4

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

128821

JUN 26 1996

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6F04641- Imazapyr on Field Corn. Review of Analytical Methods and Residue Data. First Food Use Review.

(MRID #'s 438615-02, 438615-03, 438615-04, 438615-05, 438615-06, 438615-16, 438615-17, 438615-18)

(CBTS #16723)

FROM: Nancy Dodd, Chemist *Nancy Dodd*
Tolerance Petition Section II
Chemistry Branch I- Tolerance Support
Health Effects Division (7509C)

THROUGH: Edward Zager, Acting Chief *Edward Zager*
Chemistry Branch I- Tolerance Support
Health Effects Division (7509C)

TO: Debbie McCall, Acting Section Head
Registration Section
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

Attached is the first food use Residue Chemistry review for imazapyr on field corn. This information was compiled by Dynamac Corporation under supervision of CBTS, HED. This review has undergone secondary review by CBTS and has been revised to reflect Agency policies.

Product Chemistry data for technical imazapyr has been previously reviewed in connection with non-food/non-feed uses. Product Chemistry data for the proposed formulation AC 513,996 (MRID #'s 438615-07, 438615-08, and 438615-09) are under the purview of Registration Division.

Some Residue Chemistry data deficiencies exist. These deficiencies pertain to the proposed formulation, the Section B/label, an EPA petition method validation, submission of an analytical reference standard, storage stability data, and the Section F.

cc: RF, Circu., N. Dodd (CBTS), E. Haeberer (CBTS), PM #25, PP#6F04641, Rich Griffin (RCAB)

RDI: R. Loranger: 6/24/96
7509C:CBTS:CM#2:Rm804F:305-5681:N. Dodd:nd:6/26/96

IMAZAPYR
Shaughnessy No. 128821
(CBTS No. 16723; DP Barcode D222027)

PP#6F04641: REQUEST FOR THE ESTABLISHMENT OF PERMANENT TOLERANCES FOR RESIDUES OF IMAZAPYR IN/ON FIELD CORN COMMODITIES

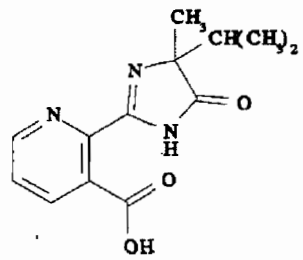
May 23, 1996

Contract No. 68-D4-0010

Submitted to:
U.S. Environmental Protection Agency
Arlington, VA

Submitted by:
Dynamac Corporation
The Dynamac Building
2275 Research Boulevard
Rockville, MD 20850-3268

IMAZAPYR



PP#6F04641: REQUEST FOR THE ESTABLISHMENT OF PERMANENT TOLERANCES FOR RESIDUES OF IMAZAPYR IN/ON FIELD CORN COMMODITIES

(CBTS NO. 16723; DP BARCODE D222027)

INTRODUCTION

The petitioner, American Cyanamid Company, is proposing the establishment of permanent tolerances for residues of the herbicide imazapyr (AC 243,997) [2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-3-pyridinecarboxylic acid] in/on the following commodities:

Field corn grain, fodder, and forage . . . . . 0.05 ppm

In conjunction with the above tolerance request, the petitioner is seeking the registration of an end-use product formulation (AC 513,996) containing a premix of imazapyr (17.5%) and another related herbicide, imazethapyr (52.5%), for use on imidazolinone-tolerant field corn (IMI-corn™ hybrids) for early postemergence control of weeds. The current tolerance petition is the first tolerance request for imazapyr use on food/feed crops.

Imazapyr (AC 243,997) is a broad-spectrum imidazolinone herbicide which is presently registered for weed control in non-crop areas. The petitioner believes that imazapyr deserves to be classified as a "reduced risk pesticide" owing to its Group E classification (as per EPA Carcinogenicity Peer Review Committee, 4/26/95) and also because if imazapyr becomes registered for use on corn it has the potential to replace a number of herbicides which are currently in Special Review (e.g., triazines and acetanilides). The petitioner claims that the proposed maximum use rate of 0.014 lb ae/A for imazapyr use on corn is 100x lower than the currently registered use for imazapyr on non-crop areas and results in nondetectable residues.

In support of this petition, the petitioner has submitted eight volumes of residue chemistry data which are evaluated for adequacy in fulfilling data requirements under Subdivision O of the Pesticide Assessment Guidelines.

CONCLUSIONS

1a. Product chemistry data for technical imazapyr (EPA Reg. No. 214-286) have previously been reviewed to establish the current non-food/non-feed uses. Review of product chemistry data for the formulation AC 513,996 Herbicide is under the purview of Registration Division.

1b. The established tolerance for imazethapyr (40 CFR 180.447) on corn fodder, forage, and grain is for imazethapyr as its ammonium salt. No tolerance is established for imazethapyr technical (acid). Since the proposed formulation AC 513,996 contains imazethapyr in the technical (acid) form according to the submitted Confidential Statement of Formula (CSF), either the proposed formulation AC 513,996 must be changed so that imazethapyr is present as the ammonium salt or a tolerance petition proposing the establishment of a tolerance for imazethapyr (as the acid) is needed.

1c. The field trial residue data for imazapyr were conducted using a salt of imazapyr (Arsenal®) rather than imazapyr technical (acid). Since the proposed formulation AC 513,996 contains imazapyr in the technical (acid) form according to the submitted CSF, either the proposed formulation must be changed so that imazapyr is present as the salt which is in Arsenal® and a revised Section F must be submitted which proposes a tolerance for imazapyr as the salt or additional field trials are needed using the imazapyr technical (acid). Three side-by-side trials comparing the ammonium salt and acid formulations would be adequate provided residues from the two products are similar.

2a. The proposed Section B/label indicates a 45-day preharvest/pregrazing interval. If the petitioner wants a 30-day preharvest/pregrazing interval as indicated in the summary of field residue trials (Exhibit 11 of the administrative materials of this petition), the proposed Section B/label would have to be revised.

2b. A revised Section B/label is required. The requirement for growers to contact processor companies for recommendations concerning plant back intervals (PBI's) for sweet corn grown for processing is inappropriate and must be removed from the label. Based on the available rotational crop study, the label should be revised to indicate a 4-month plant back interval for small grains and a 9-month plant back interval for all other commodities. However, plant back intervals longer than 12 months may remain on the label if the petitioner states that they are required due to phytotoxicity.

3. The qualitative nature of the residue in field corn is adequately understood. Following a single foliar broadcast application of [^{14}C]imazapyr to imidazolinone-resistant corn (IMI-corn™ hybrid) at 0.025 lb ae/A (1.8x the proposed maximum application rate), ^{14}C-residues were 0.004-0.010 ppm in/on forage harvested 30 and 62 days after treatment (DAT), and 0.009 ppm in/on fodder and 0.029 ppm in/on grain harvested at maturity. Following a single foliar broadcast application of [^{14}C]imazapyr to IMI-corn™ at 0.071 lb ae/A (5.1x the proposed maximum application rate) ^{14}C-residues were 0.025-0.026

5

ppm in/on forage harvested 30 and 62 DAT, and 0.028 ppm in/on fodder and 0.086 ppm in grain harvested at maturity. Following extraction and HPLC analysis of treated field corn matrices, the principal component identified in field corn was imazapyr. The identity of imazapyr was confirmed by GC/MS.

In the field corn treated at 5.1X, imazapyr accounted for 55.8% of the total radioactive residue (TRR) in early forage (30 DAT), 53.3% of the TRR in late forage (62 DAT), 11.7% of the TRR in fodder (114 DAT), and 63.7% of the TRR in grain (114 DAT). The metabolites CL 9,140, CL 60,032, CL 263,078, CL 252,974, CL 252,663, and CL 271,045 were also identified in field corn matrices, each at <10% of the TRR. (See Figure 1 for the chemical names and structures of imazapyr metabolites identified in field corn matrices.) Unknown 2 accounted for 8.1% of the TRR (0.012 ppm) in the green plant (14 DAT), 6.5% of the TRR (0.002 ppm) in early forage (30 DAT), 10.1% of the TRR (0.003 ppm) in late forage (62 DAT), 19.2% of the TRR (0.006 ppm) in the fodder (114 DAT), and <0.1% of the TRR (<0.001 ppm) in grain (114 DAT). The remainder of the characterized radioactivity in the field corn treated at 5.1X consisted of 9 unknowns, none comprising >7% of the TRR. Total identified and characterized residues in the field corn treated at 5.1X accounted for 82.0% of the TRR in the green plant (14 DAT), 85.8% of the TRR in early forage (30 DAT), 86.8% of the TRR in late forage (62 DAT), 69.9% of the TRR in fodder (114 DAT), and 89.6% of the TRR in grain (114 DAT).

