQ and LOD are 0.01 and 0.003 ppm, respectively, for aminopyralid in each tested matrix.

The method was adequately validated using samples of untreated cattle milk, kidney, and fat and poultry egg, liver, and muscle fortified with aminopyralid at 0.01 and 2 ppm. The recovery ranges for these matrices were 90-119% for bovine matrices (average of 98% with a standard deviation of 5.7%) and 82-111% for poultry matrices (average of 95% with a standard deviation of 5.9%). The fortification levels and samples used in method validation are adequate to bracket expected residue levels. Radiovalidation data are not needed for Method GRM 07.08 as the extraction procedures are very similar to those of Method GRM 03.18.

The method includes instructions for monitoring up to three ion transitions for aminopyralid; therefore, confirmatory analysis procedures are not needed.

The method is very similar to the current enforcement method, LC/MS/MS Method GRM 03.18. Because Method GRM 07.08 is considered to be an improvement to Method GRM 03.18, no independent laboratory validation or validation by ACB is needed.

Conclusions. The submitted livestock analytical method data are adequate to satisfy data requirements. Method GRM 07.08 satisfies all requirements for an enforcement method for livestock commodities. The method will be forwarded to FDA for publication in PAM Vol. II.

860.1360 Multiresidue Methods

Residue Chemistry Memo D305665, M. Doherty, 7/12/05

Adequate multiresidue method testing data have been submitted previously for aminopyralid. The results of the study indicate that the FDA multiresidue methods in PAM Vol. I are not suitable for the determination of aminopyralid.

860.1380 Storage Stability

DER Reference: 46661301.der.doc
Residue Chemistry Memo D305665, M. Doherty, 7/12/05

Dow AgroSciences has submitted the final report of a storage stability study with aminopyralid on grass forage and hay, and wheat grain and straw. An interim report for this study, reflecting storage intervals of up to ~6 months, was previously reviewed under PP#4F6827. Samples of untreated grass forage, grass hay, wheat grain, and wheat straw were fortified with aminopyralid at 0.1 ppm and stored frozen (~-20°C). Storage intervals tested were 0, 28, 130, 187, and 488 days (grass forage and hay) or 0, 113, 168/175, 273, and 469 days (wheat grain and straw).

Samples of grass hay and forage, and wheat grain and straw were analyzed for residues of aminopyralid using LC/MS/MS Method GRM 02.31. The method was adequate for data collection based on acceptable concurrent method recoveries; the reported LOQ was 0.01 ppm for each commodity.

The study results indicate that residues of aminopyralid are stable during frozen storage for up to ~16 months in/on grass forage and hay, and for up to ~15 months in/on wheat grain and straw.

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

Table 4. Summary of Storage Conditions and Durations of Samples from Field Corn Crop Field Trial and Processing Studies.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Field corn forage	~-20	435-518 days (14.3-17.0 months)	Residues of aminopyralid are stable during frozen storage for up to ~16 months in/on grass forage and hay, and for up to ~15 months in/on wheat grain and straw.
Field corn grain		375-448 days (12.3-14.7 months)	
Field corn stover		377-448 days (12.4-14.7 months)	
Field corn AGF		350 days (11.5 months)	No storage stability data are available for field corn processed commodities.
Flour		355 days (11.7 months)	
Grits		384 days (12.6 months)	
Meal		355 days (11.7 months)	
Starch		341 days (11.2 months)	
Refined oil (wet milled)		387 days (12.7 months)	
Refined oil (dry milled)		350 days (11.5 months)	

[1] From harvest/collection to extraction for analysis.

Conclusions. The submitted storage stability study is adequate to fulfill data requirements for samples of field corn forage, grain, and stover from the submitted field trial and processing studies. The data indicate that no correction for residue decline during storage will be needed for these commodities.

The data are also adequate to support the storage conditions and durations of field corn processed commodities from the processing study submitted to support this petition. Although a storage stability study with aminopyralid residues in field corn processed commodities was not submitted, the available storage stability data for the wheat and grass commodities will be considered to be adequate to support the field corn processing study. The OECD guideline "Stability of Pesticide Residues in Stored Commodities" (adopted 10/16/2007) states that storage stability data for processed foods are not needed if residue decline is not observed across the range of five commodity categories. In this case, HED considers the data for grain and grass commodities to be adequate in light of the minimal metabolism of aminopyralid in living plants. Conjugation is the only significant metabolic pathway, and the resulting conjugates are determined by the analytical method.

The dates of analysis were not provided for the subject field trial and processing studies. For future submissions, the petitioner should note that dates of extraction and analysis should be provided for all samples.

Submission of the final report of the grass and wheat storage stability study satisfies the data requirements for storage stability identified in PP#4F6827 (Memo, D305665, M. Doherty, 7/12/05). No correction for residue decline is needed for any of the grass or wheat commodity samples submitted under PP#4F6827.

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

Residue Chemistry Memo: D305665, M. Doherty, 7/12/05

There are several livestock feedstuffs associated with the registered and proposed uses of aminopyralid, including AGF (and milled byproducts); grass forage, grass hay, field corn grain, field corn forage, field corn stover, wheat grain, wheat forage, wheat hay, and wheat straw. The dietary burdens of aminopyralid to livestock, based on reasonably balanced diets, are presented in Table 5. The estimated dietary burdens are 8.7 ppm for beef cattle, 45 ppm for dairy cattle, 0.15 ppm for poultry, and 0.17 ppm for swine.

Table 5. Calculation of Dietary Burdens of Aminopyralid Residues to Livestock.

Feedstuff	Type[1]	% Dry Matter[2]	% Diet[2]	Established/ Recommended Tolerance (ppm)	Dietary Contribution (ppm)[3]
Beef Cattle					
Grass hay	R	88	15	50	8.5
Corn, field, grain	CC	88	80	0.20	0.18
PC without registered uses	PC	--	5	--	--
TOTAL BURDEN	--	--	100	--	**8.7**
Dairy Cattle					
Grass, forage	R	25	45	25	45
Corn, field, grain	CC	88	45	0.20	0.10
PC without registered uses	PC	--	10	--	--
TOTAL BURDEN	--	--	100	--	**45**
Poultry					
Corn, field, grain	CC	88	75	0.20	0.15
PC without registered uses	PC	--	25	--	--
TOTAL BURDEN	--	--	100	--	**0.15**
Swine					
Corn, field, grain	CC	88	85	0.20	0.17
PC without registered uses	PC	--	15	--	--
TOTAL BURDEN	--	--	100	--	**0.17**

[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.

Ruminants: The dietary burdens of aminopyralid to livestock were previously calculated to be 60 ppm for beef and dairy cattle and 0.075 ppm for swine. Based on an adequate dairy cattle feeding study, reflecting dosing of dairy cattle with aminopyralid at levels of 32.8, 64.5, 181.5, or 644.7 ppm in the diet, RAB2 concluded that tolerances were needed for livestock commodities at 0.03 ppm for milk; 0.02 ppm for the meat and meat byproducts, excluding kidney, of cattle, goats, horses, and sheep; 0.02 ppm for the fat of cattle, goats, horses, and sheep; and 0.30 ppm for the kidney of cattle, goats, horses, and sheep. It was also concluded that no tolerances were needed for swine commodities. Because the re-calculated dietary burdens for beef and dairy cattle are lower than the previously calculated values, no changes to the existing tolerances for cattle, goat, horse, and sheep commodities are needed to support the proposed uses.

The lowest dosing level in the cattle feeding study represents 190x the maximum theoretical dietary burden to swine. Aminopyralid residues in milk and tissues from the lowest dosing level in the cattle feeding study were ≤0.01 ppm in all commodities except kidney and were 0.10 ppm in kidney. HED concludes that tolerances for hog commodities are not needed to support the proposed and registered uses of aminopyralid.

Poultry: No poultry feeding study with aminopyralid has been submitted. RAB2 previously concluded that tolerances for poultry commodities were not needed based on the results of the poultry metabolism study and the previously calculated dietary burden of 0.075 ppm.

The poultry metabolism study represented a dosing level of 12 ppm and TRR were <0.01 ppm in eggs and all poultry tissues at this dosing level. The dosing level corresponds to 80x the current dietary burden aminopyralid to poultry. Therefore, HED concludes that the proposed and registered uses of aminopyralid result in a 40 CFR §180.6(a)(3) situation for poultry commodities; i.e., there is no reasonable expectation of finite residues in poultry commodities. No poultry feeding study is needed to support the subject petition. If additional uses of aminopyralid with significant poultry feed items are proposed in the future, then a poultry feeding study might be required.

860.1500 Crop Field Trials

DER Reference: 47572601.de1.doc (includes review of MRID 47572603)

Dow AgroSciences submitted field trial data for aminopyralid on field corn. Twenty field corn trials were conducted in the United States during the 2006 growing season. One trial each was performed in Zones 1 (PA), 2 (GA), and 6 (TX). Seventeen trials were performed in Zone 5 (IA (3), IL (3), IN (1), MI (1), MN (2), MO (1), ND (2), NE (2), OH (1), and WI (1)).

Each treated plot received a single foliar application of an SL formulation containing the TIPA salt of aminopyralid at 2 lb ae/gal. Applications were made at the 4- to 6-leaf growth stage (BBCH 14-16 or V4-V6). There were two treated plots at each location. One treated plot received an application at ~0.031 lb ae/A (~1x the proposed maximum seasonal rate) and the other plot received an application at ~0.062 lb ae/A (~2x). Applications were made in ~15-24 gal/A spray volumes, using ground equipment. A non-ionic surfactant was added to the spray mixture at ~0.25% (v/v). Field corn commodities were harvested at normal harvest times. Forage was harvested at the dent stage, at a 60- to 87-day preharvest interval (PHI), and grain and stover were harvested at maturity, at a 105- to 138-day PHI. In addition, to evaluate residue decline, forage samples were harvested at the Wisconsin trial and at one of the Illinois trials at 0-, 7-, 13- to 14-, 21-, and 28-day PHIs.

Samples of field corn forage, grain, and stover were analyzed for residues of aminopyralid using LC/MS/MS Method GRM 07.07. The validated LOQ was 0.01 ppm for each matrix. The method was adequate for data collection based on acceptable concurrent method recovery data.

Sample storage conditions and durations are reported in Table 4. Adequate storage stability data are available to support the storage conditions and durations of samples from the submitted field corn study.

A summary of the study results is presented in Table 6. Following foliar application of the 2 lb ae/gal SL formulation at approximately a 1x application rate (0.030-0.034 lb ae/A), maximum residues of aminopyralid were 0.262 ppm in/on forage (60- to 87-day PHI), 0.164 ppm in/on grain (105- to 138-day PHI), and 0.176 ppm in/on stover (105- to 138-day PHI). Following foliar application at approximately a 2x application rate (0.060-0.069 lb ae/A), maximum residues of aminopyralid were 0.293 ppm in/on forage, 0.212 ppm in/on grain, and 0.387 ppm in/on stover.

In the four forage residue decline trials, average residues of aminopyralid decreased from the 0-day to either the 14-day PHI or 21-day PHI and then generally did not decrease further (from the 14- or 21-day PHI to harvest at 66 or 72 days posttreatment).

Table 6. Summary of Residue Data from Crop Field Trials with Aminopyralid.

Crop matrix	PHI (days)	Total Applic. Rate (lb ai/A)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
FIELD CORN (proposed use = 0.027 lb ai/A total application rate, 0-day PHI for grain and 8-day for forage and silage)									
Field corn forage	60-87	0.030-0.034	40	<0.01	0.262	0.226	0.041	0.059	0.053
		0.060-0.069	39	0.018	0.293	0.240	0.083	0.105	0.069
Field corn grain	105-138	0.030-0.034	40	<0.01	0.164	0.155	0.090	0.036	0.032
		0.060-0.069	40	<0.01	0.212	0.209	0.049	0.060	0.048
Field corn stover	105-138	0.030-0.034	40	<0.01	0.176	0.153	0.032	0.048	0.041
		0.060-0.069	40	0.020	0.387	0.360	0.059	0.084	0.077

[1] HAFT = Highest average field trial result.

Conclusions. The submitted field corn crop field trial data are adequate to fulfill data requirements provided the proposed use is amended as requested under 860.1200. The number and locations of the corn field trials are in accordance with those specified in OPPTS Guideline 860.1500 for use on field corn. Field trials were conducted at ~1x the proposed maximum seasonal rate, and application was made at the growth stage specified on the proposed label. However, it should be noted that the proposed PHIs of 0 days for grain and 8 days for forage and silage are not supported.

The available data support the proposed tolerances of 0.30 ppm for field corn forage, 0.20 ppm for field corn grain, and 0.20 ppm for field corn stover. Refer to Appendix I for the tolerance calculation.

Residue data for field corn aspirated grain fractions were submitted and are discussed below with the field corn processing data.

860.1520 Processed Food and Feed

DER Reference: 47572601.de2.doc (includes review of MRID 47572604)

Dow AgroSciences submitted a processing study for aminopyralid on field corn. During the 2006 growing season, a single field corn trial was conducted in the United States in Zone 5 (Illinois). A single foliar broadcast application of an SL formulation containing the TIPA salt of aminopyralid at 2 lb ae/gal was made to field corn at the BBCH 14-15 growth stage at 0.060 lb ae/A (~2x the proposed maximum seasonal rate). The application was made using ground equipment in a 17.4 gal/A spray volume and a non-ionic surfactant was added to the spray mixture. A single bulk sample of field corn grain was harvested at a 138-day PHI, and processed using simulated commercial procedures into aspirated grain fractions (AGF), as well as flour, grits, meal, and refined oil (dry milling), and starch and refined oil (wet milling).

Samples of field corn grain raw agricultural commodity (RAC) and processed fractions were analyzed for residues of aminopyralid using LC/MS/MS Method GRM 07.07. The validated LOQ was 0.01 ppm for each matrix. The method was adequate for data collection based on acceptable concurrent method recovery data.

Sample storage conditions and durations are reported in Table 4. Adequate storage stability data are available to support the storage conditions and durations of samples of field corn grain and processed commodities from the processing study.

Residues of aminopyralid were 0.0787 ppm in field corn grain (RAC) harvested 138 days after a single foliar application of aminopyralid at 0.060 lb ae/A. Residues of aminopyralid were 0.0270 ppm in AGF, 0.0747 ppm in flour, 0.0886 ppm in grits, 0.1019 ppm in meal, and <0.01 ppm in starch and wet and dry milled refined oil. The processing factors for field corn processed commodities are presented in Table 7. Residues of aminopyralid did not concentrate in corn AGF (0.3x), flour (0.9x), starch (<0.1x), or refined oil (<0.04x for both wet and dry milled), but concentrated slightly in corn grits (1.1x) and meal (1.3x).

The observed processing factors are below the maximum theoretical concentration factor of 25x for corn (OPPTS 860.1520, Table 1).

Table 7. Summary of Processing Factors for Aminopyralid.

RAC	Processed Commodity	Processing Factor
Field corn, grain	Aspirated grain fractions	0.3x
	Flour	0.9x
	Grits	1.1x
	Meal	1.3x
	Refined oil (dry milling)	<0.04x
	Refined oil (wet milling)	<0.04x
	Starch	<0.1x

Conclusions. The submitted processing data are adequate to satisfy data requirements.

The processing data indicate that no tolerances are needed for field corn flour, starch, or refined oil, and that no change in the existing tolerance for aspirated grain fractions, at 0.20 ppm, is needed as a result of the proposed uses on field corn.

The processing data indicate that aminopyralid residues might concentrate in field corn grits and meal. Based on the HAFT residues for aminopyralid in/on field corn grain (0.155 ppm), and the processing factors, expected residues of aminopyralid in corn grits and meal following treatment at 1x would be 0.17 and 0.20 ppm, respectively. Because these values are not greater than the proposed tolerance of 0.20 ppm for field corn grain, no tolerances are needed for grits and meal.

860.1650 Submittal of Analytical Reference Standards

An analytical standard for aminopyralid is currently available in the EPA National Pesticide Standards Repository, with an expiration date of 8/28/2010 (electronic communication, Dallas Wright (ACB) to D. Dotson, 9/15/2009).

860.1850 Confined and Field Accumulation in Rotational Crops

Residue Chemistry Memo: D305665, M. Doherty, 7/12/05 (PP#4F6827)

A confined rotational crop study was submitted previously. In that study, [2,6-^{14}C]aminopyralid was applied directly to sandy loam soil in lined wooden boxes at 0.009 lb ai/A, which was 1x the proposed maximum seasonal rate for wheat (the only annual crop in PP#4F6827), and rotational lettuce, sorghum, and turnips were planted at plantback intervals (PBIs) of 90 and 120 days. TRR accumulated at ≥0.01 ppm in 90- and 120-day PBI early sorghum forage (0.027 ppm and 0.017 ppm, respectively), 90-day PBI sorghum stover (0.027 ppm), and 120-day PBI mature turnip tops (0.010 ppm); residues in all other rotational crop commodities ranged <0.001-0.007 ppm. TRR were generally found to decrease from the 90-day PBI to the 120-day PBI. Total identified residues ranged from 17 to 44% TRR in sorghum early forage and stover as well as in turnip tops, and consisted entirely of free aminopyralid. Residue profiles were similar between the matrices. Aminopyralid was found at 0.012 ppm in 90-day PBI sorghum early forage, 0.005 ppm in 120-day PBI sorghum early forage, 0.005 ppm in 90-day PBI sorghum stover, and 0.002 ppm in 120-day PBI turnip tops. In PP#4F6827, HED concluded that the residues of concern in rotational crop commodities are the same as for primary crop commodities, free and conjugated aminopyralid. HED further concluded that there is potential for quantifiable residues of aminopyralid in rotated cereal grain forage at a 3-month PBI. No field rotational crop study was submitted. It was concluded that the available rotational crop data support a 0-day plantback interval for wheat and a 4-month plant-back interval for barley, canola, flax, grasses, field corn, grain sorghum, oats, mustard, popcorn, and sweet corn (the requested rotated crops in PP#4F6827).

With the proposed use on field corn, the maximum seasonal rate to annual crops has increased from 0.009 lb ai/A to 0.027 lb ai/A. The available rotational crop data reflect application at a rate of 0.3x the proposed maximum seasonal rate. Because the identified residues in the confined rotational crop study consisted solely of free and conjugated aminopyralid, a new confined rotational crop study (conducted at 0.027 lb ai/A) will not be required to support the proposed use. Although the available confined data indicate that quantifiable residues of aminopyralid could occur in grasses and cereal grain foliage with a PBI of 4 months, the only crops with requested PBIs of less than one year (i.e., wheat, grasses, and field corn) will be treated as primary crops and will have tolerances. Therefore, the petitioner does not need to submit a limited field rotational crop study for aminopyralid reflecting a PBI of 4 months. HED considers the rotation intervals listed on the supplemental label for field corn to be adequate.

The supplemental label specifies that wheat may be planted at any time after harvest. Grasses and field corn may be planted at a 4-month plantback interval. Barley, canola (rapeseed), flax, grain sorghum, mustard, oats, sweet corn, and popcorn may be planted at a 12-month plantback interval. The crop rotational interval for all other crops not listed on the label is 24 months.

860.1550 Proposed Tolerances

DowAgroSciences has proposed tolerances for residues of aminopyralid (2-pyridine carboxylic acid, 4-amino-3,6-dichloro-), expressed as total parent, free and conjugated, in/on field corn commodities. The proposed tolerances are listed in Table 8.

HED recommends that 40CFR §180.610(a)(1) be amended by replacing the tolerance expression with the following: "Tolerances are established for residues of aminopyalid (4-amino-3,6-dichloro-2-pyridinecarboxylic acid), 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 free and conjugated aminopyralid." HED further recommends that 40CFR §180.610(a)(2) be amended by replacing the tolerance expression with the following: "Tolerances are established for residues of aminopyralid, 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 aminopyralid."

Codex and Canadian MRLs have been established for residues of aminopyralid; however, no MRLs have been established for the requested crop commodities. No Mexican MRLs have been established for aminopyralid.

Adequate field trial data have been submitted for field corn. The Agency's *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* was used for determining appropriate tolerance levels for field corn raw agricultural crop commodities. See Appendix I for tolerance calculations. The available data will support the proposed tolerances of 0.30 ppm for field corn forage, 0.20 ppm for field corn grain, and 0.20 ppm for field corn stover.

The field corn processing study is adequate. It indicates that no tolerances are required for field corn flour, grits, meal, refined oil, or starch, and that no change in the existing tolerance for aspirated grain fractions, at 0.20 ppm, is needed as a result of the proposed uses on field corn.

No changes to the existing tolerances for livestock commodities are needed as a result of the proposed uses.

The proposed tolerances should be revised to reflect the correct commodity definitions as specified in Table 8.