The HED Metabolism Committee will be consulted for a determination of the residue of concern in corn commodities.

4. The qualitative nature of the residue in ruminants is adequately understood. Following oral administration of [6-pyridine-^{14}C]imazapyr to two goats at 17.7 ppm or 42.5 ppm (~190x or 460x the maximum theoretical dietary burden) in the diet for 7 days, the TRR (expressed as imazapyr equivalents) ranged from <0.01 ppm (nondetectable) to 0.02 ppm in milk and were 0.08 ppm and 0.11 ppm, respectively, in the kidneys of the low and high dose goats. The TRR in remaining tissues (fat, liver, and leg and loin muscle) were nondetectable (<0.05 ppm) and were not further characterized. The study sufficiently characterized and identified detectable residues in extracts of milk and kidney by TLC and HPLC. Imazapyr *per se* was the sole radioactive component identified, comprising ~50% of TRR in milk and ~95% of TRR in kidney.

5. The qualitative nature of the residue in poultry is adequately understood. Following oral administration of [6-pyridine-^{14}C]imazapyr to two groups of hens at 1.98 ppm or 9.72 ppm (~50x and 240x the maximum theoretical dietary burden) in the diet for 7 days, the TRR were <0.01 ppm (nondetectable) in eggs, liver, kidneys, muscle, and skin with adhering fat. Because residues in poultry eggs and tissues of concern were nondetectable, no further analyses were attempted or are required. It is noted that imazapyr *per se* was the sole radioactive component identified in the excreta of treated hens.

6a. The petitioner is proposing GC/MS Method M 2468 for use as an enforcement method for field corn commodities. This method was used for data collection in the submitted corn field trials and processing studies. Based on the concurrent method recovery data submitted with the field trials and processing studies, GC/MS Method M 2468 is adequate for collection of residue data for imazapyr *per se* from samples of field corn forage, silage, grain, fodder, meal, and oil. The method has successfully undergone independent laboratory validation (as per PR Notice 88-5) and has been radiovalidated using samples from the plant metabolism study. The radiovalidation data indicated that the method adequately recovered residues of imazapyr from samples of IMI-corn™ green plant and grain treated with [^{14}C]imazapyr.

6b. EPA needs to conduct a petition method validation. CBTS will forward the method to EPA's Analytical Chemistry Laboratory for petition method validation.

6c. The petitioner must submit an analytical reference standard for imazapyr and the material safety data sheet (MSDS) to the EPA repository. The petitioner should then submit the repository code number for the analytical reference standard to CBTS so that CBTS will know that the standard has been sent.

6d. The petitioner stated that FDA multi-residue methods have been found to be inappropriate for analysis of other imidazolinone pesticides in food/feed commodities, and cited examples in which attempts to analyze samples for imidazolinone pesticides using Protocols A-C were unsuccessful. The petitioner concluded that FDA multi-residue methods did not exhibit sufficient detectability and sensitivity to other imidazolinone herbicides, and thus there is no reasonable expectation that these methods would prove to be useful for determining residues of imazapyr. CBTS concurs with this conclusion.

7a. Storage stability data submitted with the field corn metabolism study indicate that residues of [^{14}C]imazapyr are stable in/on field corn forage, fodder, and grain during frozen storage between the first analyses (1-7 months after sample collection) and the second analyses at least two years later.

7b. Additional storage stability data are required as follows:

i. Data reflecting residue analyses at zero time for the on-going storage stability study are needed to establish the baseline residue levels present at the time samples were placed into storage.

ii. The petitioner must submit the final report for the on-going storage stability study reflecting storage of field corn commodities for up to 24 months.

7

iii. Information pertaining to the date and location where the grain samples were processed was not included. These data must be submitted so that the exact intervals from processing to analysis can be determined for corn oil and meal.

8a. The geographic representation and number of conducted field trials are adequate for establishment of pesticide residue tolerances. A total of 19 trials reflecting the proposed maximum use pattern was conducted in IA, IL, IN, MI, MN, MO, NC, NE, OH, PA, SD, TX, and WI. These test states encompass Regions 1, 2, 5, 6, and 7.

8b. The submitted residue data for field corn indicate that residues of imazapyr *per se* were below the limit of quantitation (<0.05 ppm) in/on field corn forage samples harvested 29-62 days and in/on grain and fodder samples harvested 103-149 days following a single early postemergence broadcast application of either Arsenal® 2 ASU (2 lb ae/gal) or Arsenal® 20 WP at the rate of 0.024 lb ae/A (1.7x the maximum proposed single/seasonal application rate). These field trial data indicate that residues of imazapyr in/on field corn forage, fodder, and grain resulting from application of Arsenal® 2 ASU or Arsenal® 20 WP will not exceed the proposed tolerances of 0.05 ppm, the limit of quantitation (LOQ) of the proposed enforcement method.

8c. The petitioner is requested to submit a revised Section F to separately propose tolerances for the correct field corn RACs as follows:

corn, field, stover (fodder).....0.05 ppm
corn, field, forage.....0.05 ppm
corn, field, grain.....0.05 ppm

8d. The proposed use would allow use of a nonionic surfactant or crop oil. All of the residue studies included nonionic surfactant. Since no residue data have been submitted in which crop oil was applied, either a revised Section B/label must be submitted which deletes references to crop oil or additional residue data in which crop oil is included must be submitted.

8e. No residue data for field corn aspirated grain fractions (grain dust) were submitted with this petition. Because the proposed use is an early season use (before corn is 12 inches in height) and residues of imazapyr were below the LOQ in/on field corn grain following treatment at 1.7x, no residue data on aspirated grain fractions are required for the purposes of this petition.

9. The abbreviated field corn processing study indicates that residues of imazapyr did not concentrate in oil but concentrated slightly in meal (1.1-1.2x) processed/extracted from field corn grain bearing detectable residues and treated at 17x the maximum proposed single/seasonal application rate. CBTS recognizes that obtaining samples with significant residues with an early season herbicide is difficult, and considers the submitted abbreviated processing study to be adequate in demonstrating that residues of

8

imazapyr will not significantly concentrate in the processed commodities of field corn at the proposed use pattern. For the purposes of this petition request, no Section 409 tolerances are required for imazapyr residues in the processed commodities of field corn.

10. In consideration of the exaggerated feeding levels utilized in the animal metabolism studies which resulted in nondetectable radioactive residues (<0.01 or <0.05 ppm depending on the matrix) in goat muscle, goat liver, and goat fat, and all poultry matrices along with small amounts of radioactive residues in milk and goat kidney, there is no reasonable expectation that finite imazapyr residues will occur in meat, milk, poultry, and eggs (Category 3 of 40 CFR §180.6) as a result of the proposed use pattern on field corn. Residues of imazapyr were also below the validated limit of quantitation (<0.05 ppm) in/on field corn forage, grain, and fodder following application of imazapyr at 1.7x. Therefore, animal feeding studies or tolerances for meat, milk, poultry, and eggs are not required for purposes of this petition request. However, CBTS reserves the right to request animal feeding studies if additional uses on crops with livestock feed items are proposed for registration in the future.

11. The submitted confined rotational crop study is adequate. ^{14}C-Residues were <0.002 ppm in the RACs of wheat from a 4-month plant back interval (PBI) and in the RACs of radishes, lettuce, and soybeans from a 9-month PBI. The proposed label specifies rotational crop PBIs of 4 months for rye and wheat, 8.5 months for field corn, and ≥9.5 months for all other crops. Based on the submitted data, no PBIs longer than 9 months are required. No limited or extensive field rotational crop studies or rotational crop tolerances are required for purposes of this petition. However, a revised Section B/label must be submitted which specifies rotational crop plant back intervals of 4 months for small grains and 9 months for all other crops unless the petitioner states that longer intervals are needed due to phytotoxicity concerns.

RECOMMENDATIONS

CBTS recommends against establishment of the proposed permanent tolerances for imazapyr on field corn forage, fodder and grain for the reasons given in Conclusions #'s 1b, 1c, 2a, 2b, 6b, 6c, 7b, 8c, and 8d above.

DETAILED CONSIDERATIONS

Product Chemistry

Product chemistry data for technical imazapyr (EPA Reg. No. 214-286) have previously been reviewed to establish the current non-food/non-feed uses. Review of product chemistry data for the formulation AC 513,996 Herbicide is under the purview of Registration Division.

The established tolerance for imazethapyr (40 CFR 180.447) on corn fodder, forage, and grain is for imazethapyr as its ammonium salt. No tolerance is established for imazethapyr technical (acid). Since the proposed formulation AC 513,996 contains imazethapyr in the technical (acid) form according to the submitted Confidential Statement of Formula (CSF), either the proposed formulation AC 513,996 must be changed so that imazethapyr is present as the ammonium salt or a tolerance petition proposing the establishment of a tolerance for imazethapyr (as the acid) is needed.

The field trial residue data for imazapyr were conducted using a salt of imazapyr (Arsenal®) rather than imazapyr technical (acid). Since the proposed formulation AC 513,996 contains imazapyr in the technical (acid) form according to the submitted CSF, either the proposed formulation must be changed so that imazapyr is present as the salt which is in Arsenal® and a revised Section F must be submitted which proposes a tolerance for imazapyr as the salt or additional field trials are needed using the imazapyr technical (acid). Three side-by-side trials comparing the ammonium salt and acid formulations would be adequate provided residues from the two products are similar.

Proposed Use

Section B of the subject petition contained a specimen label for a proposed wettable powder (WP) formulation (Product Name = AC 513,996 DG Herbicide) containing the active ingredients imazapyr (17.5%) and imazethapyr (52.5%). The 17.5% WP imazapyr formulation is proposed for a single early broadcast postemergence application (before weeds exceed a height of 4 inches, and before corn is 12 inches in height) on imidazolinone-tolerant corn only (IMI-corn™ hybrids) at 0.014 lb ae/A. The postemergence application requires the addition of an adjuvant (i.e., nonionic or organosilicone surfactant, or crop oil concentrate such as petroleum or vegetable oil) and liquid fertilizer solution (preferably nitrogen-based such as 28%N, 32%N or 10-34-0). Application may be made alone or as a tank mix with other recommended herbicides using ground (in 10 or more gallons of water per acre) or aerial (in 5 or more gallons of water per acre) equipment; application using any type of irrigation system is prohibited. The label proposes a maximum of one application per growing season and a 45-day preharvest/pregrazing interval. We note that in the summary of field residue trials (Exhibit 11 of the administrative materials of this petition), the petitioner states that they are proposing a 30-day feeding/grazing restriction.

The following geographic restrictions are being proposed: (i) imazapyr application may be made with a non-ionic surfactant only (liquid fertilizer not required) in the boot-heel of MO, TN, SC, LA, and GA; (ii) imazapyr use is prohibited in CA and NY; and (iii) imazapyr application to IMI-corn™ hybrids is prohibited in ND or in MN north of State Highway 210.

The following rotational crop restrictions are being proposed: (i) IMI-corn™ hybrids may be planted anytime following application; (ii) a 4-month PBI for rye and wheat; (iii) an 8.5-month plant back interval (PBI) for field corn and field corn grown for seed; (iv) a 9.5-month PBI for alfalfa, barley, edible beans, peas, peanuts, soybeans, and tobacco; (v) an 18-month PBI for cotton, lettuce, oats, popcorn, safflower, sorghum, and sweet corn; (vi) a 26-month PBI for potatoes; and (vii) a 46-month PBI for all crops not listed above.

Exceptions to the above rotational restrictions are proposed for corn inbred seed lines and sweet corn and popcorn varieties. According to the petitioner, due to the proprietary nature of seed production, they have not been given access to data by seed companies for corn inbred seed lines. Growers are directed to call the seed company for information and recommendations concerning appropriate PBI(s) for popcorn and corn grown for seed. The proposed plant back interval is 18 months for sweet corn and popcorn for all states except IA, IL, IN, OH, WI, and MN (south of Highway No. 210 only) where a 12-month PBI is being proposed. Growers are directed to call the processor company for information and recommendations concerning appropriate PBI(s) for sweet corn grown for processing. The proposed PBI for fresh market sweet corn is 18 months.

Conclusion

The proposed Section B/label indicates a 45-day preharvest/pregrazing interval. If the petitioner wants a 30-day preharvest/pregrazing interval as indicated in the summary of field residue trials (Exhibit 11 of the administrative materials of this petition), the proposed Section B/label would have to be revised.

A revised Section B/label is required. The requirement for growers to contact processor companies for recommendations concerning plant back intervals (PBI's) for sweet corn grown for processing is inappropriate and must be removed from the label. Based on the available rotational crop study, the label should be revised to indicate a 4-month plant back interval for small grains and a 9-month plant back interval for all other commodities. However, plant back intervals longer than 12 months may remain on the label if the petitioner states that they are required due to phytotoxicity.

Qualitative Nature of the Residue in Plants

Field Corn (1995; MRID 438615-03)

In-life phase

American Cyanamid submitted data depicting the metabolism of [6-pyridine-^{14}C]imazapyr in imidazolinone-tolerant field corn (IMI-corn™). The field phase of the study was conducted by American Agricultural Services Incorporated (AASI; Lucama, NC), and the analytical phase was conducted by American Cyanamid Company (Princeton, NJ). The radiolabelled test substance, [6-pyridine-^{14}C]imazapyr (specific activity 43.6 µCi/mg, radiochemical purity 98.6%), was dissolved in acetone to a final specific activity of 21.2 µCi/mg; [6-pyridine-^{13}C]imazapyr was added as a mass marker. The radioactive test substance was formulated with nonlabelled imazapyr, water, and a non-ionic spreader, and applied as an ammonium salt formulation to two separate field plots of IMI-corn™ plants at the 3- to 4-leaf stage. Each plot received a single broadcast foliar application of [^{14}C]imazapyr at either 0.025 or 0.071 lb ae/A (1.8x or 5.1x the proposed maximum use rate) 18 days after planting. Applications were made in 47.6 gal/A using ground equipment.

Whole plant samples were harvested 0, 14, 30, and 62 days after treatment (DAT). At crop maturity (114 DAT), shucked ears and stalks plus husks were collected. Samples were frozen immediately after harvest and were stored at ≤-19 °C for 1-7 days prior to overnight shipment on dry ice to the analytical laboratory.

Total radioactive residues (TRR)

At the analytical laboratory, field corn grain was removed from cobs, and the cobs were combined with husks and stalks to form the fodder sample. All samples were then ground frozen and stored at ~-20 °C until analysis. Triplicate subsamples of each sample were combusted and radioassayed by liquid scintillation spectrometry (LSS). The limit of detection (LOD) for the radioassay was 0.002 ppm for all commodities. The TRR in IMI-corn™ matrices are presented in Table 1. Radioactive residues in all control matrices were <0.002 ppm. Sample calculations were submitted.

Table 1. Total radioactive residues in/on IMI-corn™ commodities harvested following a single foliar application of [^{14}C]imazapyr at 0.025 lb ae/A or 0.071 lb ae/A (1.8x or 5.1x the proposed maximum use rate).

Commodity	Posttreatment Interval (days)	TRR (expressed as ppm [^{14}C]imazapyr equivalents)	
		0.025 lb ae/A	0.071 lb ae/A
Green plant [a]	0	2.471	8.711
	14	0.058	0.153
Early forage	30	0.010	0.026
Late forage	62	0.004	0.025
Fodder [b]	114	0.009	0.028
Grain	114	0.029	0.086

[a] These samples are not representative of the RAC field corn forage because of the early harvest interval.
[B] Fodder sample consists of husks, stalks, and cobs with grain removed.