Table 8. Tolerance Summary for Aminopyralid.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Corn, forage	0.30	0.30	*Corn, field, forage*
Corn, grain	0.20	0.20	*Corn, field, grain*
Corn, stover	0.20	0.20	*Corn, field, stover*

References

D305665, Aminopyralid. Petition for the Establishment of Permanent Tolerances for Use of Aminopyralid on Grasses and Wheat. Summary of Analytical Chemistry and Residue Data. PP#4F6827, M. Doherty, 7/12/05, MRIDs: 46235708-46235712, 46235714, 46235716-46235719, 46235721-46235725

D312724, PP# 4F6827. Review of Method for the Establishment of Permanent Tolerances in Aminopyralid in/on Plant and Livestock Commodities. ACL Project #:B05-12, D. Wright, 11/3/05, MRIDs: 46235712, 46235714, 46235716, 46235717

Attachments:
International Residue Limit Status sheet
Appendix I - Tolerance Assessment Calculations

INTERNATIONAL RESIDUE LIMIT STATUS

Chemical Name: 4-amino-3,6-dichloro-2-pyridinecarboxylic acid	Common Name: Aminopyralid	X Proposed tolerance ☐ Reevaluated tolerance ☐ Other	Date: 5/8/09
Codex Status (Maximum Residue Limits)		U. S. Tolerances	
☐ No Codex proposal step 6 or above X No Codex proposal step 6 or above for the crops requested		Petition Number: PP#8F7455 DP#: 360100 Other Identifier: Decision # 401475	
Residue definition (step 8/CXL): aminopyralid and its conjugates that can be hydrolysed, expressed as aminopyralid		Reviewer/Branch: D. Dotson/C.Swartz/RAB1	
		Residue definition: Aminopyralid, free and conjugated residues	
Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		Corn, forage	0.30
		Corn, grain	0.20
		Corn, stover	0.20
Limits for Canada		Limits for Mexico	
☐No Limits X No Limits for the crops requested		X No Limits ☐ No Limits for the crops requested	
Residue definition: 4-amino-3,6-dichloro-2-pyridinecarboxylic acid (free and conjugated)		Residue definition: N/A	
Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)
Notes/Special Instructions: S.Funk, 05/13/2009.			

Appendix I. Tolerance Assessment Calculations.

For the field corn commodities listed below, the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* (SOP), along with the tolerance spreadsheet (January 2008 version), was used for calculating recommended tolerances. As specified in the SOP, the minimum of the 95% upper confidence limit (UCL) on the 95th percentile and the point estimate of the 99th percentile was selected as the tolerance value because the datasets were large (40 samples each) and reasonably lognormal. The rounding procedures specified in the SOP were also used.

The datasets used to establish tolerances for aminopyralid on field corn forage, grain, and stover consisted of field trial data representing application rates of 0.03-0.034 lb ae/A (single application) with a 60- to 87-day PHI for forage and a 105- to 138-day PHI for grain and stover. The field trial application rates are within 25% of the maximum label application rate; however, the PHIs are much greater than the proposed PHIs of 0 days for grain and 8 days for forage and silage. No residue data were submitted for field corn commodities reflecting the proposed PHIs. The residue values that were entered into the tolerance spreadsheet are provided in Table I-1.

For forage and stover, 39 out of 40 field trial sample results for aminopyralid were above the LOQ (LOQ = 0.01 ppm), and for field corn grain, 35 out of 40 field trial results were above the LOQ. Visual inspection of the lognormal probability plot (Figures I-1, I-3, and I-5) and the results from the approximate Shapiro-Francia test statistic (Figures I-2, I-4, and I-6) indicated that the datasets were reasonably lognormal.

Using the tolerance spreadsheet, the recommended tolerances are 0.25 ppm for field corn forage, 0.15 ppm for field corn grain, and 0.20 ppm for field corn stover. However, for both forage and grain, the recommended tolerances are slightly less than the highest residue value observed in the field trials, of 0.262 ppm and 0.164 ppm, respectively. Therefore, HED recommends in favor of tolerances of 0.30 ppm for field corn forage and 0.20 ppm for field corn grain.

Table I-I. Residue data used to calculate tolerances for residues of aminopyralid on field corn forage, grain, and stover.

Regulator:	EPA	EPA	EPA
Chemical:	Aminopyralid	Aminopyralid	Aminopyralid
Crop:	Field corn forage	Field corn grain	Field corn stover
PHI:	60-87 Days	105-138 Days	105-138 Days
App. Rate:	0.030-0.034 lb ac/A	0.030-0.034 lb ae/A	0.030-0.034 lb ae/A
Submitter:	Dow AgroSciences	Dow AgroSciences	Dow AgroSciences
MRID Citation:	MRID 47572601	MRID 47572601	MRID 47572601
	Residues of Aminopyralid (ppm)		
	0.045	0.015	0.019
	0.041	0.026	0.020
	0.039	0.043	0.036
	0.022	0.021	0.017
	0.065	0.052	0.068
	0.042	0.030	0.030
	0.113	0.033	0.176
	0.057	0.030	0.029
	0.012	0.015	0.014
	0.119	<0.01	0.091
	0.189	0.145	0.167
	0.035	0.023	0.064
	0.021	0.053	<0.01
	<0.01	<0.01	0.012
	0.035	0.038	0.060
	0.021	0.020	0.028
	0.037	0.012	0.021
	0.036	<0.01	0.035
	0.046	0.031	0.033
	0.084	0.051	0.071
	0.034	0.014	0.018
	0.024	0.032	0.030
	0.041	0.047	0.034
	0.050	0.025	0.012
	0.086	0.052	0.108
	0.044	0.032	0.021
	0.128	0.037	0.131
	0.052	0.028	0.037
	0.030	0.016	0.029
	0.145	0.081	0.075
	0.262	0.164	0.107
	0.056	0.021	0.060

Table I-1. Residue data used to calculate tolerances for residues of aminopyralid on field corn forage, grain, and stover.

Regulator:	EPA	EPA	EPA
Chemical:	Aminopyralid	Aminopyralid	Aminopyralid
Crop:	Field corn forage	Field corn grain	Field corn stover
PHI:	60-87 Days	105-138 Days	105-138 Days
App. Rate:	0.030-0.034 lb ae/A	0.030-0.034 lb ae/A	0.030-0.034 lb ae/A
Submitter:	Dow AgroSciences	Dow AgroSciences	Dow AgroSciences
MRID Citation:	MRID 47572601	MRID 47572601	MRID 47572601
	Residues of Aminopyralid (ppm)		
	0.016	0.031	0.011
	0.012	<0.01	0.011
	0.045	0.035	0.046
	0.042	0.020	0.046
	0.025	0.011	0.025
	0.016	<0.01	0.028
	0.038	0.036	0.023
	0.149	0.056	0.072

Figure I-1. Lognormal probability plot of aminopyralid field trial data for field corn forage.

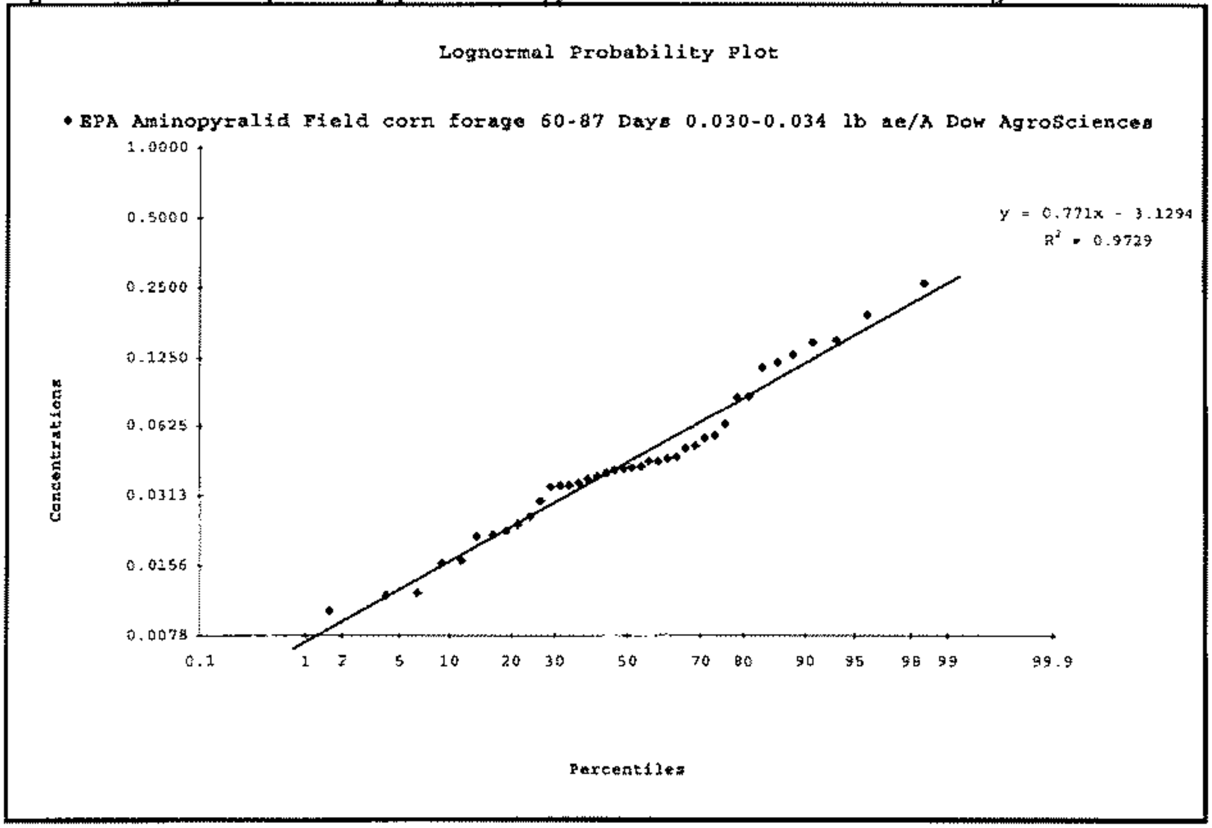


Figure I-2. Tolerance spreadsheet summary of aminopyratid field trial data for field corn forage.

	Regulator: EPA **Chemical:** Aminopyralid **Crop:** Field corn forage **PHI:** 60-87 Days **App. Rate:** 0.030-0.034 lb ae/A **Submitter:** Dow AgroSciences **n:** 40 **min:** 0.01 **max:** 0.26 **median:** 0.04 **average:** 0.06		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.15 (0.20)	0.20 (0.25)	0.25 (--)
95/99 Rule	0.20 (0.25)	0.30 (0.45)	0.50 (--)
EU Method II Distribution-Free		0.15	
Mean+3SD		0.25	
UCLMedian95th		0.25	
Approximate Shapiro-Francia Normality Test		0.9729 p-value > 0.05 : Do not reject lognormality assumption	

Figure I-3. Lognormal probability plot of aminopyralid field trial data for field corn grain.

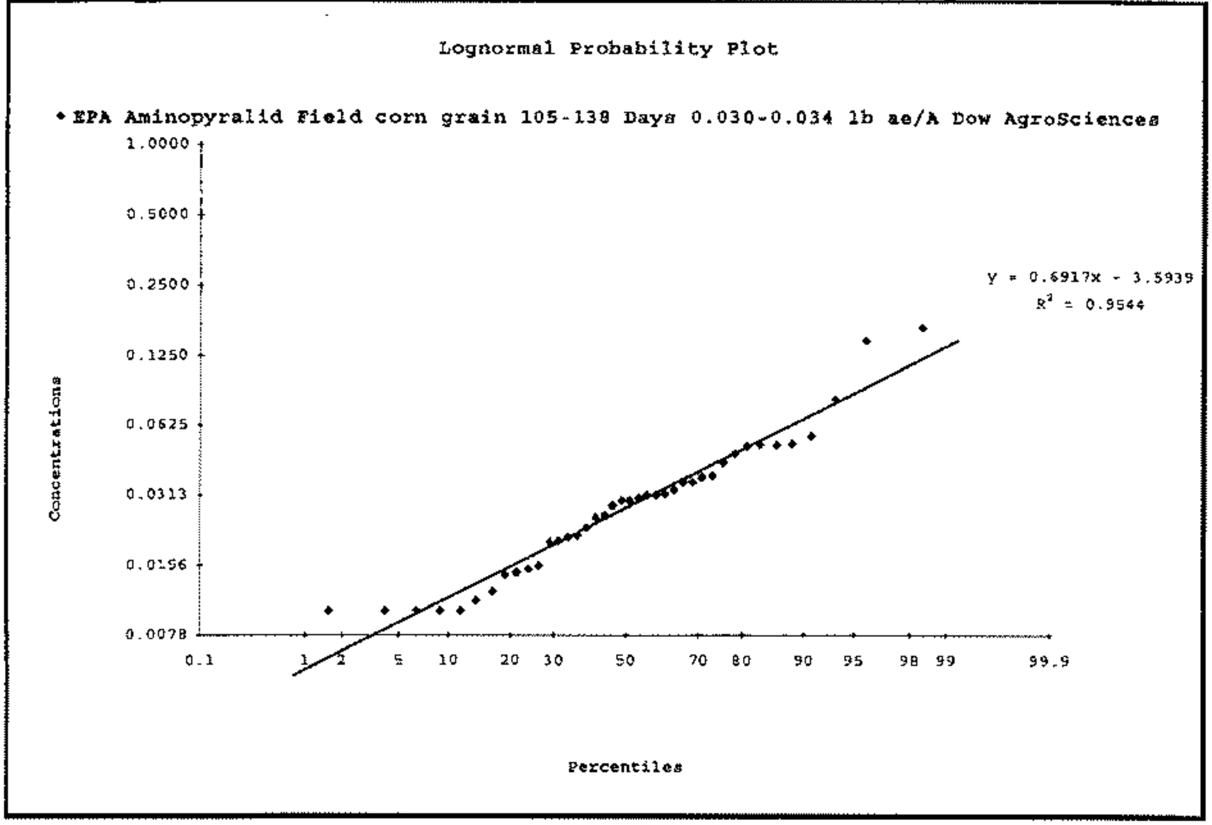
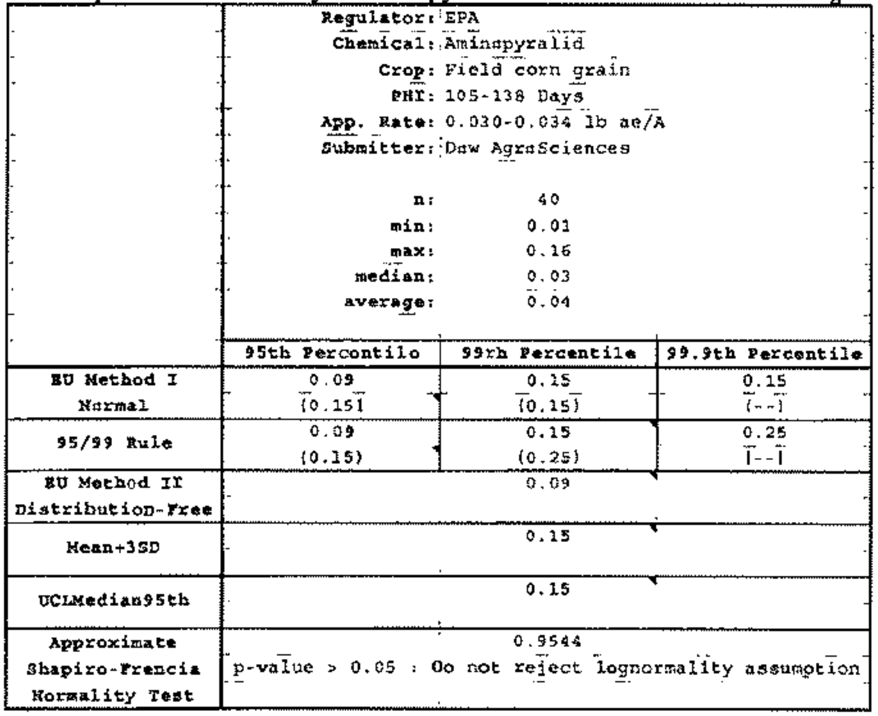


Figure I-4. Tolerance spreadsheet summary of aminopyralid field trial data for field corn grain.



Regulator: EPA
Chemical: Aminopyralid
Crop: Field corn grain
PHI: 105-138 Days
App. Rate: 0.030-0.034 lb ae/A
Submitter: Dow AgroSciences

n:	40
min:	0.01
max:	0.16
median:	0.03
average:	0.04

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.09 (0.15)	0.15 (0.15)	0.15 (--)
95/99 Rule	0.09 (0.15)	0.15 (0.25)	0.25 (--)
EU Method II Distribution-Free	0.09		
Mean+3SD	0.15		
UCLMedian95th	0.15		
Approximate Shapiro-Francia Normality Test	0.9544 p-value > 0.05 : Do not reject lognormality assumption		

Figure I-5. Lognormal probability plot of aminopyralid field trial data for field corn stover.

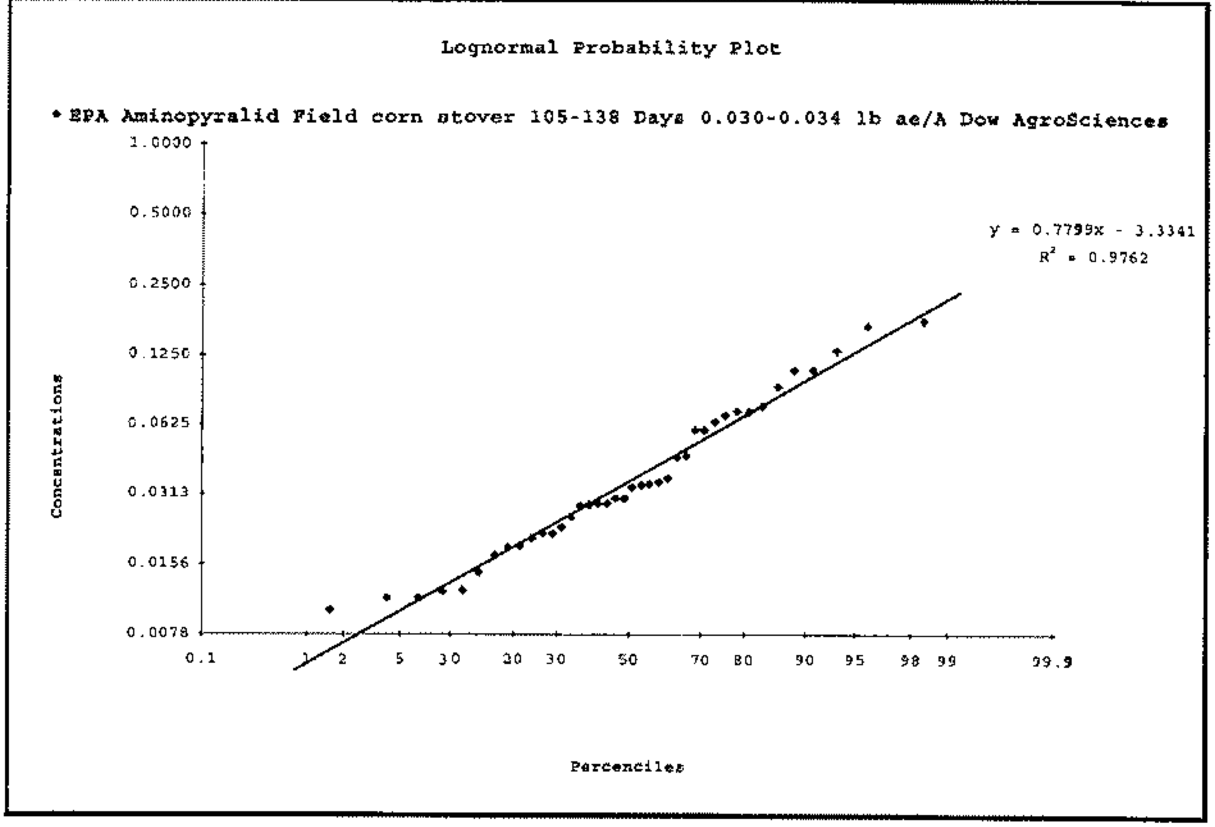
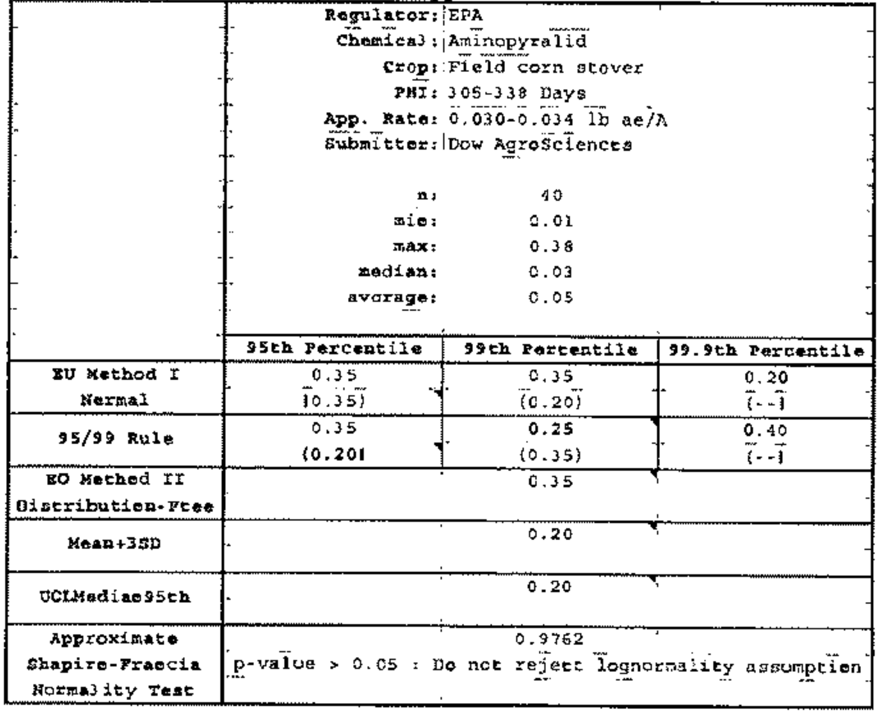


Figure I-6. Tolerance spreadsheet summary of aminopyralid field trial data for field corn stover.