Extraction of residues

Samples of 62-DAT forage and fodder from the 1.8x-treatment were not further analyzed because TRR were <0.01 ppm; the 0-DAT green plant sample from the 5.1x treatment was also not analyzed. The remaining samples of whole green plants (0 and 14 DAT) and forage (30 and 62 DAT) were extracted three times with methanol (MeOH) and filtered. Fodder samples were extracted with MeOH:water:HCl (80:18:2, v:v:v) for one hour and filtered; the extraction was repeated three additional times. Grain samples were initially extracted with hexane for one hour, then extracted with MeOH:water:HCl as for fodder.

The nonextractable solids were not further analyzed. In addition, the MeOH extract from the 30 DAT early forage sample (1.8x-treatment) and the hexane fractions from grain were not further analyzed because ^{14}C-residues were <0.01 ppm in these fractions. The MeOH and MeOH:water:HCl fractions from the remaining samples were reserved for analysis by TLC and reverse-phase HPLC. The distribution of ^{14}C-residues in IMI-corn™ commodities are presented in Tables 2 and 3.

To validate the extraction procedure, the petitioner fortified an untreated sample of 14-DAT green plant with [^{14}C]imazapyr and extracted the sample using the above procedures. Following extraction 99.9% of the fortified radioactivity was recovered in the MeOH extract. Subsequent HPLC analysis indicated that 92.8% of the radioactivity co-chromatographed with imazapyr.

Characterization/identification of residues

Although the petitioner analyzed extracts using TLC, the TLC data are not presented here because the petitioner indicated that results were unsatisfactory. Radioactive residues in field

13

corn extracts was analyzed by HPLC using Supelcosil LC-8DB and LC-18DB columns and a gradient mobile phase of acidified water (pH 2.1) changing to acidified water:acetonitrile (1:1, v:v) over 50 minutes. Radioactivity was quantitated by fraction collection followed by LSS. Residues were identified by co-chromatography with the following reference standards: imazapyr, CL 9,140, CL 60,032, CL 252,663, CL 252,974, CL 263,078, and CL 247,087.

To confirm identification of imazapyr, the MeOH extracts from 62-DAT forage and grain (5.1x-treatment) were further purified using antibody affinity chromatography to isolate imazapyr, which was then identified by GC/MS. The distribution and characterization/identification of ^{14}C-activity in extracts of field corn commodities are presented in Tables 2 and 3; a summary of the characterized and identified ^{14}C-residues for each treatment is presented in Tables 4 and 5. Representative chromatograms and spectra were included in the submission. The chemical names and structures of imazapyr and its metabolites identified in field corn commodities are presented in Figure 1.

Table 2. Distribution and characterization/identification of ^{14}C-residues in IMI-corn™ matrices following application of [^{14}C]imazapyr at 0.025 lb ae/A (1.8x the proposed maximum application rate).

Fraction	%TRR	ppm [a]	Characterization/Identification [b]
Green plant - 0 DAT (TRR = 2.471 ppm)			
MeOH	96.3	2.379	HPLC analysis resolved: Imazapyr 80.9% TRR 1.997 ppm CL 9,140 <0.1% TRR <0.001 ppm CL 60,032 0.1% TRR 0.002 ppm CL 263,078 1.0% TRR 0.025 ppm CL 252,974 1.0% TRR 0.026 ppm CL 252,663 3.2% TRR 0.078 ppm CL 271,045 1.7% TRR 0.042 ppm Unknown 2 1.1% TRR 0.028 ppm Plus 8 unknowns each accounting for 0.2-2.7% TRR (0.005-0.067 ppm).
Solids	3.7	0.093	N/A.
Green plant - 14 DAT (TRR = 0.058 ppm)			
MeOH	78.6	0.046	HPLC analysis resolved: Imazapyr 50.0% TRR 0.029 ppm CL 9,140 2.0% TRR 0.001 ppm CL 60,032 1.1% TRR 0.001 ppm CL 263,078 2.2% TRR 0.001 ppm CL 252,974 2.9% TRR 0.002 ppm CL 252,663 1.6% TRR 0.001 ppm CL 271,045 1.7% TRR 0.001 ppm Unknown 2 5.9% TRR 0.003 ppm Plus 8 unknowns each accounting for 0.4-2.9% TRR (<0.001-0.002 ppm).
Solids	21.4	0.012	N/A.
Early forage - 30 DAT (TRR = 0.010 ppm)			
MeOH	84.2	0.008	N/A
Solids	15.7	0.002	N/A.
Grain - 114 DAT (TRR = 0.029 ppm)			
Hexane	1.5%	<0.001	N/A.
MeOH:H_2O:HCl	80.0	0.023	HPLC analysis resolved: Imazapyr 40.8% TRR 0.012 ppm CL 9,140 1.9% TRR 0.001 ppm CL 60,032 0.9% TRR <0.001 ppm CL 263,078 3.2% TRR 0.001 ppm CL 252,974 2.9% TRR 0.001 ppm CL 252,663 5.1% TRR 0.001 ppm CL 271,045 1.7% TRR 0.001 ppm Unknown 2 6.9% TRR 0.002 ppm Plus 9 unknowns each accounting for 1.0-3.2% of the TRR (<0.001-0.001 ppm).
Solids	18.5	0.005	N/A.

[a] Expressed in imazapyr acid equivalents.

[b] %TRR calculated by reviewer from % of injected radioactivity recovered in each peak. Unknown 2 eluted in HPLC fraction 2 immediately before CL 9,140.

15

Table 3. Distribution and characterization/identification of ^{14}C-residues in IMI-corn™ matrices following application of [^{14}C]imazapyr at 0.071 lb ae/A (5.1x the proposed maximum application rate).

Fraction	%TRR	ppm [a]	Characterization/Identification [b]
Green plant - 14 DAT (TRR = 0.153 ppm)			
MeOH	81.9	0.126	HPLC analysis resolved: Imazapyr 53.1% TRR 0.082 ppm CL 9,140 0.7% TRR 0.001 ppm CL 60,032 0.9% TRR 0.001 ppm CL 263,078 2.3% TRR 0.004 ppm CL 252,974 2.3% TRR 0.004 ppm CL 252,663 2.7% TRR 0.004 ppm CL 271,045 1.4% TRR 0.002 ppm Unknown 2 8.1% TRR 0.012 ppm Plus 8 unknowns each accounting for 0.3-4.1% TRR (<0.001-0.006 ppm).
Solids	18.1	0.028	N/A.
Early forage - 30 DAT (TRR = 0.026 ppm)			
MeOH	85.8	0.022	HPLC analysis resolved: Imazapyr 55.8% TRR 0.014 ppm CL 9,140 1.1% TRR <0.001 ppm CL 60,032 0.8% TRR <0.001 ppm CL 263,078 2.1% TRR 0.001 ppm CL 252,974 3.1% TRR 0.001 ppm CL 252,663 2.6% TRR 0.001 ppm CL 271,045 1.4% TRR <0.001 ppm Unknown 2 6.5% TRR 0.002 ppm Plus 8 unknowns each accounting for 0.5-3.3% TRR (<0.001-0.001 ppm).
Solids	14.2	0.004	N/A.
Late forage - 62 DAT (TRR = 0.025 ppm)			
MeOH	86.8	0.022	HPLC analysis resolved: Imazapyr 53.3% TRR 0.013 ppm CL 9,140 1.2% TRR <0.001 ppm CL 60,032 0.6% TRR <0.001 ppm CL 263,078 3.3% TRR 0.001 ppm CL 252,974 2.5% TRR 0.001 ppm CL 252,663 2.5% TRR 0.001 ppm CL 271,045 1.1% TRR <0.001 ppm Unknown 2 10.1% TRR 0.003 ppm Plus 7 unknowns each accounting for 0.1-4.5% TRR (<0.001-0.001 ppm). Imazapyr was isolated by affinity chromatography and its identity was confirmed by GC/MS.
Solids	13.3	0.003	N/A.

(continued; footnotes follow)

Table 3 *(continued)*.

Fraction	%TRR	ppm [a]	Characterization/Identification [b]
Fodder - 114 DAT (TRR = 0.028 ppm)			
MeOH:H_2O:HCl	69.9	0.020	HPLC analysis resolved: Imazapyr 11.7% TRR 0.003 ppm CL 9,140 6.7% TRR 0.002 ppm CL 60,032 0.8% TRR <0.001 ppm CL 263,078 6.3% TRR 0.002 ppm CL 252,974 3.2% TRR 0.001 ppm CL 252,663 2.3% TRR 0.001 ppm CL 271,045 0.8% TRR <0.001 ppm Unknown 2 19.2% TRR 0.006 ppm Plus 9 unknowns each accounting for 0.9-3.8% TRR (<0.001-0.001).
Solids	30.1	0.008	N/A.
Grain - 114 DAT (TRR = 0.086 ppm)			
Hexane	0.8%	<0.001	N/A.
MeOH:H_2O:HCl	88.8	0.076	HPLC analysis resolved: Imazapyr 63.8% TRR 0.055 ppm CL 9,140 0.4% TRR <0.001 ppm CL 263,078 3.3% TRR 0.003 ppm CL 252,974 3.3% TRR 0.003 ppm CL 252,663 7.2% TRR 0.006 ppm CL 271,045 0.9% TRR 0.001 ppm Unknown 2 <0.1% TRR <0.001 ppm Plus 9 unknowns each accounting for <0.1-3.5% TRR (<0.001-0.003 ppm). Imazapyr was isolated by affinity chromatography and its identity was confirmed by GC/MS.
Solids	10.3	0.009	N/A.

[a] Expressed in imazapyr acid equivalents.
[b] %TRR calculated by reviewer from % of injected radioactivity recovered in each peak. Unknown 2 eluted in HPLC fraction 2 immediately before CL 9,140.

17

Table 4. Summary of radioactive residues characterized/identified in IMI-corn™ commodities receiving a single foliar application of [^{14}C]imazapyr at 0.025 lb ae/A (1.8x the maximum application rate).

Fraction	Green Plant - 0 DAT		Green Plant - 14 DAT		Grain - 114 DAT	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Identified						
Imazapyr	80.9	1.997	50.0	0.029	40.8	0.012
CL 9,140	<0.1	<0.001	2.0	0.001	1.9	0.001
CL 60,032	0.1	0.002	1.1	0.001	0.9	<0.001
CL 263,078	1.0	0.025	2.2	0.001	3.2	0.001
CL 252,974	1.0	0.026	2.9	0.002	2.9	0.001
CL 252,663	3.2	0.078	1.6	0.001	5.1	0.001
CL 271,045	1.7	0.042	1.7	0.001	1.7	0.001
Total identified	**87.9**	**2.172**	**61.4**	**0.036**	**56.5**	**0.016**
Characterized						
Unknown 2	1.1	0.028	5.9	0.003	6.9	0.002
Other unknowns [b]	7.3	0.181	11.4	0.009	16.5	0.005
Hexane	--	--	--	--	1.5	<0.001
Total identified/characterized[a]	**96.3**	**2.379**	**78.7**	**0.046**	**81.5**	**0.024**
Nonextractable[a]	3.7	0.093	21.4	0.012	18.5	0.005

[a] Expressed as imazapyr acid equivalents.
[b] Including up to 9 individual components, none comprising >4% TRR.

Table 5. Summary of radioactive residues characterized/identified in IMI-corn™ commodities receiving a single foliar application of [^{14}C]imazapyr at 0.071 lb ae/A (5.1x the maximum application rate).

Fraction	Green Plant - 14 DAT		Early Forage - 30 DAT		Late Forage - 62 DAT		Fodder - 114 DAT		Grain - 114 DAT	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Identified										
Imazapyr	53.1	0.082	55.8	0.014	53.3	0.013	11.7	0.003	63.7	0.055
CL 9,140	0.7	0.001	1.1	<0.001	1.2	<0.001	6.7	0.002	0.4	<0.001
CL 60,032	0.9	0.001	0.8	<0.001	0.6	<0.001	0.8	<0.001	--	--
CL 263,078	2.3	0.004	2.1	0.001	3.3	0.001	6.3	0.002	3.3	0.003
CL 252,974	2.3	0.004	3.1	0.001	2.5	0.001	3.2	0.001	3.3	0.003
CL 252,663	2.7	0.004	2.6	0.001	2.5	0.001	2.3	0.001	7.2	0.006
CL 271,045	1.4	0.002	1.4	<0.001	1.1	<0.001	0.8	<0.001	0.9	0.001
Total identified	**63.3**	**0.097**	**66.9**	**0.017**	**64.6**	**0.016**	**31.8**	**0.009**	**78.9**	**0.068**
Characterized										
Unknown 2	8.1	0.012	6.5	0.002	10.1	0.003	19.2	0.006	<0.1	<0.001
Other unknowns[b]	10.6	0.016	12.5	0.003	12.1	0.003	18.9	0.005	9.9	0.009
Hexane	--	--	--	--	--	--	--	--	0.8	<0.001
Total identified/ characterized[a]	**82.0**	**0.125**	**85.8**	**0.022**	**86.8**	**0.022**	**69.9**	**0.020**	**89.6**	**0.077**
Nonextractable[a]	18.1	0.028	14.2	0.004	13.3	0.003	30.1	0.008	10.3	0.009

[a] Expressed as imazapyr acid equivalents.
[b] Including up to 9 individual components, none comprising >7% TRR.

Storage stability

Samples of IMI-corn™ green plant, forage, fodder, and grain were stored frozen (≤-19 °C) for 1-7 months between sample collection and analysis. To assess the stability of [^{14}C]imazapyr residues in frozen field corn matrices from the metabolism study, the petitioner re-extracted and analyzed samples of 30-DAT forage fodder, and grain samples from the 5.1x treatment after storage for ~2 years at -20 °C. The stored samples were extracted and analyzed using the procedures described above. The results of the storage stability study are presented in Table 6.

The levels [^{14}C]imazapyr in stored samples of fodder and grain were similar to levels found in the metabolism study. The increase in concentration of ^{14}C-residues observed in forage samples was attributed to desiccation of the forage sample during storage. The submitted data indicate that imazapyr is stable in/on samples of field corn forage, fodder, and grain during frozen storage between the first analyses and the second analyses at least two years later. Supporting chromatograms and data were included in the submission. No additional storage stability data are required to support the field corn metabolism study.

Table 6. Stability of [^{14}C]imazapyr in IMI-corn™ matrices stored at -20 °C for at least two years.

	First Analyses (6/93-11/93)			Second Analyses (11/95)		
		Imazapyr			Imazapyr	
Sample	TRR	%TRR	ppm	TRR	%TRR	ppm [a]
Early forage (30 DAT)	0.026	55.8	0.014	0.031	71.0	0.022
Fodder (114 DAT)	0.028	11.7	0.003	0.052	11.5	0.006
Grain (114 DAT)	0.086	63.8	0.055	0.086	57.1	0.049

[a] Expressed in imazapyr acid equivalents.

Radiovalidation of the proposed enforcement method (1995; MRID 43861516)

To validate the proposed enforcement method (GC/MS Method M 2468) for determination of residues of imazapyr in/on field corn commodities, the petitioner submitted data reflecting analysis of duplicate subsamples of 14-DAT green plant and grain from field corn plants from the metabolism study treated at the 5.1x rate. Method M 2468 is described in the "Residue Analytical Methods" section. The results of the radiovalidation study are presented in Table 7. Sample calculations and representative spectra were provided.

Concurrent method recovery data were submitted to demonstrate the adequacy of Method M 2468. Untreated samples of each crop matrix were fortified with imazapyr at 0.05 ppm; concurrent recoveries were 101% and 112% for green plant and grain samples, respectively.

The level of imazapyr residues in the green plant was found to be higher using Method M 2468 than for the metabolism study. The petitioner attributed this difference in residue levels to the dessication of the samples during storage.

The submitted data indicate that the proposed enforcement method, Method M 2468, adequately recovers residues of [^{14}C]imazapyr from field corn matrices.

Table 7. Comparison of the recovery of [^{14}C]imazapyr from treated IMI-corn™ matrices analyzed during the metabolism study and the proposed GC/MS residue method (M 2468).