	Regulator: EPA Chemical: Aminopyralid Crop: Field corn stover PHI: 305-338 Days App. Rate: 0.030-0.034 lb ae/A Submitter: Dow AgroSciences n: 40 min: 0.01 max: 0.38 median: 0.03 average: 0.05		
	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.35 (0.35)	0.35 (0.20)	0.20 (--)
95/99 Rule	0.35 (0.20)	0.25 (0.35)	0.40 (--)
EU Method II Distribution-Free		0.35	
Mean+3SD		0.20	
UCLMedian95th		0.20	
Approximate Shapiro-Francia Normality Test		0.9762 p-value > 0.05 : Do not reject lognormality assumption	

Primary Evaluator Douglas Dotson Date: 10/22/2009
Douglas Dotson, Ph.D., Chemist, RABII

Peer Reviewer Date: 10/22/2009
Michael Doherty, Ph.D., Chemist, RABII

This DER was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850; submitted 5/14/2009). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

47572601 Rosser, S. (2008) Residues of Aminopyralid in Corn Forage, Grain, Stover and Processed Products. Project Number: 060014, IL2. Unpublished study prepared by Dow AgroSciences, LLC and GLP Technologies. 131 p.

47572604 Rosser, S. (2008) Study Profile for Residues of Aminopyralid in Corn Forage, Grain, Stover and Processed Products. Project Number: 060014/SPT2. Unpublished study prepared by Dow AgroSciences, LLC. 23 p.

EXECUTIVE SUMMARY:

Dow AgroSciences submitted a processing study for aminopyralid on field corn. During the 2006 growing season, a single field corn trial was conducted in the United States in Zone 5 (Illinois). A single foliar broadcast application of a liquid soluble concentrate (SL) formulation containing the triisopropanolammonium (TIPA) salt of aminopyralid at 2 lb ae/gal was made to field corn at the BBCH 14-15 growth stage at 0.060 lb ae/A. The application was made using ground equipment in a 17.4 gal/A spray volume and a non-ionic surfactant was added to the spray mixture. A single bulk sample of field corn grain was harvested at a 138-day PHI, and processed using simulated commercial procedures. The processed fractions that were obtained included aspirated grain fractions (AGF) as well as flour, grits, meal, and refined oil from dry milling, and starch and refined oil from wet milling.

Samples of field corn grain raw agricultural commodity (RAC) and processed fractions were analyzed for residues of aminopyralid using a high performance liquid chromatography method with tandem mass spectrometry detection (LC/MS/MS), Method GRM 07.07. The validated limit of quantitation (LOQ) was 0.01 ppm for each matrix. The method was adequate for data collection based on acceptable concurrent method recovery data. Overall method recoveries ranged 75-98% from corn grain and its processed commodities.

Samples of field corn commodities were stored frozen from harvest/collection to extraction, for 12.9 months for grain, 11.5 months for AGF and refined oil (dry milled), 11.7 months for flour and meal, 12.6 months for grits, 11.2 months for starch, and 12.7 months for refined oil (wet milled). The available storage stability data indicate that residues of aminopyralid are stable during frozen storage for up to ~15 months in/on wheat grain (refer to the DER for MRID 46661301). These data are adequate to support the storage conditions and durations of samples of field corn grain from the submitted study, but are not adequate to support the storage conditions and durations of processed corn commodities. No supporting storage stability data are available for processed field corn commodities.

Residues of aminopyralid were 0.0787 ppm in field corn grain (RAC) harvested 138 days following a single foliar application of aminopyralid at 0.060 lb ae/A. Residues of aminopyralid were 0.0270 ppm in AGF, 0.0747 ppm in flour, 0.0886 ppm in grits, 0.1019 ppm in meal, and <0.01 ppm in starch and wet and dry milled refined oil. In the field corn processing study, residues of aminopyralid did not concentrate in corn AGF (0.3x), flour (0.9x), starch (<0.1x), or refined oil (<0.04x for both wet and dry milled). However, residues concentrated slightly in corn grits (1.1x) and meal (1.3x).

The observed processing factors are below the maximum theoretical concentration factor of 25x for corn (OPPTS 860.1520, Table 1).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the processed commodity residue data are tentatively classified as scientifically acceptable, pending submission of supporting storage stability data for field corn processed commodities reflecting frozen storage for up to 13 months.

The acceptability of this study for regulatory purposes is addressed in the U.S. EPA Residue Chemistry Summary Document, D360100, D. Dotson, 10/22/2009.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Aminopyralid is a systemic postemergence herbicide that belongs to the pyridine carboxylic acid class of herbicides. It is currently registered for use on rangeland, permanent grass pastures, and wheat. In addition, it is registered for use on wildlife habitat and industrial vegetation management areas, including right-of-way for roads, railroads, and utility lines. Under PP#8F7455, Dow AgroSciences is proposing aminopyralid for use on field corn. The end-use product (EP) proposed for use on field corn is a SL formulation, Milestone Specialty Herbicide (EPA Reg. No. 62719-519), in which aminopyralid is formulated as the TIPA salt. The product contains 40.6% aminopyralid TIPA salt at an acid equivalent (ae) of 21.1% or 2 lb ae/gal.

The chemical structure and nomenclature of aminopyralid and aminopyralid TIPA salt, and the physicochemical properties of the technical grade of aminopyralid are presented in Tables A.1 and A.2.

TABLE A.1. Test Compound Nomenclature.

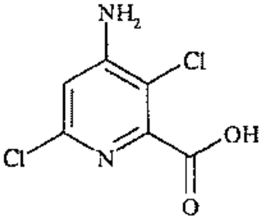
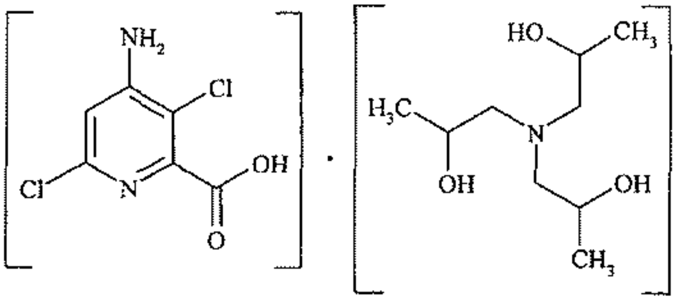
Compound	
Common name	Aminopyralid
Company experimental name	XDE-750
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid
CAS name	4-amino-3,6-dichloro-2-pyridinecarboxylic acid
CAS registry number	150114-71-9
Compound	
Common name	Aminopyralid, triisopropanolammonium (TIPA) salt
PC Code	005209
Company experimental name	XDE-750 TIPA salt
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid - (2RS,2'RS,2"RS)-1,1',1"-nitrilotripropan-2-ol (1:1)
CAS name	4-amino-3,6-dichloropyridine-2-carboxylic acid compound with 1,1',1"-nitrilotris[2-propanol] (1:1)
CAS registry number	566191-89-7
End-use product (EP)	Milestone Specialty Herbicide (2 lb ae/gal SL; EPA Reg. No. 62719-519)

TABLE A.2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value	Reference
Melting point/range	163.5°C	MRID 46235703
pH	2.31 at 23.4°C (1% solution in water)	MRID 46235703
Density	1.72 at 20°C	MRID 46235703
Water solubility	2.48 g/L unbuffered water at 18°C 212 g/L pH 5 buffer at 20°C 205 g/L pH 7 buffer at 20°C 203 g/L pH 9 buffer at 20°C	MRID 46235703

TABLE A.2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value	Reference
Solvent solubility at 20°C	methanol 52.2 g/L acetone 29.2 g/L n-octanol 3.9 g/L ethyl acetate 3.9 g/L 1,2-dichloroethane 0.2 g/L xylene 0.04 g/L heptane <10 µg/mL	MRID 46235703
Vapor pressure	2.59 x 10^{-8} Pa at 25°C; 9.52 x 10^{-9} Pa at 20°C	MRID 46235703
Dissociation constant, pK_a	2.56	MRID 46235703
Octanol/water partition coefficient, Log(K_{OW})	0.201 unbuffered water at 19°C -1.76 at pH 5 -2.87 at pH 7 -2.96 at pH 9	MRID 46235703
UV/visible absorption spectrum	Solution / Wavelength λ max, nm / Extinction coefficient L/(mol*cm) Neutral 217 29100 Basic (pH 12.6) 220 26100 Basic (pH 12.6) 245 10150 Acidic (pH 1.4) 217 22800 Acidic (pH 1.4) 270 9140	MRID 46235703

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

During the 2006 growing season, a single field corn trial was conducted in the United States in Zone 5 (Illinois). The trial included an untreated and a treated plot. In the treated plot, a single foliar broadcast application of a SL formulation containing the TIPA salt of aminopyralid at 2 lb ae/gal was made to field corn (var. B-T 6516 RR 2YG) at the BBCH 14-15 (4- to 6-leaf) growth stage at 0.060 lb ae/A. The application was made using ground equipment in a spray volume of 17.4 gal/A. A non-ionic surfactant was included as an adjuvant at 0.25% v/v. The study use pattern is presented in Table B.1.1. The trial was conducted in conjunction with the field corn crop field trials (refer to the 860.1500 DER for MRID 47572601).

The petitioner stated that farming practices were typical of corn production; a list of the maintenance pesticides and fertilizers that were used was provided. Average monthly minimum and maximum temperatures and monthly rainfall amounts were presented, along with historical values. The petitioner reported no unusual weather occurrences for the study period. No irrigation was used at this trial.

TABLE B.1.1. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants
		Method; Timing	Volume (gal/A)	Rate (lb ae/A)	RTI[2] (days)	Total Rate (lb ae/A)	
Carlyle, IL; 2006 (060014-IL2)	2 lb ae/gal SL	1. Foliar broadcast; BBCH 14-15	17.4	0.060	NA	0.060	NIS[3] 0.25% v/v

[1] EP = End-use Product

[2] RTI = Retreatment Interval; NA = not applicable as treatment was a single application.

[3] NIS = Non-ionic surfactant.

B.2. Sample Handling and Processing Procedures

A single bulk sample of field corn grain was harvested mechanically from each plot at normal maturity at a 138-day PHI. The grain was stored at ambient conditions overnight and shipped via freezer truck the following day to GLP Technologies (Navasota, TX) for processing. Samples were stored frozen (≤-12°C) at GLP Technologies prior to processing. Processing was initiated 36 days after sample harvest and completed within 68 days of harvest.

To generate AGF, the grain was dried and placed in a dust generation room and grain dust was removed by aspiration. The collected grain dust was then classified by sieving into six categories of particle size. All material of the <2360 µm particle size was combined to produce the AGF sample. Separate subsamples of grain were then processed using simulated commercial procedures. Flour, grits, meal, and refined oil were obtained from dry milling, and starch and refined oil were obtained from wet milling. Flowcharts of the processing procedures, copied without alteration from MRID 47572601, are presented in Figure 1.

Processed matrices were frozen after collection, and RAC and processed commodities were shipped frozen to Dow AgroSciences (Indianapolis, IN) for analysis. At the analytical facility, samples remained in frozen storage (~-20°C) except while being homogenized, prepared, and extracted for analysis. Samples of grain and grits were prepared for analysis by freezing using liquid nitrogen and then grinding.

FIGURE 1. Processing Flowcharts for Field Corn.

MATERIAL BALANCE for GENERATION, CLASSIFICATION, AND ASH CONTENT
DETERMINATION OF ASPIRATED GRAIN FRACTIONS

Sample # 2 (Treated, Trt. 3) Code # 060014-066-0002

COMMODITY 710.3 lbs.

Drying 692.4 lbs. (after drying)

692.4 lbs. used for generation

Aspiration 0.4 lbs.

Classification

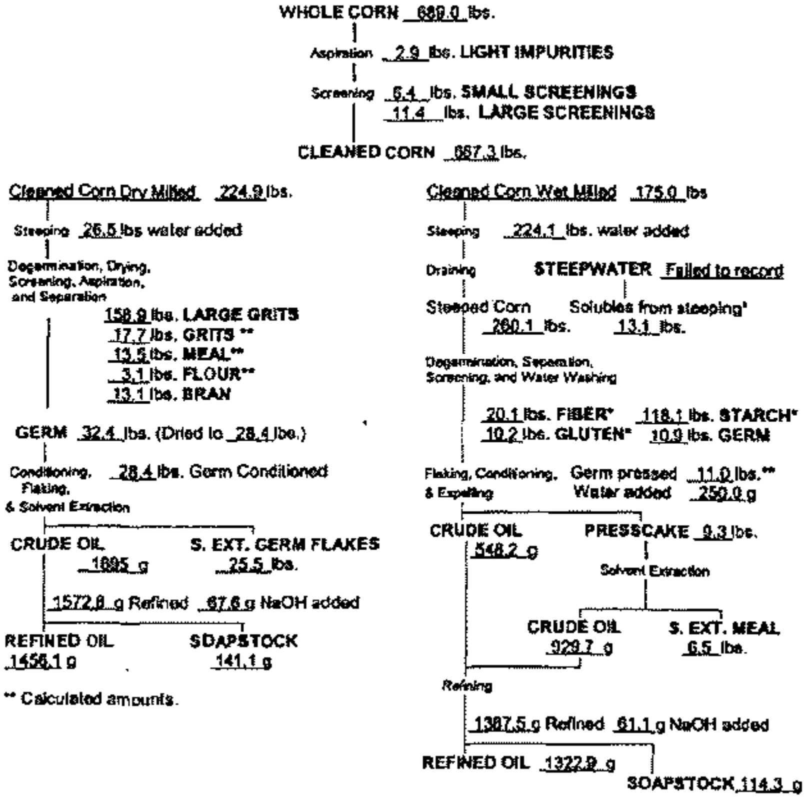
- **ASPIRATED GRAIN FRACTION > 2360 micron** 42.9 g
  (Grain Dust)
- **ASPIRATED GRAIN FRACTION > 2000 micron** 9.1 g
  (Grain Dust)
- **ASPIRATED GRAIN FRACTION > 1180 micron** 20.9 g
  (Grain Dust)
- **ASPIRATED GRAIN FRACTION > 850 micron** 7.4 g
  (Grain Dust)
- **ASPIRATED GRAIN FRACTION > 425 micron** 7.5 g
  (Grain Dust)
- **ASPIRATED GRAIN FRACTION < 425 micron** 84.7 g
  (Grain Dust)

ASH CONTENT: 5.8 %

All fractions less than 2360 micron were re-combined to produce one 129.0 g AGF fraction.

CORN PROCESSING MATERIAL BALANCE

Sample # 2 (Treated, Trt. 3) Code # 060014-066-0002



** Calculated amounts.

* Calculated amounts based on commercial recovery percentages and starting weight of corn used for wet milling.

** Weight Gain of 0.1 lbs.

B.3. Analytical Methodology

Samples of field corn grain (RAC) and processed fractions were analyzed for residues of aminopyralid using LC/MS/MS method GRM 07.07 (refer to the DER for MRID 47572602 for a complete description of the method). The petitioner stated that an adapted version of the method was used, but did not specify how the method was adapted. Only a brief description of the method was included in MRID 47572601.

Briefly, residues were extracted from field corn commodities, except refined oil (dry milling), using 0.1 N NaOH, which hydrolyzes bound residues and base-labile conjugates to yield free aminopyralid. The hydrolysate is acidified with 2 N HCl. The refined oil (dry milling) samples were extracted with acetone and the extract was evaporated to dryness, redissolved in hexane, and partitioned into water. The aqueous phase was mixed with 0.2 N NaOH (to hydrolyze bound residues and base-labile conjugates to yield free aminopyralid) then acidified with 3 N HCl. For all samples, the acidified extract was heated at 80°C for 90 minutes, which hydrolyzes acid-labile

32

conjugates to yield free aminopyralid and further solubilizes bound residues. The extract was then purified using anion-exchange solid phase extraction, using ethyl acetate:trifluoroacetic acid (99:1, v:v) to elute residues. An internal standard ($^{13}C_2{}^2H^{15}N$-aminopyralid) was added to the eluate, which was evaporated to dryness, reconstituted in acetonitrile:pyridine:1-butanol (22:2:1, v:v:v; derivatization coupling reagent) and derivatized with butyl chloroformate to form the 1-butyl esters of the analyte and the internal standard. The mixture was diluted with a solution of methanol:water (40:60, v:v) containing 0.05% formic acid and 5 mM ammonium formate solution for LC/MS/MS analysis. The limit of detection (LOD) and the LOQ are 0.003 and 0.01 ppm, respectively, for aminopyralid in each corn matrix.

The method was validated concurrently with the analysis of processing samples using samples of untreated grain, AGF, flour, grits, meal, refined oil, and starch fortified with aminopyralid at 0.01 and 2 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations are summarized in Table C.2. Field corn commodity samples were stored frozen from harvest/collection to extraction for analysis. Dates of analysis were not provided. The petitioner should note for future submissions that dates of extraction and analysis should be provided for all samples. Sample storage intervals were 394 days (12.9 months) for grain, 350 days (11.5 months) for AGF and refined oil (dry milled), 355 days (11.7 months) for flour and meal, 384 days (12.6 months) for grits, 341 days (11.2 months) for starch, and 387 days (12.7 months) for refined oil (wet milled). The available storage stability data indicate that residues of aminopyralid are stable during frozen storage for up to ~15 months in/on wheat grain (refer to the DER for MRID 46661301). These data are adequate to support the storage conditions and durations of samples of field corn grain from the submitted study, but are not adequate to support the storage conditions and durations of processed corn commodities. Storage stability data must be submitted for field corn processed commodities.

Concurrent method recovery data are presented in Table C.1. Method GRM 07.07 (LC/MS/MS) is adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were within the acceptable range of 70-120% from field corn grain, AGF, flour, grits, meal, wet and dry milled refined oil, and starch fortified with aminopyralid at 0.01 and 2 ppm. Fortification levels were adequate to bracket residues found in treated samples. Apparent residues of aminopyralid were below the LOD (<0.003 ppm) in/on one control sample each of field corn grain RAC, AGF, flour, grits, meal, wet and dry milled refined oil, and starch. Adequate sample calculations and chromatograms were provided.

Residue data from the field corn processing study are reported in Table C.3. Residues of aminopyralid were 0.0787 ppm in field corn grain (RAC) harvested 138 days following a single foliar application of aminopyralid at 0.060 lb ae/A. Residues of aminopyralid were 0.0270 ppm in AGF, 0.0747 ppm in flour, 0.0886 ppm in grits, 0.1019 ppm in meal, and <0.01 ppm in starch and wet and dry milled refined oil. Aminopyralid residues did not concentrate in corn AGF (0.3x), flour (0.9x), starch (<0.1x), or refined oil (<0.04x for both wet and dry milled), but concentrated slightly in corn grits (1.1x) and meal (1.3x).

The observed processing factors are below the maximum theoretical concentration factor (OPPTS 860.1520, Table 1) of 25x for corn.