Sample	Metabolism Study				Method M 2468 - GC/MS Method [a]			
	TRR	Extractability (%TRR)	Imazapyr		TRR	Extractability (%TRR)	Imazapyr	
			%TRR	ppm [b]			%TRR	ppm [b]
Green plant (14 DAT)	0.153	81.9	53.1	0.082	0.317	84, 91	47.6, 51.4	0.151, 0.163
Grain (114 DAT)	0.086	88.8	63.8	0.055	0.080	96, 97	82.5, 106.0	0.066, 0.085

[a] Samples were analyzed in duplicate.
[b] Expressed in [^{14}C]imazapyr equivalents.

Conclusion

The qualitative nature of the residue in corn is adequately understood. Following a single foliar broadcast application of [^{14}C]imazapyr to imidazolinone-resistant corn (IMI-corn™ hybrid) at 0.025 lb ae/A (1.8x the proposed maximum application rate), ^{14}C-residues were 0.004-0.010 ppm in/on forage harvested 30 and 62 days after treatment (DAT), and 0.009 ppm in/on fodder and 0.029 ppm in/on grain harvested at maturity. Following a single foliar broadcast application of [^{14}C]imazapyr to IMI-corn™ at 0.071 lb ae/A (5.1x the proposed maximum application rate) ^{14}C-residues were 0.025-0.026 ppm in/on forage harvested 30 and 62 DAT, and 0.028 ppm in/on fodder and 0.086 ppm in grain harvested at maturity. Following extraction and HPLC analysis of treated field corn matrices, the principal component identified in field corn was imazapyr. The identity of imazapyr was confirmed by GC/MS.

In the field corn treated at 5.1X, imazapyr accounted for 55.8% of the total radioactive residue (TRR) in early forage (30 DAT), 53.3% of the TRR in late forage (62 DAT), 11.7% of the TRR in fodder (114 DAT), and 63.7% of the TRR in grain (114 DAT). The metabolites CL 9,140, CL 60,032, CL 263,078, CL 252,974, CL 252,663, and CL 271,045 were also identified in field corn matrices, each at <10% of the TRR. (See Figure 1 for the chemical names and structures of imazapyr metabolites identified in field corn matrices.) Unknown 2 accounted for 8.1% of the TRR (0.012 ppm) in the green plant (14 DAT), 6.5%

of the TRR (0.002 ppm) in early forage (30 DAT), 10.1% of the TRR (0.003 ppm) in late forage (62 DAT), 19.2% of the TRR (0.006 ppm) in the fodder (114 DAT), and <0.1% of the TRR (<0.001 ppm) in grain (114 DAT). The remainder of the characterized radioactivity in the field corn treated at 5.1X consisted of 9 unknowns, none comprising >7% of the TRR. Total identified and characterized residues in the field corn treated at 5.1X accounted for 82.0% of the TRR in the green plant (14 DAT), 85.8% of the TRR in early forage (30 DAT), 86.8% of the TRR in late forage (62 DAT), 69.9% of the TRR in fodder (114 DAT), and 89.6% of the TRR in grain (114 DAT).

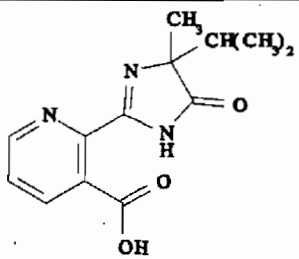
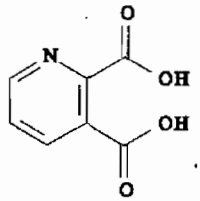
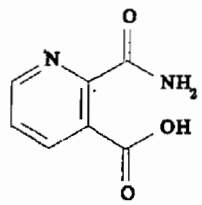
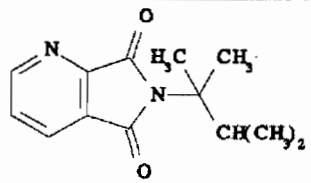
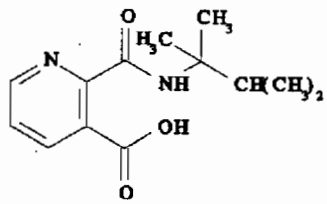
The HED Metabolism Committee will be consulted for a determination of the residue of concern in corn commodities.

Storage stability data submitted with the field corn metabolism study indicate that residues of [^{14}C]imazapyr are stable in/on field corn forage, fodder, and grain during frozen storage between the first analyses (1-7 months after sample collection) and the second analyses at least two years later.

The radiovalidation data for the proposed enforcement method (M 2468) are adequate to satisfy radiovalidation data requirements. The method adequately recovered residues of imazapyr from samples of IMI-corn™ green plant and grain treated with [^{14}C]imazapyr. No additional radiovalidation data are required.

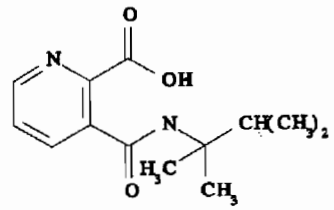
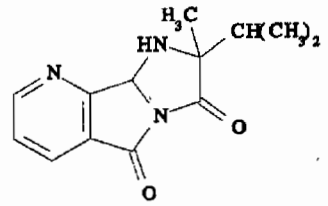
22

Figure 1. Chemical structures of imazapyr and its metabolites in field corn (MRID 43861503) and goat (MRID 43861504) commodities.

Common Name Chemical Name	Structure	Substrate
Imazapyr 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-3-pyridinecarboxylic acid		Field corn forage, fodder, and grain Goat milk and kidney
CL 9,140 2,3-pyridine dicarboxylic acid		Field corn forage, fodder, and grain
CL 60,032 2-carbamoyl-nicotinic acid		Field corn forage, fodder, and grain
CL 252,663 (S)-(-)-5,7-dihydro-α-methyl-5,7-dioxo-6H-pyrrolo[3,4-b]pyridine-6-acetamide		Field corn forage, fodder, and grain
CL 252,974 2-[(1-carbamoyl-1,2-dimethylpropyl)-carbamoyl]-nicotinic acid		Field corn forage, fodder, and grain

(continued; footnotes follow)

Figure 1 *(continued)*.

Common Name Chemical Name	Structure	Substrate
CL 263,078 3-[(1-carbamoyl-1,2-dimethylpropyl)-carbamoyl]-picolinic acid		Field corn forage, fodder, and grain
CL 271,045 (R)-(+)-1,9-α-dihydro-3β-isopropyl-3-methyl-5H-imidazo[1',2':1,2]pyrrolo[3,4-b]pyridine-2(3H)-5-dione		Field corn forage, fodder, and grain

Qualitative Nature of the Residue in Animals

Ruminants (1992; MRID 43861504)

American Cyanamid submitted data depicting the metabolism of [6-pyridine-^{14}C]imazapyr in lactating goats. The in-life portion of the study was conducted at Biological Test Center (BTC; Irvine, CA) and the analytical portion of the study was conducted at Xenobiotic Laboratories, Inc. (Princeton, NJ).. Gelatin dose capsules were prepared from [^{14}C]imazapyr (specific activity 43.41 μCi/mg, radiochemical purity 98.3%) to a final specific activity of 4.04 μCi/mg. Two goats were orally dosed with [^{14}C]imazapyr for seven consecutive days; Goat A at 17.7 ppm and Goat B at 42.5 ppm. These feeding levels respectively represent ~190x and 460x the maximum theoretical dietary burden; see "Magnitude of the Residue in Meat, Milk, Poultry, and Eggs" section for calculation of the dietary burden for ruminants. A third goat was used as a control and received gelatin capsules containing lactose only. The goats were orally dosed with gelatin capsules once daily in the morning.

During the testing period, the goats were fed alfalfa hay and a dietary supplement designed for lactating goats and were allowed water *ad libitum*. Milk was collected twice daily (in the a.m. prior to dosing and in the p.m.), and the daily samples were composited; triplicate aliquots of each daily milk sample were collected for radioassay at BTC, and the remaining subsamples were stored frozen. Blood samples were also collected on days 0, 1, 3, and 7 prior to daily dosing. The petitioner provided sufficient information concerning daily feed intake, body weights, and milk production. Goats were sacrificed ~22 hours after the last

dose. The entire liver and kidneys and representative samples of leg and loin muscle and omental fat were collected, diced, and frozen immediately. Samples were shipped on dry ice to Xenobiotic Laboratories where they were stored at ~-15 °C prior to analysis for residue characterization and identification.

Total radioactive residues (TRR)

At Xenobiotic Laboratories triplicate aliquots of homogenized tissues were combusted and radioassayed by liquid scintillation spectroscopy (LSS); milk samples were radioassayed directly by LSS. The limits of detection were 0.05 ppm for tissues and 0.01 ppm for milk. The TRR, expressed as [^{14}C]imazapyr equivalents, are presented in Table 8.

Table 8. Total radioactive residues found in milk and tissues from lactating goats orally dosed with [^{14}C]imazapyr for 7 days at 17.7 ppm and 42.5 ppm.

Matrix		TRR (expressed as ppm [^{14}C]imazapyr equivalents)	
		Goat A (17.7-ppm dose)	Goat B (42.5-ppm dose)
Milk	Day 1	<0.01	0.01
	Day 2	0.01	0.02
	Day 3	<0.01	0.01
	Day 4	<0.01	0.01
	Day 5	0.01	0.01
	Day 6	0.01	0.02
	Day 7	0.01	0.02
Fat		<0.05	<0.05
Kidney		0.08	0.11
Liver		<0.05	<0.05
Muscle		<0.05	<0.05

Samples of urine and feces were also collected to estimate the extent of excretion of the test substance. The petitioner provided data that indicated that 65.32% and 16.11% of the applied dose was eliminated in the urine and feces, respectively, of Goat A, and 60.35% and 18.97% of the applied dose was eliminated in the urine and feces, respectively, of Goat B. In addition, the TRR in blood samples from goats at both dosing levels were <0.05 ppm.

Extraction and hydrolysis of residues

Samples of milk and kidney from Goat B (42.5 ppm dose) were subjected to extraction and hydrolysis procedures for residue characterization and identification. During the fractionation procedures, aliquots of extracts and nonextractable residues were analyzed for radioactivity by LSS or combustion/LSS. The general extraction procedures are summarized below. Because

25

the TRR in fat, liver, and muscle were <0.05 ppm and reflected high dosing levels, these tissues were not subjected to characterization/identification procedures.

Milk: A subsample of milk (day 7) was extracted with acetonitrile (ACN) and centrifuged. The nonextractable residues were extracted twice with ACN:water (2.5:1, v:v) and centrifuged, then extracted twice with hexane and centrifuged. The supernatants from all extraction steps were combined and separated into a hexane fraction (Hexane-1) and an ACN:water fraction (Aqueous-1) using a separatory funnel. The ACN:water fraction was concentrated to remove ACN, then extracted three times with hexane and three times with ethyl acetate (EtOAc). The resulting hexane (Hexane-2), EtOAc, and aqueous (Aqueous-2) fractions were then concentrated by rotary evaporation. The Aqueous-2 fraction was acidified with concentrated HCl to a pH of ~4.5 and eluted with methanol on a C_{18} Sep-Pak cartridge. The methanol fraction was then concentrated prior to further analysis.

Kidney: A subsample of kidney was homogenized with methanol:water:chloroform (11:5:5, v:v:v) and centrifuged. The nonextractable residues were again extracted with chloroform and blended. The supernatants were combined and separated into a chloroform fraction and a methanol:water fraction using a separatory funnel. The methanol:water fraction was concentrated to remove methanol, then eluted with methanol on a C_{18} Sep-Pak cartridge. The methanol extract was concentrated and centrifuged prior to further analysis.

The distribution of total radioactive residues in the extracts of goat matrices is presented in Table 9.

Characterization and identification of ^{14}C-residues

The Aqueous-2 extract of milk and the methanol:water extract of kidney were subjected to two-dimensional TLC on silica gel plates with fluorescent indicator using the solvent systems 2-propanol:NH_4OH (80:20, v:v) in one dimension and methanol:water:EtOAc (25:25:50, v:v:v) in the other dimension. Radioactive residues were detected by a radioanalytic imager. Radioactivity was quantitated using the radioanalytic imager. The only reference standard used was imazapyr; the nonlabelled imazapyr standard was visualized using UV light.

The milk and kidney extracts were also analyzed by HPLC to confirm identification of imazapyr. The HPLC system consisted of a Zorbax R_x column, a UV detector (254 nm), and a radioactivity monitor. A gradient mobile phase of acidified water (0.25 mL phosphoric acid/L) changing to 100 ACN over 20 minutes (milk) or 40 minutes (kidney) was used.

Because of the low levels of TRR in milk and kidney, identification of imazapyr in milk and kidney extracts by TLC and HPLC was confirmed by GC/MS analysis of the same radioactive component in urine. The petitioner reported that imazapyr was the sole radioactive component identified in the Aqueous-2 fraction of milk and in the methanol:water fraction of kidney, and provided representative TLC and HPLC chromatograms and a mass spectrum.

Table 9. Distribution of total radioactive residues in milk and kidney from a lactating goat orally dosed with [^{14}C]imazapyr at 42.5 ppm in the diet for 7 days.

Fraction	% TRR	ppm	Characterization/Identification [a]
Milk (Day 7; TRR = 0.02 ppm)			
Hexane-1	11.29	<0.01	Not further analyzed (N/A).
Hexane-2	6.36	<0.01	N/A.
EtOAc	6.39	<0.01	N/A.
Aqueous-2	49.36	0.01	Imazapyr was identified by TLC and HPLC analysis (49.36% TRR, 0.01 ppm).
Nonextractable	26.60	0.01	N/A.
Kidney (TRR = 0.11 ppm)			
Chloroform	4.53	0.01	N/A.
Methanol:water	95.47	0.11	Imazapyr identified by TLC and HPLC analysis (95.47% TRR, 0.11 ppm).
Nonextractable	0.00	<0.01	N/A.

[a] Metabolites were identified/resolved by TLC and HPLC, and identification was confirmed by GC/MS analysis of the same component in goat urine.

Storage stability

All samples were stored frozen (~-15 °C) prior to extraction, and extracts were stored under refrigeration prior to analysis. The petitioner provided the dates of sample collection, and final analysis. Samples were stored for ≤6.4 months prior to final analysis. No additional storage stability data are required.

Conclusion

The qualitative nature of the residue in ruminants is adequately understood. Following oral administration of [6-pyridine-^{14}C]imazapyr to two goats at 17.7 ppm or 42.5 ppm (~190x or 460x the maximum theoretical dietary burden) in the diet for 7 days, the TRR (expressed as imazapyr equivalents) ranged from <0.01 ppm (nondetectable) to 0.02 ppm in milk and were 0.08 ppm and 0.11 ppm, respectively, in the kidneys of the low and high dose goats. The TRR in remaining tissues (fat, liver, and leg and loin muscle) were nondetectable (<0.05 ppm) and were not further characterized. The study sufficiently characterized and identified detectable residues in extracts of milk and kidney by TLC and HPLC. Imazapyr *per se* was the sole radioactive component identified, comprising ~50% of TRR in milk and ~95% of TRR in kidney.

Poultry (1995; MRID 43861505)

American Cyanamid submitted data depicting the metabolism of [6-pyridine-^{14}C]imazapyr in hens. The in-life and analytical portions of the study were conducted at American Cyanamid (Princeton, NJ). Gelatin dose capsules were prepared from [^{14}C]imazapyr (specific activity 43.41 µCi/mg, radiochemical purity 98.2%) to a final specific activity of 4.15 µCi/mg; [6-pyridine-^{13}C]imazapyr was included as a mass marker. Two groups of eight hens each were orally dosed with [^{14}C]imazapyr for 7 consecutive days; Group A at 1.98 ppm and Group B at 9.72 ppm. These feeding levels respectively represent ~50x and 240x the maximum theoretical dietary burden; see "Magnitude of the Residue in Meat, Milk, Poultry, and Eggs" section for calculation of the dietary burden for poultry. A third group of hens was used as a control and received gelatin capsules containing lactose only. The hens were orally dosed with gelatin capsules once daily in the morning.