TABLE C.1. Summary of Concurrent Recoveries of Aminopyralid from Field Corn Matrices.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev.[1] (%)
Grain	0.01	6	85, 87, 88, 89, 92, 97	90 ± 4
	2	6	75, 76, 78, 80, 81, 81	78 ± 3
Field corn AGF	0.01	2	91, 94	92
	2	2	80, 82	81
Flour	0.01	2	91, 92	92
	2	2	75, 77	76
Grits	0.01	2	95, 97	96
	2	2	92, 94	93
Meal	0.01	2	97, 98	97
	2	2	79, 81	80
Refined oil (wet milled)	0.01	2	81, 85	83
	2	2	79, 81	80
Refined oil (dry milled)	0.01	2	83, 90	87
	2	2	81, 83	82
Starch	0.01	2	88, 91	90
	2	2	78, 80	79

[1] Standard deviation is only calculated for sample sizes ≥3.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Field corn grain (RAC)	-20	394 days (12.9 months)	Residues of aminopyralid are stable during frozen storage for up to ~15 months in/on wheat grain.[2]
Field corn AGF		350 days (11.5 months)	No storage stability data are available for field corn processed commodities.
Flour		355 days (11.7 months)	
Grits		384 days (12.6 months)	
Meal		355 days (11.7 months)	
Starch		341 days (11.2 months)	
Refined oil (wet milled)		387 days (12.7 months)	
Refined oil (dry milled)		350 days (11.5 months)	

[1] Storage duration from harvest (RAC) or processing to extraction. Analysis dates were not provided.
[2] Refer to the DER for MRID 46661301.

TABLE C.3. Residue Data from Field Corn Processing Study with Aminopyralid.

RAC	Processed Commodity	Total Rate (lb ae/A)	PHI (days)	Residues (ppm)[1]	Processing Factor
Field Corn	Grain (RAC)	0.060	138	0.0787	--
	AGF			0.0270	0.3x
	Flour			0.0747	0.9x
	Grits			0.0886	1.1x
	Meal			0.1019	1.3x
	Starch			(0.0075)	<0.1x
	Refined oil (wet milled)			<0.003	<0.04x
	Refined oil (dry milled)			<0.003	<0.04x

[1] Residues reported between the LOD (0.003 ppm) and the LOQ (0.01 ppm) are presented in parentheses.

D. CONCLUSION

The field corn processing study indicates that residues of aminopyralid do not concentrate in corn AGF (0.3x), flour (0.9x), starch (<0.1x), or refined oil (<0.04x for both wet and dry milled) but might concentrate slightly in corn grits (1.1x) and meal (1.3x).

An acceptable method was used for the quantitation of residues of aminopyralid in/on field corn matrices, and adequate storage stability data are available to support sample storage conditions and durations for aminopyralid residues in grain. However, no storage stability data have been submitted to support storage conditions and durations for field corn processed commodities. These data must be submitted.

E. REFERENCES

None.

F. DOCUMENT TRACKING

Petition Number: 8F7455
DP#: 360100
PC Codes: 005100 and 005209

Primary Evaluator Douglas Dotson Date: 10/22/2009
Douglas Dotson, Ph.D., Chemist, RABII

Peer Reviewer Michael Doherty Date: 10/22/2009
Michael Doherty, Ph.D., Chemist, RABII

This DER was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850; submitted 5/14/2009). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46661301 Lindsay, D. (2004) Frozen Storage Stability of XDE-750 in Range Land and Pasture Grass and Hay and Wheat Straw and Wheat Grain. Project Number: 030004/01. Unpublished study prepared by Dow Agrosciences LLC. 59 p.

EXECUTIVE SUMMARY:

Dow AgroSciences submitted the final report of a storage stability study with aminopyralid on grass forage and hay and wheat grain and straw. An interim report for this study, reflecting storage intervals of up to ~6 months, was previously reviewed in conjunction with a petition for grasses and wheat (PP#4F6827; DP# 305665, 7/12/05, M. Doherty; DER 46235719.1380.der.wpd). Samples of untreated grass forage, grass hay, wheat grain, and wheat straw were fortified with aminopyralid at 0.1 ppm and stored frozen (~-20 °C). Storage intervals tested were 0, 28, 130, 187, and 488 days (grass forage and hay) or 0, 113, 168/175, 273, and 469 days (wheat grain and straw).

Samples of grass hay and forage and wheat grain and straw were analyzed for residues of aminopyralid using high performance liquid chromatography method with tandem mass spectrometry detection (LC/MS/MS), Method GRM 02.31. A complete description of the method is provided in the DER for MRID 46235712 (46235712.1340.plant.der.wpd). The method was adequate for data collection based on acceptable concurrent method recoveries; the reported limit of quantitation (LOQ) was 0.01 ppm for each commodity.

The study results indicate that residues of aminopyralid are stable during frozen storage for up to ~16 months in/on grass forage and hay and for up to ~15 months in/on wheat grain and straw.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the storage stability data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the U.S. EPA Residue Chemistry Summary Document, D360100, D. Dotson, 10/22/2009.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported.

A. BACKGROUND INFORMATION

Aminopyralid is a systemic postemergence herbicide that belongs to the pyridine carboxylic acid class of herbicides. It is currently registered for use on rangeland, permanent grass pastures, and wheat. In addition, it is registered for use on wildlife habitat and industrial vegetation management areas, including right-of-way for roads, railroads, and utility lines. Under PP#8F7455, Dow AgroSciences is proposing aminopyralid for use on field corn. The end-use product (EP) proposed for use on field corn is a liquid soluble concentrate (SL), Milestone Specialty Herbicide (EPA Reg. No. 62719-519), in which aminopyralid is formulated as the triisopropanolammonium (TIPA) salt. The product contains 40.6% aminopyralid TIPA salt at an acid equivalent (ae) of 21.1% or 2 lb ae/gal.

The chemical structure and nomenclature of aminopyralid and the physicochemical properties of the technical grade of aminopyralid are presented in Tables A.1 and A.2.

TABLE A.1. Test Compound Nomenclature.

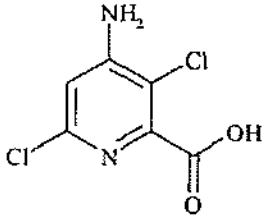
Compound	
Common name	Aminopyralid
Company experimental name	XDE-750
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid
CAS name	4-amino-3,6-dichloro-2-pyridinecarboxylic acid
CAS registry number	150114-71-9
End-use product (EP)	Not applicable

TABLE A.2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value	Reference
Melting point/range	163.5°C	MRID 46235703
pH	2.31 at 23.4°C (1% solution in water)	MRID 46235703
Density	1.72 at 20°C	MRID 46235703
Water solubility	2.48 g/L unbuffered water at 18°C 212 g/L pH 5 buffer at 20°C 205 g/L pH 7 buffer at 20°C 203 g/L pH 9 buffer at 20°C	MRID 46235703
Solvent solubility at 20°C	methanol 52.2 g/L acetone 29.2 g/L n-octanol 3.9 g/L ethyl acetate 3.9 g/L 1,2-dichloroethane 0.2 g/L xylene 0.04 g/L heptane <10 µg/mL	MRID 46235703
Vapor pressure	2.59×10^{-8} Pa at 25°C; 9.52×10^{-9} Pa at 20°C	MRID 46235703
Dissociation constant, pK_a	2.56	MRID 46235703
Octanol/water partition coefficient, Log(K_{OW})	0.201 unbuffered water at 19°C -1.76 at pH 5 -2.87 at pH 7 -2.96 at pH 9	MRID 46235703
UV/visible absorption spectrum	Solution / Wavelength λ max, nm / Extinction coefficient L/(mol*cm) Neutral 217 29100 Basic (pH 12.6) 220 26100 Basic (pH 12.6) 245 10150 Acidic (pH 1.4) 217 22800 Acidic (pH 1.4) 270 9140	MRID 46235703

B. EXPERIMENTAL DESIGN

B.1. Sample Handling and Preparation

The study was conducted by Dow AgroSciences Regulatory Laboratories (Indianapolis, IN). Samples of untreated grass hay and forage and wheat grain and straw (obtained from Dow AgroSciences) were fortified with aminopyralid at 0.1 ppm. The aminopyralid fortification standard was prepared in methanol. Fortified and unfortified samples were then stored frozen (~-20°C) in HDPE containers. Stored and fresh fortification samples of grass hay and forage were analyzed after 0, 28, 130, 187, and 488 days of frozen storage, and stored and fresh fortification samples of wheat grain and straw were analyzed after 0, 113, 168/175, 273, and 469 days of frozen storage; the tested intervals were approximately 0, 1 (hay and forage), 4, 6, 9 (grain and straw), and 15-16 months. At each tested interval, one untreated sample, two freshly fortified samples, and three stored-fortified samples were analyzed. The 0-day grass hay and forage samples were actually fortified and analyzed concurrently with the 28-day stored samples, and the 0-day wheat grain and straw samples were fortified and analyzed a day before the 113-day stored samples.

B.2. Analytical Methodology

Samples of grass hay and forage and wheat grain and straw were analyzed for residues of aminopyralid using LC/MS/MS Method GRM 02.31. A complete description of the method is provided in the residue analytical method DER for MRID 46235712 (46235712.1340.plant.der.wpd).

Briefly, homogenized samples of grass hay and forage and wheat grain and straw were extracted using 0.1 N sodium hydroxide and centrifuged. Residues were concentrated and purified using solid phase extraction cartridges. The internal standard, $^{13}C_2$-^{15}N-aminopyralid, was added to the eluate, which was then evaporated to dryness. Residues were redissolved in coupling reagent, derivatized with butyl chloroformate to form the 1-butyl ester of aminopyralid and the internal standard, and diluted with mobile phase for analysis by LC/MS/MS. The LOQ was 0.01 ppm.

C. RESULTS AND DISCUSSION

Concurrent method recovery data are presented in Table C.1. Recoveries of aminopyralid from samples of grass and wheat fortified at 0.1 ppm were within the acceptable range of 70-120%. The data indicate that the LC/MS/MS method is adequate for the determination of residues of aminopyralid in/on grass forage and hay and wheat grain and straw. Apparent residues were nonquantifiable (<0.01 ppm) in all unfortified samples (one control sample each of grass hay and forage, and wheat grain and straw).

The results of the storage stability study are presented in Table C.2. The interim results previously reviewed by HED (DER 46235719.1380.der.wpd) are re-presented herein for completeness. Based on the submitted data, residues of aminopyralid are stable in/on grass forage, grass hay, wheat grain, and wheat straw during frozen storage (-20°C) for up to ~16 months. A graph of the storage stability of residues of aminopyralid in grass forage and hay, and wheat grain and straw is provided in Figure C.1.

The review of the interim report of this storage stability study noted that raw data for the 6-month storage interval for wheat straw were missing. These raw data have been included in the final report of the study.

TABLE C.1. Summary of Concurrent Recoveries of Aminopyralid from Grass and Wheat Matrices.

Matrix	Spike Level (ppm)	Storage Interval (days)	Sample Size (n)	Recoveries (%)	Mean (%)
Grass forage	0.1	0	2	91, 94	92
		28	2	95, 95	95
		130	2	71, 78	74
		187	2	82, 85	83
		488	2	86, 88	87
Grass hay	0.1	0	2	93, 94	94
		28	2	91, 93	92
		130	2	73, 79	76
		187	2	81, 83	82
		488	2	88, 88	88
Wheat grain	0.1	0	2	85, 87	86
		113	2	89, 90	90
		168	2	93, 97	95
		273	2	100, 106	103
		469	2	88, 90	89
Wheat straw	0.1	0	2	82, 84	83
		113	2	80, 88	84
		175	2	87, 96	91
		273	2	101, 101	101
		469	2	84, 86	85

TABLE C.2. Stability of Aminopyralid Residues in Grass and Wheat Matrices Following Storage at Approximately -20°C.

Commodity	Spike Level (ppm)	Storage Interval (days)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected Recovery[1] (%)
Grass forage	0.1	0	0.0767, 0.0898, 0.0908	0.0858	86	93
		28	0.0904, 0.0907, 0.0922	0.0911	91	96
		130	0.0678, 0.0790, 0.0803	0.0757	76	102
		187	0.0771, 0.0863, 0.0870	0.0835	83	100
		489	0.0846, 0.0888, 0.0918	0.0884	88	102
Grass hay	0.1	0	0.0862, 0.0885, 0.0898	0.0882	88	94
		28	0.0880, 0.0909, 0.0944	0.0911	91	99
		130	0.0684, 0.0689, 0.0763	0.0712	71	93
		187	0.0769, 0.0784, 0.0807	0.0787	79	96
		489	0.0848, 0.0858, 0.0890	0.0865	87	98
Wheat grain	0.1	0	0.0824, 0.0853, 0.0867	0.0848	85	99
		113	0.0800, 0.0898, 0.0900	0.0866	87	96
		168	0.0882, 0.0883, 0.0911	0.0892	89	94
		273	0.0976, 0.0978, 0.0978	0.0977	98	95
		469	0.0903, 0.0908, 0.0920	0.0910	91	103

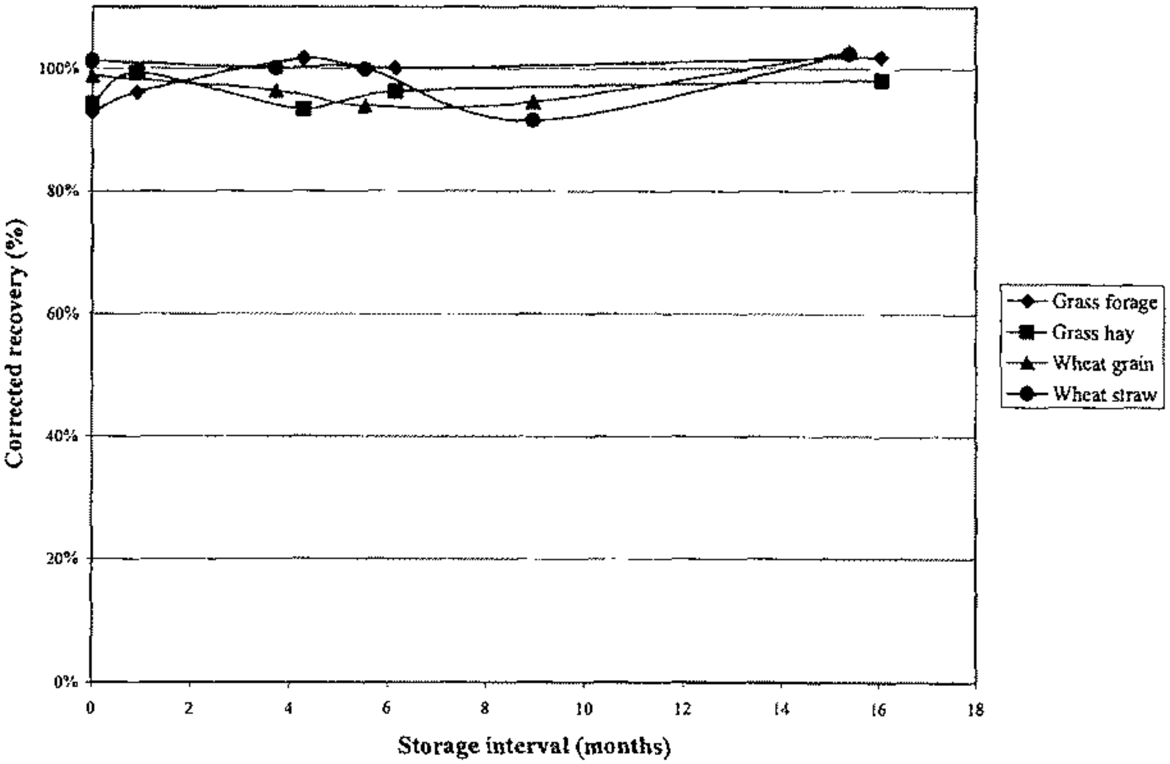
36

TABLE C.2. Stability of Aminopyralid Residues in Grass and Wheat Matrices Following Storage at Approximately -20°C.

Commodity	Spike Level (ppm)	Storage Interval (days)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected Recovery[1] (%)
Wheat straw	0.1	0	0.0816, 0.0847, 0.0854	0.0839	84	101
		113	0.0821, 0.0821, 0.0878	0.0840	84	100
		175	0.0897, 0.0918, 0.0920	0.0912	91	100
		273	0.0885, 0.0943, 0.0944	0.0924	92	91
		469	0.0857, 0.0873, 0.0876	0.0869	87	102

[1] Corrected for mean concurrent recovery (see Table C.1.).

FIGURE C.1. **Graph of residue stability in grass and wheat matrices.**



D. CONCLUSION

The submitted storage stability study adequately demonstrates the stability of residues of aminopyralid in/on grass forage, grass hay, wheat grain, and wheat straw stored frozen (~-20°C) for up to 16 months. An adequate method was used for quantitation of residues in the tested matrices.

E. REFERENCES

D305665, PP#4F6827, Aminopyralid. Petition for the Establishment of Permanent Tolerances for Use of Aminopyralid on Grasses and Wheat. Summary of Analytical Chemistry and Residue Data, M. Doherty, 7/12/05, MRIDs: 46235708-46235712, 46235714, 46235716-46235719, and 46235721-46235725

D305665, Aminopyralid. Residue Analytical Method: Plant. DER 46235712.1340.plant.der.wpd, M. Doherty, 6/28/05, MRID: 46235712

D305665, Aminopyralid. Storage Stability - Grasses and Wheat. DER 46235719.1380.der.wpd, M. Doherty, 6/28/05, MRID: 46235719

F. DOCUMENT TRACKING

Petition Number: 8F7455
DP#: 360100
PC Codes: 005100 and 005209

Primary Evaluator Douglas Dotson Date: 10/22/2009
Douglas Dotson, Ph.D., Chemist, RABII

Peer Reviewer Michael A Doherty Date: 10/22/2009
Michael Doherty, Ph.D., Chemist, RABII

This DER was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850; submitted 05/21/2009). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46729001 Oberling, E. (2006) A Confirmatory Technique for the Determination of Residues of Aminopyralid in Agricultural Commodities by Liquid Chromatography with Tandem Mass Spectrometry Detection. Project Number: GH/C/5830, GRM/02/31. Unpublished study prepared by Dow Agrosciences LLC. 25 p.

EXECUTIVE SUMMARY:

The petitioner previously proposed LC/MS/MS Method GRM 02.31 for the enforcement of tolerances for residues of aminopyralid in grass and wheat commodities, and LC/MS/MS Method GRM 03.18 for the enforcement of tolerances for residues of aminopyralid in livestock commodities. In review of the methods, HED expressed concern that the proposed enforcement methods might not be able to differentiate between aminopyralid, picloram, and clopyralid, and requested that the petitioner complete an interference study using these three compounds (Memo, D305665, M. Doherty, 7/12/05).

Dow AgroSciences has submitted the requested interference study for the derivatization and LC/MS/MS analysis procedures of Method GRM 02.31. To investigate the potential inference of picloram and clopyralid in the determination of aminopyralid, the petitioner prepared analytical standards of picloram and clopyralid, as well as aminopyralid, and derivatized the standards to form the 1-butyl esters of the compounds using the procedures of Method GRM 02.31. The derivatized compounds were then analyzed by LC/MS/MS.

The analysis of the 1-butyl esters of aminopyralid, clopyralid, and picloram demonstrated that the three compounds have different retention times, and that there was no interference in the ion transitions. Therefore, clopyralid and picloram do not interfere in the determination of aminopyralid residues. Because the derivatization and LC/MS/MS analysis procedures of Method GRM 02.31 are the same as those of Method GRM 03.18, clopyralid and picloram will not interfere in aminopyralid determination using Method GRM 02.31 or GRM 03.18.

The petitioner noted that, since the original aminopyralid methods were developed, minor changes in the LC conditions and MS/MS parameters have been made to improve the sensitivity and selectivity of the method, including the addition of two ion transitions to monitor for the confirmation of aminopyralid residues. Representative chromatograms from the analysis of a grass forage sample were provided for the quantitation ion transition and the two confirmation ion transitions. The changes in the LC and MS/MS conditions are reflected in the revised methods that were submitted with this tolerance petition: Method GRM 07.07 for crop commodities and Method GRM 07.08 for livestock commodities (refer to the DERs for MRID 47572602: 47572602.de1.doc and 47572602.de2.doc).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the analytical method test data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the U.S. EPA Residue Chemistry Summary Document, D360100, D. Dotson, 10/22/2009.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. The GLP and Quality Assurance statements stated that the study was a non-GLP study, presumably because the study pertains to method development and does not contain any quantitative data (such as recoveries).

A. BACKGROUND INFORMATION

Aminopyralid is a systemic postemergence herbicide that belongs to the pyridine carboxylic acid class of herbicides. It is currently registered for use on rangeland, permanent grass pastures, and wheat. In addition, it is registered for use on wildlife habitat and industrial vegetation management areas, including right-of-way for roads, railroads, and utility lines. Under PP#8F7455, Dow AgroSciences is proposing aminopyralid for use on field corn. The end-use product (EP) proposed for use on field corn is a liquid soluble concentrate (SL), Milestone Specialty Herbicide (EPA Reg. No. 62719-519), in which aminopyralid is formulated as the triisopropanolammonium (TIPA) salt. The product contains 40.6% aminopyralid TIPA salt at an acid equivalent (ae) of 21.1% or 2 lb ae/gal.

The chemical structure and nomenclature of aminopyralid and the physicochemical properties of the technical grade of aminopyralid are presented in Tables A.1 and A.2.

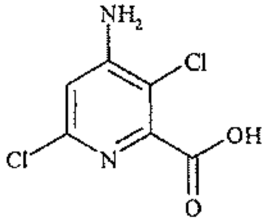
TABLE A.1. Test Compound Nomenclature.	
Compound	
Common name	Aminopyralid
Company experimental name	XDE-750
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid
CAS name	4-amino-3,6-dichloro-2-pyridinecarboxylic acid
CAS registry number	150114-71-9
End-use product (EP)	Not applicable

TABLE A.2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value	Reference
Melting point/range	163.5°C	MRID 46235703
pH	2.31 at 23.4°C (1% solution in water)	MRID 46235703
Density	1.72 at 20°C	MRID 46235703
Water solubility	2.48 g/L unbuffered water at 18°C 212 g/L pH 5 buffer at 20°C 205 g/L pH 7 buffer at 20°C 203 g/L pH 9 buffer at 20°C	MRID 46235703
Solvent solubility at 20°C	methanol 52.2 g/L acetone 29.2 g/L n-octanol 3.9 g/L ethyl acetate 3.9 g/L 1,2-dichloroethane 0.2 g/L xylene 0.04 g/L heptane <10 µg/mL	MRID 46235703
Vapor pressure	2.59×10^{-8} Pa at 25°C; 9.52×10^{-9} Pa at 20°C	MRID 46235703
Dissociation constant, pK_a	2.56	MRID 46235703
Octanol/water partition coefficient, $Log(K_{OW})$	0.201 unbuffered water at 19°C -1.76 at pH 5 -2.87 at pH 7 -2.96 at pH 9	MRID 46235703
UV/visible absorption spectrum	Solution / Wavelength λ max, nm / Extinction coefficient L/(mol*cm) Neutral 217 29100 Basic (pH 12.6) 220 26100 Basic (pH 12.6) 245 10150 Acidic (pH 1.4) 217 22800 Acidic (pH 1.4) 270 9140	MRID 46235703

B. MATERIALS AND METHODS

B.1. Data-Gathering Method

Not applicable to this submission.

B.2. Enforcement Method

The petitioner previously proposed LC/MS/MS Method GRM 02.31 for the enforcement of tolerances for residues of aminopyralid in grass and wheat commodities and LC/MS/MS Method GRM 03.18 for the enforcement of tolerances for residues of aminopyralid in livestock commodities. In review of the methods, HED expressed concern that the proposed enforcement methods might not be able to differentiate between aminopyralid, picloram, and clopyralid, and requested that the petitioner complete an interference study using these three compounds (Memo, D305665, M. Doherty, 7/12/05).

Dow AgroSciences has submitted an interference study for the derivatization and LC/MS/MS analysis procedures of Method GRM 02.31.

B.2.1. Principle of the Method:

Briefly, for Method GRM 02.31, homogenized samples are extracted with 0.1 N sodium hydroxide, releasing bound residues and hydrolyzing base-labile conjugates in order to free aminopyralid. The extract is then acidified with hydrochloric acid and heated to release acid-labile conjugates. Following hydrolysis, the extract is cleaned up through an anion-exchange solid-phase extraction column. The internal standard, $^{13}C_2{}^{15}N$-aminopyralid, is added to the eluate and residues are derivatized with butyl chloroformate to form the 1-butyl esters of aminopyralid for LC/MS/MS analysis.

To investigate the potential inference of picloram and clopyralid in the determination of aminopyralid, the petitioner prepared analytical standards of picloram and clopyralid in acetonitrile, as well as aminopyralid, and derivatized the standards to form the 1-butyl esters of the compounds using the procedures of Method GRM 02.31. The derivatized compounds were then analyzed by LC/MS/MS.

TABLE B.2.1. Summary Parameters for the Analytical Enforcement Method Used for the Quantitation of Aminopyralid Residues in Crop and Livestock Matrices.
Not applicable to this submission. The method parameters are presented in 46235712.1340.plant.der.wpd and 46235714.1340.livestock.der.wpd (Memo, D305665, M. Doherty, 7/12/05).

C. RESULTS AND DISCUSSION

C.1. Data-Gathering Method

Not applicable to this submission.

C.2. Enforcement Method

LC/MS/MS analysis of the analytical standards of the 1-butyl esters of aminopyralid, clopyralid, and picloram demonstrated that the three compounds have different retention times (approximately 5.9 minutes for aminopyralid butyl ester, 6.45 minutes for clopyralid butyl ester, and 6.5 minutes for picloram butyl ester). There was no evidence of interference in the ion transitions. Therefore, clopyralid and picloram do not interfere in the determination of aminopyralid residues. The derivatization and LC/MS/MS analysis procedures of Method GRM 02.31 are the same as those of Method GRM 03.18; therefore, clopyralid and picloram will not interfere in aminopyralid determination using Method GRM 02.31 or GRM 03.18.

The petitioner noted that since the original aminopyralid methods were developed, minor changes in the LC conditions and MS/MS parameters have been made to improve the sensitivity and selectivity of the method. The LC column was changed from the C18 column to a Zorbax SB-C8 column. The mobile phase was changed from methanol/water containing 0.1% acetic acid to methanol/water containing 0.05% formic acid and 5 mM ammonium formate. Two additional ion transitions have been included for the confirmation of aminopyralid residues.

The petitioner stated that calculation of the peak area ratios of the additional ion transitions (*m/z* 263→161 and 263→189) to the quantitation ion transition (*m/z* 263→134) may be used for confirmation of analyte presence. The ratio should be within ±20% of the average ratio for the standards to confirm aminopyralid residues. A sample of grass forage from previously submitted field trials (Memo, D305665, M. Doherty, 7/12/05) was fortified with aminopyralid and the unfortified and fortified samples were analyzed using Method GRM 02.31. The chromatograms for all three ion transitions were included in the submission, along with calculation of the peak area ratios for the confirmation ions and comparison of these ratios with the averages for the standards. For the fortified sample, the peak area ratios differed from the averages by 12.5% and 13.4%. For an aminopyralid standard, the peak area ratios differed by 5.9% and 8.7%.

The above changes in LC and MS/MS conditions are reflected in the revised methods that were submitted with this tolerance petition: Method GRM 07.07 for crop commodities and Method GRM 07.08 for livestock commodities (refer to the DERs for MRID 47572602: 47572602.de1.doc and 47572602.de2.doc).

TABLE C.2.1. Recovery Results from Method Validation Using the Enforcement Analytical Method.

Matrix	Spiking Level (ppm)	Recoveries Obtained	Mean Recovery ± Std. Dev. $[CV]^2$ (%)
Not applicable to this submission.			

TABLE C.2.2. Characteristics for the Enforcement Analytical Method Used for the Quantitation of Aminopyralid Residues in Crop and Livestock Matrices.
Not applicable to this submission. The method characteristics are presented in 46235712.1340.plant.der.wpd and 46235714.1340.livestock.der.wpd (Memo, D305665, M. Doherty, 7/12/05).

C.3. Independent Laboratory Validation

Not applicable to this submission.

D. CONCLUSION

The submitted interference data indicate that residues of picloram and/or clopyralid will not interfere in the determination of residues of aminopyralid when samples are analyzed using LC/MS/MS Method GRM 02.31 or GRM 03.18.

E. REFERENCES

D305665, PP#4F6827, Aminopyralid. Petition for the Establishment of Permanent Tolerances for Use of Aminopyralid on Grasses and Wheat. Summary of Analytical Chemistry and Residue Data, M. Doherty, 7/12/05, MRIDs: 46235708-46235712, 46235714, 46235716- 46235719, 46235721-46235725

D305665, Aminopyralid. Residue Analytical Method: Plant, DER 46235712.1340.plant.der, M. Doherty, 6/28/05, MRID: 46235712

D305665, Aminopyralid. Residue Analytical Method: Ruminant, DER 46235714.1340.livestock, M. Doherty, 6/28/05, MRID 46235714

F. DOCUMENT TRACKING

Petition Number: 8F7455
DP#: 360100
PC Codes: 005100 and 005209

Primary Evaluator	Douglas Dotson Douglas Dotson, Ph.D., Chemist, RABII	Date: 10/22/2009
Peer Reviewer	Michael Doherty Michael Doherty, Ph.D., Chemist, RABII	Date: 10/22/2009

This DER was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850; submitted 5/14/2009). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

47572601 Rosser, S. (2008) Residues of Aminopyralid in Corn Forage, Grain, Stover and Processed Products. Project Number: 060014, IL2. Unpublished study prepared by Dow AgroSciences, LLC and GLP Technologies. 131 p.

47572603 Rosser, S. (2008) Study Profile Template for Residues of Aminopyralid in Corn Forage, Grain, Stover and Processed Products. Project Number: 060014/SPT1. Unpublished study prepared by Dow AgroSciences, LLC. 31 p.

EXECUTIVE SUMMARY:

Dow AgroSciences has submitted field trial data for aminopyralid on field corn. Twenty field corn trials were conducted in the United States during the 2006 growing season. One trial each was performed in Zones 1 (PA), 2 (GA), and 6 (TX). Seventeen trials were performed in Zone 5 (IA (3), IL (3), IN (1), MI (1), MN (2), MO (1), ND (2), NE (2), OH (1), and WI (1)).

Each treated plot received a single foliar application of a liquid soluble concentrate (SL) formulation containing the triisopropanolammonium (TIPA) salt of aminopyralid at 2 lb ae/gal. Applications were made at the 4- to 6-leaf growth stage (BBCH 14-16 or V4-V6). One treated plot received an application at ~0.031 lb ae/A and the other plot received an application at ~0.062 lb ae/A. Applications were made in ~15-24 gal/A spray volumes, using ground equipment. A non-ionic surfactant was added to the spray mixture at ~0.25% (v/v). Field corn commodities were harvested at normal harvest times. Forage was harvested at the dent stage, at a 60- to 87-day preharvest interval (PHI), and grain and stover were harvested at maturity, at a 105- to 138-day PHI. In addition, to evaluate residue decline, forage samples were harvested at the Wisconsin trial and at one of the Illinois trials at 0-, 7-, 13- to 14-, 21-, and 28-day PHIs.

Samples of field corn forage, grain, and stover were analyzed for residues of aminopyralid using a high performance liquid chromatography method with tandem mass spectrometry detection (LC/MS/MS), Method GRM 07.07. The validated limit of quantitation (LOQ) was 0.01 ppm for each matrix. The method was adequate for data collection based on acceptable concurrent method recovery data. Overall method recoveries ranged from 69 to 90% in forage, from 75 to 97% in grain, and from 72 to 94% in stover.

Samples were stored frozen from harvest to extraction, for maximum durations of 17.0 months for forage and 14.7 months for grain and stover. The available storage stability data indicate that residues of aminopyralid are stable during frozen storage for up to ~16 months in/on grass forage and hay and for up to ~15 months in/on wheat grain and straw (refer to the DER for MRID 46661301). These data are adequate to support the storage conditions and durations of samples from the submitted field corn study.

Following foliar application of the 2 lb ae/gal SL formulation at 0.030-0.034 lb ae/A, maximum residues of aminopyralid were 0.262 ppm in/on forage (60- to 87-day PHI), 0.164 ppm in/on grain (105- to 138-day PHI), and 0.176 ppm in/on stover (105- to 138-day PHI). Following foliar application at 0.060-0.069 lb ae/A, maximum residues of aminopyralid were 0.293 ppm in/on forage, 0.212 ppm in/on grain, and 0.387 ppm in/on stover.

In the four forage residue decline trials, average residues of aminopyralid decreased from the 0-day to either the 14-day or 21-day PHI and then generally did not decrease further (from the 14- or 21-day PHI to harvest at 66 or 72 days posttreatment).

MRID 47572601 includes residue data for field corn aspirated grain fractions and processed commodities. Refer to the 860.1520 DER for MRID 47572601 for a discussion of these data.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the U.S. EPA Residue Chemistry Summary Document, D360100, D. Dotson, 10/22/2009.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Aminopyralid is a systemic postemergence herbicide that belongs to the pyridine carboxylic acid class of herbicides. It is currently registered for use on rangeland, permanent grass pastures, and wheat. In addition, it is registered for use on wildlife habitat and industrial vegetation management areas, including right-of-way for roads, railroads, and utility lines. Under PP#8F7455, Dow AgroSciences is proposing aminopyralid for use on field corn. The end-use product (EP) proposed for use on field corn is a SL formulation, Milestone Specialty Herbicide (EPA Reg. No. 62719-519), in which aminopyralid is formulated as the TIPA salt. The product contains 40.6% aminopyralid TIPA salt at an acid equivalent (ae) of 21.1% or 2 lb ae/gal.

The chemical structure and nomenclature of aminopyralid and aminopyralid TIPA salt, and the physicochemical properties of the technical grade of aminopyralid are presented in Tables A.1 and A.2.

TABLE A.1. Test Compound Nomenclature.

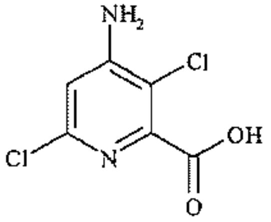
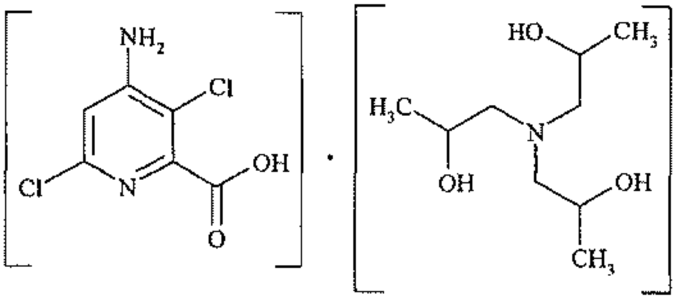
Compound	
Common name	Aminopyralid
Company experimental name	XDE-750
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid
CAS name	4-amino-3,6-dichloro-2-pyridinecarboxylic acid
CAS registry number	150114-71-9
Compound	
Common name	Aminopyralid, triisopropanolammonium (TIPA) salt
PC Code	005209
Company experimental name	XDE-750 TIPA salt
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid - (2RS,2′RS,2″RS)-1,1′,1″-nitrilotripropan-2-ol (1:1)
CAS name	4-amino-3,6-dichloropyridine-2-carboxylic acid compound with 1,1′,1″-nitrilotris[2-propanol] (1:1)
CAS registry number	566191-89-7
End-use product (EP)	Milestone Specialty Herbicide (2 lb ae/gal SL; EPA Reg. No. 62719-519)

TABLE A.2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value	Reference
Melting point/range	163.5°C	MRID 46235703
pH	2.31 at 23.4°C (1% solution in water)	MRID 46235703
Density	1.72 at 20°C	MRID 46235703
Water solubility	2.48 g/L unbuffered water at 18°C 212 g/L pH 5 buffer at 20°C 205 g/L pH 7 buffer at 20°C 203 g/L pH 9 buffer at 20°C	MRID 46235703

TABLE A.2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value	Reference
Solvent solubility at 20°C	methanol 52.2 g/L acetone 29.2 g/L n-octanol 3.9 g/L ethyl acetate 3.9 g/L 1,2-dichloroethane 0.2 g/L xylene 0.04 g/L heptane <10 µg/mL	MRID 46235703
Vapor pressure	2.59 x 10^{-8} Pa at 25°C; 9.52 x 10^{-9} Pa at 20°C	MRID 46235703
Dissociation constant, pK_a	2.56	MRID 46235703
Octanol/water partition coefficient, Log(K_{OW})	0.201 unbuffered water at 19°C -1.76 at pH 5 -2.87 at pH 7 -2.96 at pH 9	MRID 46235703
UV/visible absorption spectrum	Solution / Wavelength λ max, nm / Extinction coefficient L/(mol*cm) Neutral / 217 / 29100 Basic (pH 12.6) / 220 / 26100 Basic (pH 12.6) / 245 / 10150 Acidic (pH 1.4) / 217 / 22800 Acidic (pH 1.4) / 270 / 9140	MRID 46235703

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Twenty field corn trials were conducted in the United States during the 2006 growing season. One trial each was performed in Zones 1 (PA), 2 (GA), and 6 (TX). Seventeen trials were performed in Zone 5 (IA (3), IL (3), IN (1), MI (1), MN (2), MO (1), ND (2), NE (2), OH (1), and WI (1)).

At each trial location, two treated plots and one control plot were established. Each treated plot received a single foliar application of a SL formulation containing the TIPA salt of aminopyralid at 2 lb ae/gal. Applications were made at the 4- to 6-leaf growth stage (BBCH 14-16 or V4-V6). One treated plot received an application at ~0.031 lb ae/A and the other plot received an application at ~0.062 lb ae/A. Applications were made in ~15-24 gal/A spray volumes, using ground equipment. A non-ionic surfactant was added to the spray mixture at ~0.25% (v/v). Actual test parameters are reported in Table B.1.2.

The petitioner stated that farming practices were typical of corn production. A list of the maintenance pesticides and fertilizers that were used was provided. Trial site conditions are presented in Table B.1.1. The crop varieties grown are identified in Table C.3. For each field trial, average monthly minimum and maximum temperatures and monthly rainfall amounts were presented, along with historical values. The petitioner stated that, although there were instances at most sites in which temperatures and/or rainfall varied appreciably from historical averages, the observations appear typical of year-to-year variation in weather conditions across the area represented in the study, and there was no indication that weather conditions impacted the validity of the trials reported in the study. Irrigation was used to supplement rainfall at the Georgia, Nebraska, Pennsylvania, and Wisconsin trials.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics			
	Type	%OM	pH	CEC (meq/g)
Sycamore, GA; 2006 (060014-GA)	Loamy sand	Not provided		
Richland, IA; 2006 (060014-IA1)	Silt loam	Not provided		
Perry, IA; 2006 (060014-IA2)	Loam	Not provided		
Bagley, IA; 2006 (060014-IA3)	Silty clay loam	Not provided		
Wyoming, IL; 2006 (060014-IL1)	Silt loam	Not provided		
Carlyle, IL; 2006 (060014-IL2)	Silt loam	Not provided		
Mason, IL; 2006 (060014-IL3)	Silt loam	Not provided		
Rockville, IN; 2006 (060014-IN)	Silt loam	Not provided		
Conklin, MI; 2006 (060014-MI)	Loam	Not provided		
Theilman, MN; 2006 (060014-MN1)	Silt loam	Not provided		
Theilman, MN; 2006 (060014-MN2)	Sandy loam	Not provided		
La Plata, MO; 2006 (060014-MO)	Silty clay loam	Not provided		
Gardner, ND; 2006 (060014-ND1)	Silty clay	Not provided		
Ayr, ND; 2006 (060014-ND2)	Loam	Not provided		
York, NE; 2006 (060014-NE1)	Silt loam	Not provided		
Osceola, NE; 2006 (060014-NE2)	Sandy loam	Not provided		
New Holland, OH; 2006 (060014-OH)	Silt loam	Not provided		
Germansville, PA; 2006 (060014-PA)	Loam	Not provided		
East Bernard, TX; 2006 (060014-TX)	Clay	Not provided		
Arkansaw, WI; 2006 (060014-WI)	Sandy loam	Not provided		

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Timing[2]	Volume (gal/A)	Rate (lb ae/A)	RTI[3] (days)	Total Rate (lb ae/A)	
Sycamore, GA; 2006 (060014-GA)	2 lb ae/gal SL	1. BBCH 14-15	20.8	0.031	NA	0.031	NIS
		1. BBCH 14-15	21.0	0.063	NA	0.063	
Richland, IA; 2006 (060014-IA1)	2 lb ae/gal SL	1. BBCH 16	15.7	0.032	NA	0.032	NIS
		1. BBCH 16	15.6	0.063	NA	0.063	
Perry, IA; 2006 (060014-IA2)	2 lb ae/gal SL	1. BBCH 14-16	17.6	0.031	NA	0.031	NIS
		1. BBCH 14-16	17.6	0.062	NA	0.062	
Bagley, IA; 2006 (060014-IA3)	2 lb ae/gal SL	1. BBCH 14-16	17.3	0.030	NA	0.030	NIS
		1. BBCH 14-16	17.8	0.063	NA	0.063	
Wyoming, IL; 2006 (060014-IL1)	2 lb ae/gal SL	1. BBCH 15-16	15.9	0.030	NA	0.030	NIS
		1. BBCH 15-16	16.3	0.062	NA	0.062	
Carlyle, IL; 2006 (060014-IL2)	2 lb ae/gal SL	1. BBCH 14-15	17.7	0.031	NA	0.031	NIS
		1. BBCH 14-15	17.4	0.060	NA	0.060	

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Timing[2]	Volume (gal/A)	Rate (lb ae/A)	RTI[3] (days)	Total Rate (lb ae/A)	
Mason, IL; 2006 (060014-IL3)	2 lb ae/gal SL	1. BBCH 15-16	14.6	0.030	NA	0.030	NIS
		1. BBCH 15-16	15.2	0.063	NA	0.063	
Rockville, IN; 2006 (060014-IN)	2 lb ae/gal SL	1. BBCH 14-15	18.7	0.032	NA	0.032	NIS
		1. BBCH 14-15	18.9	0.064	NA	0.064	
Conklin, MI; 2006 (060014-MI)	2 lb ae/gal SL	1. BBCH 15-16	19.7	0.031	NA	0.031	NIS
		1. BBCH 15-16	19.7	0.062	NA	0.062	
Theilman, MN; 2006 (060014-MN1)	2 lb ae/gal SL	1. BBCH 15-16	20.4	0.032	NA	0.032	NIS
		1. BBCH 15-16	20.0	0.063	NA	0.063	
Theilman, MN; 2006 (060014-MN2)	2 lb ae/gal SL	1. BBCH 14-15	20.3	0.032	NA	0.032	NIS
		1. BBCH 14-15	20.4	0.064	NA	0.064	
La Plata, MO; 2006 (060014-MO)	2 lb ae/gal SL	1. BBCH 16-17	15.4	0.031	NA	0.031	NIS
		1. BBCH 16-17	15.3	0.062	NA	0.062	
Gardner, ND; 2006 (060014-ND1)	2 lb ae/gal SL	1. BBCH 14-15	20.5	0.032	NA	0.032	NIS
		1. BBCH 14-15	20.3	0.064	NA	0.064	
Ayr, ND; 2006 (060014-ND2)	2 lb ae/gal SL	1. BBCH 14-15	20	0.031	NA	0.031	NIS
		1. BBCH 14-15	20.1	0.063	NA	0.063	
York, NE; 2006 (060014-NE1)	2 lb ae/gal SL	1. BBCH 14-15	19.6	0.031	NA	0.031	NIS
		1. BBCH 14-15	19.4	0.061	NA	0.061	
Osceola, NE; 2006 (060014-NE2)	2 lb ae/gal SL	1. BBCH 14-15	19.7	0.031	NA	0.031	NIS
		1. BBCH 14-15	19.5	0.062	NA	0.062	
New Holland, OH; 2006 (060014-OH)	2 lb ae/gal SL	1. BBCH 15-16	15.4	0.031	NA	0.031	NIS
		1. BBCH 15-16	15.8	0.064	NA	0.064	
Germansville, PA; 2006 (060014-PA)	2 lb ae/gal SL	1. BBCH 14-16	24.2	0.034	NA	0.034	NIS
		1. BBCH 14-16	24.3	0.069	NA	0.069	
East Bernard, TX; 2006 (060014-TX)	2 lb ae/gal SL	1. BBCH 14-15	16.1	0.031	NA	0.031	NIS
		1. BBCH 14-15	16.1	0.063	NA	0.063	
Arkansaw, WI; 2006 (060014-WI)	2 lb ae/gal SL	1. BBCH 15	18.7	0.031	NA	0.031	NIS
		1. BBCH 15	18.7	0.062	NA	0.062	

[1] EP = End-use Product.

[2] All applications were foliar broadcast applications.

[3] RTI = Retreatment Interval. NA = Not applicable as treatment was a single application.

[4] Each application included a non-ionic surfactant (NIS) at approximately 0.25% (v/v).

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Field Corn		
	Submitted	Requested	
		Canada	U.S.[1]
1	1		1
1A			
2	1		1
3			
4			
5	17		17
5A			
5B			
6	1		1
7			
7A			
8			
9			
10			
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
21			
Total	20		20

[1] As per OPPTS 860.1500, Tables 1 and 5 for field corn as an individual crop.

B.2. Sample Handling and Preparation

For each trial, single samples were collected from each untreated plot and duplicate samples were collected from each treated plot. Samples were harvested by hand at normal harvest times. Forage samples were harvested at a 60- to 87-day PHI, at the ~BBCH 85 growth stage (grain dent) except for the Georgia trial where forage samples were harvested at the BBCH 73 to 75 growth stage. Samples of grain and stover were harvested at normal maturity at a 105- to 138-day PHI. In addition, to evaluate residue decline, forage samples were harvested at the Wisconsin trial and one of the Illinois trials at 0-, 7-, 13- to 14-, 21-, and 28-day PHIs. For forage samples (~≥2 kg each), the entire aerial portion of the plant was collected. For stover samples (~≥1 kg), the entire aerial portion of the plant was collected and the ears were removed. Grain samples (≥1.3 kg each) were collected from ears taken from plants throughout the plots.

The grain was removed from the ears by hand or using a sheller. Samples were placed in frozen storage within 4 hours of collection or placed in coolers with dry ice (for transport to a freezer; time to transport was not specified). The samples remained in frozen storage until shipment to Dow AgroSciences (Indianapolis, IN) for analysis. At the analytical facility, samples remained in frozen storage (~-20°C) except for homogenization, preparation, and extraction for analysis. Samples were prepared for analysis by freezing using liquid nitrogen and then grinding.

B.3. Analytical Methodology

Samples of field corn forage, grain, and stover were analyzed for residues of aminopyralid using LC/MS/MS Method GRM 07.07 (refer to the DER for MRID 47572602 for a complete description of the method). The petitioner stated that an adapted version of the method was used but did not specify how the method was adapted. Only a brief description of the method was included in MRID 47572601.

Briefly, residues of aminopyralid were extracted from field corn RAC samples using 0.1 M NaOH, which hydrolyzes bound residues and base-labile conjugates to yield free aminopyralid. The extract was acidified with HCl and heated at 80°C for 90 minutes, which hydrolyzes acid-labile conjugates to yield free aminopyralid and further solubilizes bound residues. The extract was then purified by anion-exchange solid phase extraction, using ethyl acetate:trifluoroacetic acid (99:1, v:v) to elute residues. An internal standard ($^{13}C_2{}^2H^{15}N$-aminopyralid) was added to the eluate, which was evaporated to dryness, reconstituted in acetonitrile:pyridine:1-butanol (22:2:1, v:v:v; derivatization coupling reagent) and derivatized with butyl chloroformate to form the 1-butyl esters of the analyte and the internal standard. The mixture was diluted with a solution of methanol:water (40:60, v:v) containing 0.05% formic acid and 5 mM ammonium formate solution for LC/MS/MS analysis. The limit of detection (LOD) and the LOQ are 0.003 and 0.01 ppm, respectively, for aminopyralid in each corn matrix.

The method was validated concurrently with the analysis of field samples of untreated forage, grain, and stover fortified with aminopyralid at 0.01 and 2 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations for field corn forage, grain, and stover are summarized in Table C.2. Samples were stored frozen (~-20°C) for up to 518 days (17.0 months) for forage, and up to 448 days (14.7 months) for grain and stover prior to extraction. No dates of analysis were provided. The petitioner should note for future submissions, that dates of extraction and analysis should be provided for all samples. The available storage stability data indicate that residues of aminopyralid are stable during frozen storage for up to ~16 months in/on grass forage and hay, and for up to ~15 months in/on wheat grain and straw (refer to the DER for MRID 46661301). These data are adequate to support the storage conditions and durations of samples from the submitted field corn study.

Concurrent method recovery data are presented in Table C.1. LC/MS/MS Method GRM 07.07 is adequate for data collection based on acceptable concurrent method recovery data. Recoveries were within the acceptable range of 70-120% from field corn forage, grain, and stover samples fortified with aminopyralid at 0.01 and 2 ppm, except for one forage sample fortified at 0.01 ppm (69%). Fortification levels were adequate to bracket residues found in treated samples. Adequate sample calculations and chromatograms were provided.

With the exception of one grain sample from a North Dakota site (0.0663 ppm) and a stover sample from one IL site (0.0276 ppm), apparent residues of aminopyralid were below the LOD (<0.003 ppm) in/on all samples of untreated forage, grain, and stover. The petitioner stated that no specific explanation was found for apparent residues in these two samples, but it was assumed that apparent residues resulted from contamination. For the North Dakota site (trial ID 060014-ND1), the observed quantifiable residues in/on the untreated grain sample might have been the result of sample mis-labeling, as one of the treated grain samples from the same site (treated at 0.064 lb ae/A) bore residues below the LOD.

Residue data from the field corn crop field trials are reported in Table C.3. A summary of residue data for field corn is presented in Table C.4. Following foliar application of the 2 lb ae/gal SL formulation at 0.030-0.034 lb ae/A, residues of aminopyralid ranged from <0.01 to 0.262 ppm in/on 40 samples of treated forage (60- to 87-day PHI), from <0.01 to 0.164 ppm in/on 40 samples of treated grain (105- to 138-day PHI), and from <0.01 to 0.176 ppm in/on 40 samples of treated stover (105- to 138-day PHI). Following foliar application at 0.060-0.069 lb ae/A, residues of aminopyralid ranged from 0.018 to 0.293 ppm in/on 39 samples of treated forage, from <0.01 to 0.212 ppm in/on 40 samples of treated grain, and from 0.020 to 0.387 ppm in/on 40 samples of treated stover.

In the forage residue decline trial, average residues of aminopyralid decreased from the 0-day to the 13/14-day PHI and then generally did not decrease further (from the 13/14-day PHI to harvest at 66 or 72 days posttreatment).

The petitioner questioned the validity of a nondetectable result for one treated grain sample from a Minnesota site (trial ID 060014-MN1), as the duplicate grain sample collected from the same plot bore residues of 0.0812 ppm. However, the registrant provided no explanation for the <LOD result.

TABLE C.1. Summary of Concurrent Recoveries of Aminopyralid from Corn Matrices.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Field corn forage	0.01	10	69, 73, 74, 74, 76, 81, 86, 86, 90, 90	80 ± 8
	2	10	79, 79, 80, 80, 81, 82, 83, 83, 85, 90	82 ± 3
Field corn grain	0.01	6	85, 87, 88, 89, 92, 97	90 ± 4
	2	6	75, 76, 78, 80, 81, 81	78 ± 3
Field corn stover	0.01	6	86, 87, 88, 89, 91, 94	89 ± 3
	2	6	72, 75, 75, 75, 76, 77	75 ± 2

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Field corn forage	–20	435-518 days (14.3-17.0 months)	Residues of aminopyralid are stable during frozen storage for up to ~16 months in/on grass forage and hay and for up to ~15 months in/on wheat grain and straw.[2]
Field corn grain		375-448 days (12.3-14.7 months)	
Field corn stover		377-448 days (12.4-14.7 months)	

[1] Actual storage duration from sampling/processing to extraction. Analysis dates were not provided.
[2] Refer to the DER for MRID 46661301.

TABLE C.3. Residue Data from Crop Field Trials with Aminopyralid.

Trial ID (City, State; Year)	Zone	Field Corn Variety	Total Rate (lb ae/A)	Commodity or matrix	PHI (days)	Aminopyralid (ppm)[1]
Sycamore, GA; 2006 (060014-GA)	2	Truckers Favorite	0.031	Forage	70	0.0445, 0.0342
				Grain	106	0.0147, 0.0142
				Stover	106	0.0186, 0.0184
			0.063	Forage	70	0.0851[2]
				Grain	106	0.0369, 0.0383
				Stover	106	0.0500, 0.0619
Richland, IA; 2006 (060014-IA1)	5	Golden Harvest HX9323	0.032	Forage	85	0.0410, 0.0237
				Grain	117	0.0259, 0.0317
				Stover	117	0.0201, 0.0300
			0.063	Forage	85	0.0364, 0.0550
				Grain	117	0.0665, 0.0660
				Stover	117	0.0341, 0.0321
Perry, IA; 2006 (060014-IA2)	5	36B10	0.031	Forage	70	0.0394, 0.0406
				Grain	114	0.0430, 0.0473
				Stover	114	0.0356, 0.0342
			0.062	Forage	70	0.1052, 0.1068
				Grain	114	0.0573, 0.0571
				Stover	114	0.0581, 0.0486
Bagley, IA; 2006 (060014-IA3)	5	33P65	0.030	Forage	72	0.0220, 0.0502
				Grain	115	0.0208, 0.0251
				Stover	115	0.0172, 0.0121
			0.063	Forage	72	0.0857, 0.0830
				Grain	115	0.0520, 0.0562
				Stover	115	0.0465, 0.0304

TABLE C.3. Residue Data from Crop Field Trials with Aminopyralid.

Trial ID (City, State; Year)	Zone	Field Corn Variety	Total Rate (lb ac/A)	Commodity or matrix	PHI (days)	Aminopyralid (ppm)[1]
Wyoming, IL; 2006 (060014-IL1)	5	NK N73 F3	0.030	Forage	0	1.2879, 1.0364
					7	0.1906, 0.1427
					13	0.1359, 0.1078
					21	0.0716, 0.0787
					28	0.0658, 0.0748
					66	0.0645, 0.0856
				Grain	105	0.0516, 0.0515
				Stover	105	0.0684, 0.1080
			0.062	Forage	0	1.5047, 1.1928
					7	0.2886, 0.3677
					13	0.2246, 0.2052
					21	0.1544, 0.1789
					28	0.1802, 0.1557
					66	0.1474, 0.1667
				Grain	105	0.0651, 0.0639
				Stover	105	0.1520, 0.1188
Carlyle, IL; 2006 (060014-IL2)	5	B-T 6516 RR 2YG	0.031	Forage	83	0.0420, 0.0444
				Grain	138	0.0298, 0.0315
				Stover	138	0.0303, 0.0212
			0.060	Forage	83	0.1399, 0.1288
				Grain	138	0.1123, 0.1047
				Stover	138	0.1089, 0.1473
Mason, IL; 2006 (060014-IL3)	5	Burrus 664 RWR PX4	0.030	Forage	60	0.1130, 0.1283
				Grain	108	0.0328, 0.0374
				Stover	108	0.1759, 0.1305
			0.063	Forage	60	0.2060, 0.2281
				Grain	108	0.0785, 0.0971
				Stover	108	0.3872, 0.3321
Rockville, IN; 2006 (060014-IN)	5	Wyffels 5531	0.032	Forage	69	0.0571, 0.0518
				Grain	127	0.0297, 0.0284
				Stover	127	0.0285, 0.0369
			0.064	Forage	69	0.0779, 0.0874
				Grain	127	0.0333, 0.0345
				Stover	127	0.0379, 0.0355
Conklin, MI; 2006 (060014-MI)	5	NK: N45-M2	0.031	Forage	78	0.0116, 0.0296
				Grain	111	0.0151, 0.0157
				Stover	111	0.0144, 0.0285
			0.062	Forage	78	0.0381, 0.0523
				Grain	111	0.0235, 0.0218
				Stover	111	0.0473, 0.0498

1/7

TABLE C.3. Residue Data from Crop Field Trials with Aminopyralid.

Trial ID (City, State; Year)	Zone	Field Corn Variety	Total Rate (lb ae/A)	Commodity or matrix	PHI (days)	Aminopyralid (ppm)[1]
Theilman, MN; 2006 (060014-MN1)	5	Pioneer 38G16	0.032	Forage	69	0.1188, 0.1454
				Grain	110	ND, 0.0812
				Stover	110	0.0908, 0.0750
			0.063	Forage	69	0.2042, 0.1801
				Grain	110	0.1309, 0.1461
				Stover	110	0.1358, 0.1221
Theilman, MN; 2006 (060014-MN2)	5	Pioneer 38G16	0.032	Forage	69	0.1894, 0.2616
				Grain	110	0.1452, 0.1642
				Stover	110	0.1673, 0.1072
			0.064	Forage	69	0.2260, 0.2305
				Grain	110	0.2122, 0.2056
				Stover	110	0.1138, 0.1888
La Plata, MO; 2006 (060014-MO)	5	LG 2540	0.031	Forage	83	0.0346, 0.0557
				Grain	118	0.0227, 0.0210
				Stover	118	0.0641, 0.0595
			0.062	Forage	83	0.0630, 0.0896
				Grain	118	0.0227, 0.0259
				Stover	118	0.1005, 0.0767
Gardner, ND; 2006 (060014-ND1)	5	DKC 35-51	0.032	Forage	77	0.0210, 0.0160
				Grain	117	0.0525, 0.0312
				Stover	117	(0.0093), 0.0112
			0.064	Forage	77	0.0707, 0.0746
				Grain	117	0.0342, ND
				Stover	117	0.0215, 0.0401
Ayr, ND; 2006 (060014-ND2)	5	9454349 Dekalb	0.031	Forage	76	(0.0087), 0.0119
				Grain	112	(0.0093), (0.0096)
				Stover	112	0.0119, 0.0112
			0.063	Forage	76	0.0176, 0.0208
				Grain	112	0.0183, 0.0174
				Stover	112	0.0266, 0.0282
York, NE; 2006 (060014-NE1)	5	Pioneer 34N45 RR/YG	0.031	Forage	81	0.0345, 0.0453
				Grain	112	0.0379, 0.0354
				Stover	112	0.0597, 0.0457
			0.061	Forage	81	0.0653, 0.0829
				Grain	112	0.0449, 0.0450
				Stover	112	0.0695, 0.0368
Osceola, NE; 2006 (060014-NE2)	5	NK N73-F7 RR/LL/YG	0.031	Forage	87	0.0214, 0.0415
				Grain	116	0.0199, 0.0196
				Stover	116	0.0279, 0.0463
			0.062	Forage	87	0.0687, 0.0767
				Grain	116	0.0375, 0.0434
				Stover	116	0.0643, 0.0868

TABLE C.3. Residue Data from Crop Field Trials with Aminopyralid.

Trial ID (City, State; Year)	Zone	Field Corn Variety	Total Rate (lb ae/A)	Commodity or matrix	PHI (days)	Aminopyralid (ppm)[1]
New Holland, OH; 2006 (060014-OH)	5	Crows 7R154	0.031	Forage	76	0.0368, 0.0254
				Grain	125	0.0121, 0.0111
				Stover	125	0.0214, 0.0250
			0.064	Forage	76	0.0439, 0.0465
				Grain	125	0.0185, 0.0168
				Stover	125	0.0271, 0.0279
Germansville, PA; 2006 (060014-PA)	1	TA5750	0.034	Forage	69	0.0358, 0.0164
				Grain	113	(0.0063), (0.0063)
				Stover	113	0.0349, 0.0281
			0.069	Forage	69	0.0276, 0.0204
				Grain	113	0.0104, (0.0099)
				Stover	113	0.0597, 0.0199
East Bernard, TX; 2006 (060014-TX)	6	Pioneer 31G97	0.031	Forage	74	0.0460, 0.0378
				Grain	113	0.0305, 0.0357
				Stover	113	0.0332, 0.0225
			0.063	Forage	74	0.1001, 0.0601
				Grain	113	0.0617, 0.0763
				Stover	113	0.0889, 0.0529
Arkansaw, WI; 2006 (060014-WI)	5	Pioneer 3753	0.031	Forage	0	1.5664, 1.7688
					7	0.1666, 0.1238
					14	0.0698, 0.1095
					21	0.1199, 0.0995
					28	0.0451, 0.1431
					72	0.0843, 0.1485
				Grain	116	0.0509, 0.0563
				Stover	116	0.0711, 0.0718
			0.062	Forage	0	1.8125, 3.0156
					7	0.4418, 0.4221
					14	0.0963, 0.1017
					21	0.1752, 0.2210
					28	0.2593, 0.1605
					72	0.2934, 0.1867
				Grain	116	0.0738, 0.0735
				Stover	116	0.1300, 0.0777

[1] ND = Not detected (LOD = 0.003 ppm). Residues reported between the LOD and the LOQ (0.01 ppm) are presented in parentheses.

[2] The petitioner stated that the other sample from this site was not available but did not provide an explanation.

47

TABLE C.4. Summary of Residue Data from Crop Field Trials with Aminopyralid.

Commodity	PHI (days)	Total Applic. Rate (lb ae/A)	Residue Levels [1] (ppm)						
			n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Field corn forage	60-87	0.030-0.034	40	<0.01	0.262	0.226	0.041	0.059	0.053
		0.060-0.069	39	0.018	0.293	0.240	0.083	0.105	0.069
Field corn grain	105-138	0.030-0.034	40	<0.01	0.164	0.155	0.090	0.036	0.032
		0.060-0.069	40	<0.01	0.212	0.209	0.049	0.060	0.048
Field corn stover	105-138	0.030-0.034	40	<0.01	0.176	0.153	0.032	0.048	0.041
		0.060-0.069	40	0.020	0.387	0.360	0.059	0.084	0.077

[1] For calculation of the median, mean, and standard deviation, the LOQ (0.01 ppm) was used for values reported <LOQ in Table C.3.

[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

The submitted field corn trial data are adequate. They reflect a single foliar application of a 2 lb ae/gal SL formulation of aminopyralid made at 0.030-0.034 or 0.060-0.069 lb ae/A at the 4- to 6-leaf growth stage, with a 60- to 87-day PHI for forage or a 105- to 138-day PHI for grain and stover. An acceptable method was used for quantitation of aminopyralid residues in/on field corn commodities, and the sample storage conditions and durations are supported by adequate storage stability data.

E. REFERENCES

None.

F. DOCUMENT TRACKING

Petition Number: 8F7455
DP#: 360100
PC Codes: 005100 and 005209

Primary Evaluator	Douglas Dotson Douglas Dotson, Ph.D., Chemist, RABII	Date: 10/22/2009
Peer Reviewer	Michael Doherty, Ph.D., Chemist, RABII	Date: 10/22/2009

This DER was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850; submitted 5/14/2009). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47572602 Wendelburg, B. (2008) Validation Report for Methods GRM 07.07 - Determination of Residues of Aminopyralid in Agricultural Commodities by Liquid Chromatography with Tandem Mass Spectrometric Detection, GRM 07.08 - Determination of Residues of Aminopyralid in Bovine and Poultry Tissues, Milk, and Eggs by Liquid Chromatography with Tandem Mass Spectrometric Detection, GRM 07.09 - Determination of Residues of Aminopyralid in Soil by Liquid Chromatography with Tandem Mass Spectrometric Detection, and GRM 07.10 - Determination of Residues of Aminopyralid in Drinking Water, Ground Water, and Surface Water by Liquid Chromatography with Tandem Mass Spectrometric Detection. Project Number: 071121. Unpublished study prepared by Dow AgroSciences, LLC. 207 p.

EXECUTIVE SUMMARY:

Dow AgroSciences proposed a high performance liquid chromatography (LC) method with tandem mass spectroscopy detection (MS/MS), Method GRM 07.08, for the determination of residues of aminopyralid in cattle and poultry tissues, milk, and eggs.

Briefly, sodium bicarbonate is added to homogenized livestock commodities and the mixture is extracted using methanol. The extract is purified by anion-exchange solid phase extraction (SPE), using ethyl acetate:trifluoroacetic acid (99:1, v:v) to elute residues. An internal standard ($^{13}C_2{}^2H^{15}N$-aminopyralid) is added to the eluate, which is evaporated to dryness, reconstituted in acetonitrile:pyridine:1-butanol (22:2:1, v:v:v; derivatization coupling reagent) and derivatized with butyl chloroformate to form the 1-butyl esters of the analyte and the internal standard. The mixture is diluted with a solution of methanol:water (40:60, v:v) containing 0.05% formic acid and 5 mM ammonium formate solution for LC/MS/MS analysis. The method limit of quantitation (LOQ) and limit of detection (LOD) are 0.01 and 0.003 ppm, respectively, for aminopyralid in each tested matrix.

The method description indicates that Method GRM 07.08 supersedes Method GRM 03.18, the current enforcement method for aminopyralid residues in livestock commodities (refer to Memo, D305665, M. Doherty, 7/12/05).

12

The method was adequately validated using samples of untreated cattle milk, cattle, kidney, cattle fat, poultry liver, poultry muscle, and egg fortified with aminopyralid at 0.01 and 2 ppm. The recovery ranges for these matrices were 90-119% for bovine matrices (average of 98% with a standard deviation of 5.7%) and 82-111% for poultry matrices (average of 95% with a standard deviation of 5.9%). The fortification levels and samples used in method validation are adequate to bracket expected residue levels. HED has concluded that radiovalidation data are not needed for Method GRM 07.08.

The method includes instructions for monitoring up to three ion transitions for aminopyralid; therefore, confirmatory analysis procedures are not needed.

The method is very similar to the current enforcement method, LC/MS/MS Method GRM 03.18, for which adequate independent laboratory validation data have been submitted (Memo, D305665, M. Doherty, 7/12/05). The Analytical Chemistry Branch (ACB) has concluded that Method GRM 3.18 is acceptable for enforcement purposes (DP# 312724, 11/3/05, D. Wright). Because Method GRM 07.08 is considered to be superior to Method GRM 03.18, no independent laboratory validation or validation by ACB is needed.

MRID 47572602 included validation data for method GRM 07.07, a method for crop commodities, which are reviewed separately (refer to 47572602.de1.doc). The MRID also included validation data for Methods GRM 07.09 and GRM 07.10, methods for soil and water, which will not be reviewed by HED.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the analytical method test data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the U.S. EPA Residue Chemistry Summary Document, D360100, D. Dotson, 10/22/2009.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Aminopyralid is a systemic postemergence herbicide that belongs to the pyridine carboxylic acid class of herbicides. It is currently registered for use on rangeland, permanent grass pastures, and wheat. In addition, it is registered for use on wildlife habitat and industrial vegetation management areas, including right-of-way for roads, railroads, and utility lines. Under PP#8F7455, Dow AgroSciences is proposing aminopyralid for use on field corn. The end-use product (EP) proposed for use on field corn is a liquid soluble concentrate (SL), Milestone Specialty Herbicide (EPA Reg. No. 62719-519), in which aminopyralid is formulated as the triisopropanolammonium (TIPA) salt. The product contains 40.6% aminopyralid TIPA salt at an acid equivalent (ae) of 21.1% or 2 lb ae/gal.

The chemical structure and nomenclature of aminopyralid and aminopyralid TIPA salt, and the physicochemical properties of the technical grade of aminopyralid are presented in Tables A.1 and A.2.

TABLE A.1. Test Compound Nomenclature.

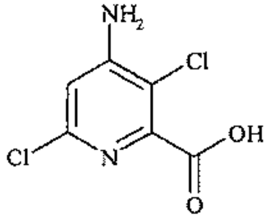
Compound	
Common name	Aminopyralid
Company experimental name	XDE-750
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid
CAS name	4-amino-3,6-dichloro-2-pyridinecarboxylic acid
CAS registry number	150114-71-9
End-use product (EP)	Not applicable

TABLE A.2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value	Reference
Melting point/range	163.5°C	MRID 46235703
pH	2.31 at 23.4°C (1% solution in water)	MRID 46235703
Density	1.72 at 20°C	MRID 46235703
Water solubility	2.48 g/L unbuffered water at 18°C 212 g/L pH 5 buffer at 20°C 205 g/L pH 7 buffer at 20°C 203 g/L pH 9 buffer at 20°C	MRID 46235703
Solvent solubility at 20°C	methanol 52.2 g/L acetone 29.2 g/L n-octanol 3.9 g/L ethyl acetate 3.9 g/L 1,2-dichloroethane 0.2 g/L xylene 0.04 g/L heptane <10 µg/mL	MRID 46235703
Vapor pressure	2.59 x 10^{-8} Pa at 25°C; 9.52 x 10^{-9} Pa at 20°C	MRID 46235703
Dissociation constant, pK_a	2.56	MRID 46235703
Octanol/water partition coefficient, $Log(K_{OW})$	0.201 unbuffered water at 19°C -1.76 at pH 5 -2.87 at pH 7 -2.96 at pH 9	MRID 46235703

47

TABLE A.2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value			Reference
	Solution	Wavelength λ max, nm	Extinction coefficient L/(mol*cm)	
UV/visible absorption spectrum	Neutral	217	29100	MRID 46235703
	Basic (pH 12.6)	220	26100	
	Basic (pH 12.6)	245	10150	
	Acidic (pH 1.4)	217	22800	
	Acidic (pH 1.4)	270	9140	

B. MATERIALS AND METHODS

B.1. Data-Gathering Method

Not applicable to this submission.

B.2. Enforcement Method

B.2.1. Principle of the Method:

The parameters of method GRM 07.08 are presented in Table B.2.1. Briefly, sodium bicarbonate is added to homogenized livestock commodities and the mixture is extracted using methanol. The extract is purified by anion-exchange SPE, using ethyl acetate:trifluoroacetic acid (99:1, v:v) to elute residues. An internal standard ($^{13}C_2{}^2H^{15}N$-aminopyralid) is added to the eluate, which is evaporated to dryness, reconstituted in acetonitrile:pyridine:1-butanol (22:2:1, v:v:v; derivatization coupling reagent) and derivatized with butyl chloroformate to form the 1-butyl esters of the analyte and the internal standard. The mixture is diluted with a solution of methanol:water (40:60, v:v) containing 0.05% formic acid and 5 mM ammonium formate solution for LC/MS/MS analysis.

The method description indicates that Method GRM 07.08 supersedes Method GRM 03.18, the current enforcement method for aminopyralid residues in livestock commodities (refer to Memo, D305665, M. Doherty, 7/12/05). The current enforcement method is an LC/MS/MS method that is very similar to Method GRM 07.08. The major differences between the two methods are that Method GRM 03.18 uses a different internal standard ($^{13}C_2{}^{15}N$-aminopyralid) and only includes instructions for the determination of residues in bovine commodities (muscle, fat, liver, kidney, and milk).

The method was validated using samples (obtained from the Dow AgroSciences Management Group) of untreated cattle milk, kidney, and fat, as well as poultry egg, liver, and muscle fortified with aminopyralid at 0.01 and 2 ppm.

TABLE B.2.1. Summary Parameters for the Analytical Enforcement Method Used for the Quantitation of Aminopyralid Residues in Livestock Matrices.

Method ID	GRM 07.08
Analyte	Aminopyralid
Extraction solvent/technique	Sodium bicarbonate is added to homogenized livestock matrices and the mixture is extracted by shaking with methanol for 60 minutes. The extract is isolated by centrifugation and diluted with water.
Cleanup strategies	The sample is purified using an anion-exchange SPE plate, eluting residues with ethyl acetate:trifluoroacetic acid (99:1, v:v). A stable isotope internal standard ($^{13}C_2{}^2H^{15}N$-aminopyralid) is added and the eluate is evaporated to dryness, reconstituted in derivatization coupling reagent]acetonitrile:pyridine:1-butanol (22:2:1, v:v:v)], and derivatized with butyl chloroformate (at ambient temperatures for 5 minutes) to form the 1-butyl esters of the analyte and the internal standard. The mixture is diluted with methanol:water (40:60, v:v) solution containing 0.05% formic acid and 5 mM ammonium formate for analysis by LC/MS/MS.
Instrument/Detector	LC/MS/MS using a Zorbax SB-C8 column and a gradient mobile phase of methanol and water each containing 0.05% formic acid and 5 mM ammonium formate. The ion transition monitored for quantitation is m/z 263.1→189.0, with m/z 263.1→161.1 and 263.1→134.1 for confirmation. The ion monitored for the internal standard is 269.1→194.9.
Standardization method	Internal and external standardization. A calibration curve is generated by plotting the ratio of the peak area of aminopyralid and the internal standard against calibration standard concentration, and aminopyralid concentration in samples is determined using the calibration curve.
Stability of std solutions	The petitioner provided data demonstrating the stability of calibration and fortification solutions during refrigerator storage for up to 198 days and 203 days, respectively.
Retention times	~5.8 minutes

C. RESULTS AND DISCUSSION

C.1. Data-Gathering Method

Not applicable to this submission.

C.2. Enforcement Method

The method was adequately validated using samples of untreated cattle milk, kidney, and fat, as well as poultry egg, liver, and muscle fortified with aminopyralid at 0.01 and 2 ppm. The method validation data are presented in Table C.2.1. The recovery ranges for these matrices were 90-119% for bovine matrices (average of 98% with a standard deviation of 5.7%) and 82-111% for poultry matrices (average of 95% with a standard deviation of 5.9%). The fortification levels and samples used in method validation are adequate to bracket expected residue levels.

The petitioner additionally conducted fortifications at 0.003 ppm with one sample of each livestock commodity to demonstrate observable residues at the LOD; observed residues ranged 0.0022-0.0035 ppm for these samples.

The LOQs and LODs were calculated as 10x and 3x, respectively, the standard deviation of recovery results at the 0.01-ppm fortification level. The calculated LOQ and LOD were 0.0060 ppm and 0.0018 ppm, respectively, for bovine commodities, and 0.0069 ppm and 0.0021 ppm, respectively, for poultry commodities. The petitioner concluded that the calculated values supported the stated LOQ of 0.01 ppm and the stated LOD of 0.003 ppm for each commodity.

Apparent residues of aminopyralid were below the stated LOD in/on two samples each of unfortified cattle milk, kidney, and fat, and poultry egg, liver, and muscle.

The method characteristics of method GRM 07.08 are presented in Table C.2.2. The method includes instructions for monitoring up to three ion transitions for aminopyralid; therefore, confirmatory analysis procedures are not needed.

No radiovalidation data were submitted for Method GRM 07.08. HED previously concluded that radiovalidation data would not be needed for Method 03.18 because the extraction solvent used in the method is similar to that used in the goat metabolism study. In the goat metabolism study (see 46235708.1300.goat.der.wpd, 6/28/05, M. Doherty), 76-96% TRR was extracted from milk, liver, and kidney samples using methanol (fat and muscle samples were not subjected to extraction procedures because of low residue levels). Because methanol is used as the extraction solvent in Method GRM 07.08, HED concludes that radiovalidation data are not needed for the method.

Method GRM 03.18 included instructions for correcting residue calculations for potential internal standard to analyte crossover contributions. Although Method GRM 07.08 includes the calculations that could be used to correct for isotopic crossover, it was stated that no mass spectral isotopic crossover was observed during method development. This is presumably the reason that the internal standard used in GRM 07.08 is slightly different from the internal standard used in GRM 03.18.

TABLE C.2.1. Recovery Results from Method Validation of Livestock Commodities using the Enforcement Analytical Method.[1]

Matrix	Spiking Level (ppm)	Recoveries Obtained	Mean Recovery ± Std. Dev. [CV] (%)
		Bovine Matrices	
Milk	0.01	93, 95, 97, 100, 101, 103	98 ± 3.8 [3.9]
	2	92, 92, 93, 95, 96	94 ± 1.8 [1.9]
Kidney	0.01	93, 98, 98, 99, 102, 104	99 ± 3.8 [3.8]
	2	90, 91, 91, 93, 96	92 ± 2.4 [2.6]
Fat	0.01	97, 99, 103, 103, 106, 119	105 ± 7.8 [7.5]
	2	94, 95, 96, 97, 100	96 ± 2.3 [2.4]
		Poultry Matrices	
Egg	0.01	82, 89, 89, 91, 102, 105	93 ± 8.7 [9.4]
	2	90, 94, 95, 95, 98	94 ± 2.9 [3.1]
Liver	0.01	93, 97, 98, 98, 99, 100	98 ± 2.4 [2.5]
	2	85, 87, 92, 96, 96	91 ± 5.1 [5.6]
Muscle	0.01	88, 95, 99, 100, 102, 111	99 ± 7.6 [7.7]
	2	90, 91, 92, 96, 97	93 ± 3.1 [3.3]

[1] Standards were prepared in ACN.

TABLE C.2.2. Characteristics for the Enforcement Analytical Method Used for the Quantitation of Aminopyralid Residues in Animal Matrices.

Method ID	GRM 07.08
Analyte	Aminopyralid
Equipment ID	MDS/Sciex API 3000 LC/MS/MS system with a Zorbax SB-C8 column (4.6 x 75 mm; 3.5 µm) using electrospray ionization in the positive ion mode.
Limit of quantitation (LOQ)	0.01 ppm The calculated LOQs were 0.0060 ppm (bovine commodities) and 0.0069 ppm (poultry commodities); the LOQs were calculated as 10x the standard deviation of recovery results at the 0.01-ppm fortification level.
Limit of detection (LOD)	0.003 ppm The calculated LODs were 0.0018 ppm (bovine commodities) and 0.0021 ppm (poultry commodities); the LODs were calculated as 3x the standard deviation of recovery results at the 0.01-ppm fortification level.
Accuracy/Precision	Percent recoveries and coefficients of variance (CVs) indicate acceptable accuracy/precision at fortification levels of 0.01 and 2 ppm for bovine milk, kidney, and fat, and hen egg, liver, and muscle. The recovery ranges (and CVs) for these matrices were 90-119% (5.8%) for bovine matrices and 82-11% (6.3%) for poultry matrices.
Reliability of the Method [ILV]	No ILV data were submitted. Because Method GRM 07.08 is considered to be superior to the current enforcement method, GRM 03.18, no ILV data are needed.
Linearity	The method/detector response was linear (coefficient of determination, r^2= 0.9997) within the range of 0.03-25 ng/mL.
Specificity	The control chromatograms generally have no peaks above the chromatographic background and the spiked sample chromatograms contain only the analyte peak of interest. Peaks were well defined and symmetrical. There appeared to be no carryover to the following chromatograms.

C.3. Independent Laboratory Validation

No ILV data have been submitted. Method GRM 07.08 is very similar to Method GRM 03.18, for which adequate ILV data have been submitted (DP# 305665, 7/12/05, M. Doherty). Because Method GRM 07.08 is considered to be superior to Method GRM 03.18, an independent laboratory validation is not needed.

D. CONCLUSION

Adequate method validation data have been submitted for LC/MS/MS Method GRM 07.08 for the determination of residues of aminopyralid in cattle and poultry tissues, milk, and eggs; the data are sufficiently representative of the expected residue levels. HED has concluded that radiovalidation data are not needed for Method GRM 07.08.

The petitioner is proposing Method GRM 07.08 for enforcement. The method is very similar to the current enforcement method, LC/MS/MS Method GRM 03.18, for which adequate independent laboratory validation data have been submitted (Memo, D305665, M. Doherty, 7/12/05). ACB has concluded that Method GRM 03.18 is acceptable for enforcement purposes (Memo, D312724, D. Wright, 11/3/05); therefore, Method GRM 07.08 does not need to be validated by the Agency.

51

E. REFERENCES

D312724, PP# 4F6827, Review of Method for the Establishment of Permanent Tolerances in Aminopyralid in/on Plant and Livestock Commodities. ACL Project #:B05-12, D. Wright, 11/3/05, MRIDs: 46235712, 46235714, 46235716, 46235717

D305665, PP#4F6827, Aminopyralid. Petition for the Establishment of Permanent Tolerances for Use of Aminopyralid on Grasses and Wheat. Summary of Analytical Chemistry and Residue Data, M. Doherty, 7/12/05, MRIDs: 46235708-46235712, 46235714, 46235716- 46235719, 46235721-46235725

D305665, Aminopyralid, Nature of the Residues in Livestock–Goat, DER46235708.1300.goat, M. Doherty, 6/28/05, MRID: 46235708

F. DOCUMENT TRACKING

Petition Number: 8F7455
DP#: 360100
PC Codes: 005100 and 005209

Primary Evaluator	Douglas Dotson Douglas Dotson, Ph.D., Chemist, RABII	Date: 10/22/2009
Peer Reviewer	Michael Doherty, Ph.D., Chemist, RABII	Date: 10/22/2009

This DER was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850; submitted 5/14/2009). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47572602 Wendelburg, B. (2008) Validation Report for Methods GRM 07.07 - Determination of Residues of Aminopyralid in Agricultural Commodities by Liquid Chromatography with Tandem Mass Spectrometric Detection, GRM 07.08 - Determination of Residues of Aminopyralid in Bovine and Poultry Tissues, Milk, and Eggs by Liquid Chromatography with Tandem Mass Spectrometric Detection, GRM 07.09 - Determination of Residues of Aminopyralid in Soil by Liquid Chromatography with Tandem Mass Spectrometric Detection, and GRM 07.10 - Determination of Residues of Aminopyralid in Drinking Water, Ground Water, and Surface Water by Liquid Chromatography with Tandem Mass Spectrometric Detection. Project Number: 071121. Unpublished study prepared by Dow AgroSciences, LLC. 207 p.

EXECUTIVE SUMMARY:

Dow AgroSciences has proposed a high performance liquid chromatography (LC) method with tandem mass spectroscopy detection (MS/MS), Method GRM 07.07, for the determination of residues of aminopyralid in crop commodities (wet, dry, acidic, and oily crops). Method GRM 07.07 was used for data collection in samples of corn forage, grain, stover, aspirated grain fractions, and processed commodities from the crop field trial and processing studies for those commodities.

Briefly, residues are extracted from homogenized agricultural commodities using 0.1 N NaOH, which hydrolyzes bound residues and base-labile conjugates to yield free aminopyralid; the hydrolysate is acidified with 2 N HCl. Oil samples are extracted with acetone and the extract is evaporated to dryness, redissolved in hexane, and partitioned into water. The aqueous phase is mixed with 0.2 N NaOH to hydrolyze bound residues and base-labile conjugates to yield free aminopyralid, and then acidified with 3 N HCl. For both crop samples and oil samples, the acidified extract is heated at 80°C for 90 minutes, which hydrolyzes acid-labile conjugates to yield free aminopyralid and further solubilizes bound residues. The extract is then purified by anion-exchange solid phase extraction (SPE), using ethyl acetate:trifluoroacetic acid (99:1, v:v) to elute residues. An internal standard ($^{13}C_2{}^2H^{15}N$-aminopyralid) is added to the eluate, which is evaporated to dryness, reconstituted in acetonitrile:pyridine:1-butanol (22:2:1, v:v:v;

derivatization coupling reagent) and derivatized with butyl chloroformate to form the 1-butyl esters of the analyte and the internal standard. The mixture is diluted with a solution of methanol:water (40:60, v:v) containing 0.05% formic acid and 5 mM ammonium formate solution for LC/MS/MS analysis. The method limit of quantitation (LOQ) and limit of detection (LOD) are 0.01 and 0.003 ppm, respectively, for aminopyralid in each tested matrix.

The method description indicates that Method GRM 07.07 supersedes Method 02.31, the current enforcement method for aminopyralid residues in crop commodities (refer to Memo, D305665, M. Doherty, 7/12/05).

Method GRM 07.07 was adequately validated using samples of untreated wet crops (broccoli and tomato), dry crops (wheat forage, grain, and straw, corn forage and grain, and grass forage and straw), acidic crops (lemon whole fruit and orange peel, pulp, and whole fruit), and oily crops (palm oil and sunflower seed) fortified with aminopyralid at 0.01 and 2 ppm for all crops other than grass forage and straw, and at 0.01 and 50 ppm for grass forage and straw. The recovery ranges for these matrices were 75-102% for wet crops (average ± standard deviation: 86% ± 6.6%), 70-102% for dry crops (86% ± 8.3%), 72-105% for acidic crops (88% ± 7.4%), and 82-106% for oily crops (93% ± 6.5%).

The fortification levels and samples used in method validation are adequate to bracket expected residue levels. Although field corn stover, aspirated grain fractions, and processed commodities were not included in the validation study, adequate concurrent method recovery data for these commodities were included with the field corn field trial and processing study submitted for field corn.

The method includes instructions for monitoring up to three ion transitions for aminopyralid; therefore, confirmatory analysis procedures are not needed.

The method is very similar to the current enforcement method, LC/MS/MS Method GRM 02.31, for which adequate radiovalidation and independent laboratory validation data have been submitted (Memo, D305665, M. Doherty, 7/12/05). The Analytical Chemistry Branch (ACB) has concluded that Method GRM 02.31 is acceptable for enforcement purposes (Memo, D312724, D. Wright, 11/3/05). Because Method GRM 07.07 is considered to be superior to Method GRM 02.31, Method GRM 07.07 does not need to be validated by the Agency.

MRID 47572602 included validation data for method GRM 07.08, a method for livestock commodities, which are reviewed separately (refer to 47572602.de2.doc); the MRID also included validation data for Methods GRM 07.09 and GRM 07.10, methods for soil and water, which will not be reviewed by HED.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the analytical method test data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the U.S. EPA Residue Chemistry Summary Document, D360100, D. Dotson, 10/22/2009.

COMPLIANCE:

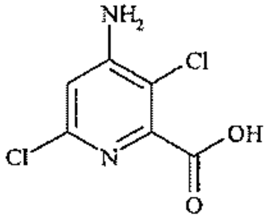
Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Aminopyralid is a systemic postemergence herbicide that belongs to the pyridine carboxylic acid class of herbicides. It is currently registered for use on rangeland, permanent grass pastures, and wheat. In addition, it is registered for use on wildlife habitat and industrial vegetation management areas, including right-of-way for roads, railroads, and utility lines. Under PP#8F7455, Dow AgroSciences is proposing aminopyralid for use on field corn. The end-use product (EP) proposed for use on field corn is a liquid soluble concentrate (SL), Milestone Specialty Herbicide (EPA Reg. No. 62719-519), in which aminopyralid is formulated as the triisopropanolammonium (TIPA) salt. The product contains 40.6% aminopyralid TIPA salt at an acid equivalent (ae) of 21.1% or 2 lb ae/gal.

The chemical structure and nomenclature of aminopyralid and the physicochemical properties of the technical grade of aminopyralid are presented in Tables A.1 and A.2.

TABLE A.1. Test Compound Nomenclature.

Compound	
Common name	Aminopyralid
Company experimental name	XDE-750
IUPAC name	4-amino-3,6-dichloropyridine-2-carboxylic acid
CAS name	4-amino-3,6-dichloro-2-pyridinecarboxylic acid
CAS registry number	150114-71-9
End-use product (EP)	Not applicable

53

TABLE A.2. Physicochemical Properties of the Technical Grade of Aminopyralid.

Parameter	Value	Reference
Melting point/range	163.5°C	MRID 46235703
pH	2.31 at 23.4°C (1% solution in water)	MRID 46235703
Density	1.72 at 20°C	MRID 46235703
Water solubility	2.48 g/L unbuffered water at 18°C 212 g/L pH 5 buffer at 20°C 205 g/L pH 7 buffer at 20°C 203 g/L pH 9 buffer at 20°C	MRID 46235703
Solvent solubility at 20°C	methanol 52.2 g/L acetone 29.2 g/L n-octanol 3.9 g/L ethyl acetate 3.9 g/L 1,2-dichloroethane 0.2 g/L xylene 0.04 g/L heptane <10 µg/mL	MRID 46235703
Vapor pressure	2.59×10^{-8} Pa at 25°C; 9.52×10^{-9} Pa at 20°C	MRID 46235703
Dissociation constant, pK_a	2.56	MRID 46235703
Octanol/water partition coefficient, $Log(K_{OW})$	0.201 unbuffered water at 19°C -1.76 at pH 5 -2.87 at pH 7 -2.96 at pH 9	MRID 46235703
UV/visible absorption spectrum	Solution — Wavelength λ max, nm — Extinction coefficient L/(mol*cm) Neutral — 217 — 29100 Basic (pH 12.6) — 220 — 26100 Basic (pH 12.6) — 245 — 10150 Acidic (pH 1.4) — 217 — 22800 Acidic (pH 1.4) — 270 — 9140	MRID 46235703

B. MATERIALS AND METHODS

B.1. Data-Gathering Method

B.1.1. Principle of the Method:

The parameters of Method GRM 07.07 are presented in Table B.1.1. Briefly, residues are extracted from homogenized agricultural commodities using 0.1 N NaOH, which hydrolyzes bound residues and base-labile conjugates to yield free aminopyralid. The hydrolysate is acidified with 2 N HCl. Oil samples are extracted with acetone and the extract is evaporated to dryness, redissolved in hexane, and partitioned into water. The aqueous phase is mixed with 0.2 N NaOH to hydrolyze bound residues and base-labile conjugates to yield free aminopyralid, and then acidified with 3 N HCl. For both crop samples and oil samples, the acidified extract is heated at 80°C for 90 minutes, which hydrolyzes acid-labile conjugates to yield free aminopyralid and further solubilizes bound residues. The extract is then purified by anion-exchange SPE, using ethyl acetate:trifluoroacetic acid (99:1, v:v; derivatization coupling reagent) to elute residues. An internal standard ($^{13}C_2{}^2H^{15}N$-aminopyralid) is added to the eluate, which is evaporated to dryness, reconstituted in acetonitrile:pyridine:1-butanol (22:2:1, v:v:v) and derivatized with butyl chloroformate to form the 1-butyl esters of the analyte and the internal standard. The mixture is diluted with a solution of methanol:water (40:60, v:v) containing 0.05% formic acid and 5 mM ammonium formate solution for LC/MS/MS analysis.

The method description indicates that Method GRM 07.07 supersedes Method 02.31, the current enforcement method for aminopyralid residues in crop commodities (refer to Memo, D305665, M. Doherty, 7/12/05).

The method was validated using samples (obtained from the Dow AgroSciences Management Group) of untreated wet crops (broccoli and tomato), dry crops (wheat forage, grain, and straw, corn forage and grain, and grass forage and straw), acidic crops (lemon whole fruit and orange peel, pulp, and whole fruit), and oily crops (palm oil and sunflower seed) fortified with aminopyralid at 0.01 and 2 ppm for all crops other than grass forage and straw, and at 0.01 and 50 ppm for grass forage and straw.

TABLE B.1.1. Summary Parameters for the Analytical Method Used for the Quantitation of Aminopyralid Residues in Crop Commodities.

Method ID	GRM 07.07
Analyte	Aminopyralid
Extraction solvent/technique	Crop samples are extracted with 0.1 N NaOH by shaking for 30 minutes; the extract is isolated by centrifugation and an aliquot is mixed with 2.0 N HCl and water. Oil samples are extracted with acetone by shaking for 30 minutes; an aliquot is evaporated to dryness, redissolved in hexane, and partitioned into water. An aliquot of the aqueous phase is mixed with 0.2 N NaOH and shaken for 30 minutes, then acidified with 3 N HCl. For both crop samples and oil samples, the acidified extract is heated at 80°C for 90 minutes; after cooling, the hydrolysate is isolated by centrifugation and diluted with 1.0 N HCl.
Cleanup strategies	The sample is purified using an anion-exchange SPE plate, eluting residues with ethyl acetate:trifluoroacetic acid (99:1, v:v). A stable isotope internal standard ($^{13}C_2{}^2H^{15}N$-aminopyralid) is added and the eluate is evaporated to dryness, reconstituted in derivatization coupling reagent [acetonitrile:pyridine:1-butanol (22:2:1, v:v:v)], and derivatized with butyl chloroformate (at ambient temperatures for 5 minutes) to form the 1-butyl esters of the analyte and the internal standard. The mixture is diluted with methanol:water (40:60, v:v) solution containing 0.05% formic acid and 5 mM ammonium formate for analysis by LC/MS/MS.
Instrument/Detector	LC/MS/MS using a Zorbax SB-C8 column and a gradient mobile phase of methanol and water each containing 0.05% formic acid and 5 mM ammonium formate. The ion transition monitored for quantitation is m/z 263.1→189.0, with m/z 263.1→161.1 and 263.1→134.1 for confirmation. The ion monitored for the internal standard is 269.1→194.9.
Standardization method	Internal and external standardization. A calibration curve is generated by plotting the ratio of the peak area of aminopyralid and the internal standard against calibration standard concentration, and aminopyralid concentration in samples is determined using the calibration curve.
Stability of std solutions	The petitioner provided data demonstrating the stability of calibration and fortification solutions during refrigerator storage for up to 198 days and 203 days, respectively.
Retention times	~5.8 minutes

78

64

B.2. Enforcement Method

The proposed enforcement method is the same as the data collection method, Method GRM 07.07. The current enforcement method, Method 02.31, is an LC/MS/MS method that is very similar to Method GRM 07.07. The major differences between the two methods are that Method GRM 02.31 uses a different internal standard ($^{13}C_2{}^{15}N$-aminopyralid) and only includes instructions for the determination of residues in barley, sorghum, wheat, and grass commodities.

HED notes that Method GRM 02.31 included instructions for correcting residue calculations for potential internal standard to analyte crossover contributions. Although Method GRM 07.07 includes the calculations that could be used to correct for isotopic crossover, it was stated that no mass spectral isotopic crossover was observed during method development. This is presumably the reason that the internal standard used in GRM 07.07 is slightly different from the internal standard used in GRM 02.31.

C. RESULTS AND DISCUSSION

C.1. Data-Gathering Method

The method was adequately validated using samples of untreated wet crops (broccoli and tomato), dry crops (wheat forage, grain, and straw, corn forage and grain, and grass forage and straw), acidic crops (lemon whole fruit and orange peel, pulp, and whole fruit), and oily crops (palm oil and sunflower seed) fortified with aminopyralid at 0.01 and 2 ppm for all crops other than grass forage and straw, and at 0.01 and 50 ppm for grass forage and straw. The method validation data are presented in Table C.1.1. The recovery ranges for these matrices were 75-102% for wet crops (average ± standard deviation was 86% ± 6.6%), 70-102% for dry crops (86% ± 8.3%), 72-105% for acidic crops (88% ± 7.4%), and 82-106% for oily crops (93% ± 6.5%). The petitioner additionally conducted fortifications at 0.003 ppm with one sample of each crop to demonstrate observable residues at the LOD; observed residues ranged 0.0024-0.0034 ppm for these samples.

The LOQs and LODs were calculated as 10x and 3x, respectively, the standard deviation of recovery results at the 0.01-ppm fortification level. Calculated LOQs ranged 0.0045-0.0083 ppm. Calculated LODs ranged 0.0014-0.0025 ppm. The petitioner concluded that the calculated values supported the stated LOQ of 0.01 ppm and the stated LOD of 0.003 ppm.

Apparent residues of aminopyralid were below the stated LOD in/on two samples each of unfortified broccoli, corn forage, corn grain, lemon, orange, orange peel, orange pulp, palm oil, sunflower seed, tomato, wheat forage, wheat grain, and wheat straw, and three samples each of unfortified grass forage and straw.

The fortification levels and samples used in method validation are adequate to bracket expected residue levels. Although field corn stover, aspirated grain fractions, and processed commodities were not included in the validation study, adequate concurrent method recovery data for these commodities were included with the field corn field trial and processing study submitted for field corn.

The method characteristics of method GRM 07.07 are presented in Table C.1.2. The method includes instructions for monitoring up to three ion transitions for aminopyralid; therefore, confirmatory analysis procedures are not needed.

No radiovalidation data were submitted for Method GRM 07.07. Adequate radiovalidation data have been submitted for the extraction procedures of Method GRM 02.31, using samples of grass and wheat commodities (refer to Memo, D305665, M. Doherty, 7/12/05). Because the extraction procedures of Method GRM 07.07 are very similar to those of Method GRM 02.31, no radiovalidation data will be required for Method GRM 07.07.

TABLE C.1.1. Recovery Results from Method Validation of Crop Commodities (Wet, Dry, Acidic, and Oily) using the Data-Gathering Analytical Method. [1]

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV] (%)
Recoveries From Wet Crops			
Broccoli	0.01	86, 87, 88, 90, 92, 95	90 ± 3.4 [3.8]
	2	79, 80, 81, 82, 83	81 ± 1.6 [2.0]
Tomato whole fruit	0.01	86, 89, 90, 91, 95, 102	92 ± 5.6 [6.1]
	2	75, 77, 81, 81, 82	79 ± 3.0 [3.8]
Recoveries From Dry Crops			
Wheat forage	0.01	89, 92, 94, 95, 100, 102	95 ± 4.9 [5.1]
	2	72, 76, 79, 79, 83	78 ± 4.1 [5.3]
Wheat grain	0.01	83, 87, 88, 90, 92, 96	89 ± 4.5 [5.0]
	2	76, 79, 80, 81, 82	80 ± 2.3 [2.9]
Wheat straw	0.01	82, 92, 96, 97, 100, 102	95 ± 7.2 [7.6]
	2	74, 75, 75, 79, 80	77 ± 2.7 [3.5]
Corn forage	0.01	72, 79, 81, 87, 87, 95	84 ± 7.9 [9.5]
	2	79, 81, 83, 86, 86, 86	84 ± 3.0 [3.6]
Corn grain	0.01	78, 82, 84, 85, 85, 94	85 ± 5.3 [6.2]
	2	77, 78, 78, 84, 84, 85	81 ± 3.7 [4.6]
Grass forage	0.01	70, 76, 88, 89, 93, 96, 99	87 ± 11 [12]
	50	82, 85, 86, 86, 89, 96	87 ± 4.8 [5.5]
Grass straw	0.01	96, 96, 98, 100, 100, 101	99 ± 2.2 [2.2]
	50	71, 81, 81, 82, 87	80 ± 5.8 [7.2]
Recoveries From Acidic Crops			
Lemon whole fruit	0.01	89, 90, 97, 100, 102, 105	97 ± 6.5 [6.7]
	2	82, 83, 84, 85, 85	84 ± 1.3 [1.6]
Orange peel	0.01	85, 88, 88, 91, 95, 97	91 ± 4.6 [5.1]
	2	76, 79, 82, 83, 84	81 ± 3.3 [4.0]
Orange pulp	0.01	91, 91, 91, 94, 96, 96	93 ± 2.5 [2.7]
	2	72, 82, 82, 84, 88	82 ± 5.9 [7.2]

TABLE C.1.1. Recovery Results from Method Validation of Crop Commodities (Wet, Dry, Acidic, and Oily) using the Data-Gathering Analytical Method. [1]

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV] (%)
Orange whole fruit	0.01	83, 86, 90, 94, 95, 101	92 ± 6.5 [7.1]
	2	75, 80, 84, 85, 85	82 ± 4.3 [5.3]
Recoveries From Oily Crops			
Palm oil	0.01	85, 93, 93, 96, 101, 102	95 ± 6.2 [6.6]
	2	82, 84, 85, 87, 89	85 ± 2.7 [3.2]
Sunflower seed	0.01	95, 97, 97, 99, 101, 106	99 ± 3.9 [4.0]
	2	88, 89, 90, 91, 93	90 ± 1.9 [2.1]

[1] Standards were prepared in acetonitrile.

TABLE C.1.2. Characteristics for the Data-Gathering Analytical Method Used for the Quantitation of Aminopyralid Residues in Crop Commodities.

Method ID	GRM 07.07
Analyte	Aminopyralid
Equipment ID	MDS/Sciex API 3000 LC/MS/MS system with a Zorbax SB-C8 column (4.6 x 75 mm; 3.5 μm) using electrospray ionization in the positive ion mode.
Limit of quantitation (LOQ)	0.01 ppm The calculated LOQs were 0.0055 ppm (acidic crops), 0.0083 ppm (dry crops), 0.0054 ppm (oily crops), and 0.0045 ppm (wet crops); the LOQs were calculated as 10x the standard deviation of recovery results at the 0.01-ppm fortification level.
Limit of detection (LOD)	0.003 ppm The calculated LODs were 0.0017 ppm (acidic crops), 0.0025 ppm (dry crops), 0.0016 ppm (oily crops), and 0.0014 ppm (wet crops); the LODs were calculated as 3x the standard deviation of recovery results at the 0.01-ppm fortification level.
Accuracy/Precision	Percent recoveries and coefficients of variance (CVs) indicate acceptable accuracy/precision at fortification levels of 0.01 and 2 ppm for broccoli; tomato; wheat forage, grain, and straw; corn forage and grain; lemon; orange peel, pulp, and whole fruit; palm oil; and sunflower seed; and 0.01 and 50 ppm for grass forage and straw. The recovery ranges (and CVs) for these matrices were 75-102% (7.7%) for wet crops, 70-102% (9.6%) for dry crops, 72-105% (8.4%) for acidic crops, and 82-106% (7.0%) for oily crops.
Reliability of the Method [ILV]	No ILV data were submitted. Because Method GRM 07.07 is considered to be superior to the current enforcement method, GRM 02.31, no ILV data are needed.
Linearity	The method/detector response was linear (coefficient of determination, r^2= 0.9995) within the range of 0.03-25 ng/mL.
Specificity	The control chromatograms generally have no peaks above the chromatographic background and the spiked sample chromatograms contain only the analyte peak of interest. Peaks were well defined and symmetrical. There appeared to be no carryover to the following chromatograms.

C.2. Enforcement Method

The proposed enforcement method is the same as the data collection method, Method GRM 07.07.

C.3. Independent Laboratory Validation

No ILV data have been submitted. Method GRM 07.07 is very similar to Method GRM 02.31, for which adequate ILV data have been submitted (Memo, D305665, M. Doherty, 7/12/05). Because Method GRM 07.07 is considered to be superior to Method GRM 02.31, an independent laboratory validation is not needed.

D. CONCLUSION

Adequate method validation data have been submitted for LC/MS/MS Method GRM 07.07 for the determination of residues of aminopyralid in crop commodities; the data are sufficiently representative of the expected residue levels for the plant commodities included in the current tolerance petition.

The petitioner is proposing Method GRM 07.07 for enforcement. The method is very similar to the current enforcement method, LC/MS/MS Method GRM 02.31, for which adequate radiovalidation and independent laboratory validation data have been submitted (Memo, D305665, M. Doherty, 7/12/05). ACB has concluded that Method GRM 02.31 is acceptable for enforcement purposes (Memo, D312724, D. Wright, 11/3/05). As a result, Method GRM 07.07 does not need to be validated by the Agency.

E. REFERENCES

D312724, PP# 4F6827. Review of Method for the Establishment of Permanent Tolerances in Aminopyralid in/on Plant and Livestock Commodities. ACL Project #:B05-12, D. Wright, 11/3/05, MRIDs: 46235712, 46235714, 46235716, 46235717

D305665, Aminopyralid. Petition for the Establishment of Permanent Tolerances for Use of Aminopyralid on Grasses and Wheat. Summary of Analytical Chemistry and Residue Data. PP#4F6827, M. Doherty, 7/12/05, MRIDs: 46235708-46235712, 46235714, 46235716-46235719, 46235721-46235725

F. DOCUMENT TRACKING

Petition Number: 8F7455
DP#: 360100
PC Codes: 005100 and 005209

56