During the testing period, the hens were fed Pennfield Layer Feed Crumbles 32000 and were allowed water *ad libitum*. Eggs were collected twice daily (in the a.m. prior to dosing and in the p.m.), and the daily samples were composited and refrigerated (1 to 5 °C). The petitioner provided sufficient information concerning daily feed intake, body weights, and egg production. Hens were sacrificed ~22 hours after the last dose. The entire liver and kidneys and representative samples of muscle, skin with adhering fat, and blood were collected, composited for each group, and frozen or refrigerated (blood) immediately. Egg and tissue samples were delivered on the day of or the next working day following collection to the Sample Preparation Laboratory where they were stored refrigerated (eggs) or frozen prior to analysis for residue characterization and identification.

Total radioactive residues (TRR)

Triplicate aliquots of homogenized tissues were combusted and radioassayed by liquid scintillation spectroscopy (LSS); egg samples were radioassayed directly by LSS. ^{14}C-Residues were nondetectable (<0.01 ppm) in eggs from days 1-7, liver, kidneys, muscle, and skin with adhering fat from hens dosed at 1.98 ppm and 9.72 ppm.

Samples of excreta were also collected to estimate the extent of excretion of the test substance. The petitioner provided data that indicated that ~90.5% and 91.7% of the applied dose was eliminated in the excreta of hens from Groups A and B, respectively.

Because ^{14}C-residues were below the limit of detection in all edible poultry commodities, the petitioner did not attempt further extraction or characterization/identification procedures. Imazapyr *per se* was identified in excreta by extraction and HPLC analysis.

Storage stability

All samples were stored refrigerated (eggs; -4 to 14 °C) or frozen (-26 to 4 °C) prior to analysis. Egg and tissue samples were prepared and analyzed within 2 weeks and 23 days,

respectively, of sampling. The petitioner provided the dates of sample collection and analysis. Because samples were stored for ≤1 month prior to final analysis, no additional storage stability data are required.

Conclusion

The qualitative nature of the residue in poultry is adequately understood. Following oral administration of [6-pyridine-^{14}C]imazapyr to two groups of hens at 1.98 ppm or 9.72 ppm (~50x and 240x the maximum theoretical dietary burden) in the diet for 7 days, the TRR were <0.01 ppm (nondetectable) in eggs, liver, kidneys, muscle, and skin with adhering fat. Because residues in poultry eggs and tissues of concern were nondetectable, no further analyses were attempted or are required. It is noted that imazapyr *per se* was the sole radioactive component identified in the excreta of treated hens.

Residue Analytical Methods

Proposed enforcement method (1995; MRID 43861506): The petitioner has proposed American Cyanamid Method M 2468, entitled "Imazapyr (CL 243,997): GC/MS Method for the Determination of CL 243,997 Residues in Corn Grain, Forage, and Fodder" for use as an enforcement method for corn commodities. For Method M 2468, residues are extracted from homogenized samples with acidified water:acetone. After blending, Celite is added to the extract, and the mixture is filtered and concentrated by rotary evaporation. The concentrated material is cleaned up by solid-phase extraction using methylene chloride to elute the residues. The resulting eluate is evaporated to dryness in a heated water bath. Residues are redissolved in methanol and trimethylphenylammonium hydroxide, evaporated to dryness, and reconstituted in methanol for GC/MS analysis using negative ion chemical ionization. The validated limit of quantitation (LOQ) is 0.05 ppm.

Data collection method: Samples of corn forage, silage, fodder, grain, meal and oil from the submitted field trials and processing studies were analyzed for residues of imazapyr per se using GC/MS Method M 2468 by Centre Analytical Laboratories (State College, PA). Concurrent recovery data were submitted for the commodities of field corn. Fifty-three untreated samples of field corn forage were fortified with imazapyr at 0.050-6.00 ppm, thirty-eight untreated samples of silage were fortified at 0.050 and 0.500 ppm, nineteen untreated samples each of grain and fodder and two untreated samples each of meal and oil were fortified at 0.050 ppm, and analyzed concurrently with the treated samples. The results of concurrent method analyses of fortified untreated samples are detailed in Table 10. Sample calculations and chromatograms were submitted.

Table 10. Concurrent method recoveries of imazapyr from fortified untreated samples of field corn forage, silage, grain, fodder, meal, and oil from the respective field trial and processing studies.

Commodity	Fortification Level (ppm)	Number of Samples	% Recovery [a]
Forage	0.050	27	73-120; 132
	0.500	1	94
	1.00	20	65, 69; 76-119; 126
	6.00	5	77-104
Silage	0.050	19	77-118
	0.500	19	64; 74-112
Grain	0.050	20 [b]	72-114
Fodder	0.050	19	75-117; 122, 124, 128, 132
Meal	0.050	2	86, 90
Oil	0.050	2	80, 99

[a] Recovery values outside the acceptable 70-120% range are listed separately.
[b] Includes one untreated grain sample from the processing study.

Radiovalidation of the proposed enforcement method: Method M 2468 was radiovalidated in conjunction with the plant metabolism study presented above. The data indicated that the method adequately recovered residues of imazapyr *per se* from samples of green plant and grain treated with [^{14}C]imazapyr.

Independent laboratory validation (ILV) of proposed enforcement method - (1995; MRID 43861506))

American Cyanamid submitted data pertaining to independent laboratory validation of the proposed enforcement method for the determination of residues of imazapyr in/on field corn forage, fodder, and grain. The method used was entitled "GC/MS Method for the Determination of CL 243,997 Residues in Corn Grain, Forage and Fodder" and is the same method used for residue data collection (Method M 2468 discussed above). The validation was conducted by Centre Analytical Laboratories (State College, PA). Some minor modifications to the method were made by the laboratory; changes involved higher solvent volumes for reconstitution of residues to avoid later dilutions and substituting the carrier gas, helium, with hydrogen.

The method validation consisted of two samples each of untreated, unfortified field corn grain, forage, and fodder, and two samples each of untreated corn grain, forage, and fodder fortified at 0.050, 0.100, and 1.00 ppm; these levels correspond to 1x, 2x, and 20x the

proposed tolerance level. The laboratory stated that analysis of a set of eight samples required approximately 8 hours. Representative chromatograms were submitted.

Recoveries of imazapyr from fortified field corn grain, forage, and fodder samples are presented in Table 11. Apparent residues of imazapyr were less than the LOQ (<0.05 ppm) in/on two samples each of unfortified field corn grain, forage, and fodder.

Table 11. Independent laboratory validation of Method M 2468 for determination of imazapyr *per se* in field corn grain, forage, and fodder (MRID 43861506).

Commodity	Fortification Level (ppm)	Imazapyr Percent Recovery [a]
Grain	0.050	119, 119
	0.100	93, 105
	1.00	93, 99
Forage	0.050	88, 97 [b]
	0.100	113, 119
	1.00	99, 102
Fodder	0.050	114, 114
	0.100	103, 110
	1.00	103, 105

[a] Recovery values represent a single fortified sample.
[b] Recoveries were corrected for control values.

Conclusion

The petitioner is proposing GC/MS Method M 2468 for use as an enforcement method for field corn commodities. This method was used for data collection in the submitted corn field trials and processing studies. Based on the concurrent method recovery data submitted with the field trials and processing studies, GC/MS Method M 2468 is adequate for collection of residue data for imazapyr *per se* from samples of field corn forage, silage, grain, fodder, meal, and oil. The method has successfully undergone independent laboratory validation (as per PR Notice 88-5) and has been radiovalidated using samples from the plant metabolism study.

EPA needs to conduct a petition method validation. CBTS will forward the method to EPA's Analytical Chemistry Laboratory for petition method validation.

The petitioner must submit an analytical reference standard for imazapyr and the material safety data sheet (MSDS) to the EPA repository. The petitioner should then submit the repository code number for the analytical reference standard to CBTS so that CBTS will know that the standard has been sent.

Multiresidue Methods

The petitioner stated that FDA multi-residue methods have been found to be inappropriate for analysis of other imidazolinone pesticides in food/feed commodities, and cited examples in which attempts to analyze samples for imidazolinone pesticides using Protocols A-C were unsuccessful. The petitioner concluded that FDA multi-residue methods did not exhibit sufficient detectability and sensitivity to other imidazolinone herbicides, and thus there is no reasonable expectation that these methods would prove to be useful for determining residues of imazapyr. CBTS concurs with this conclusion.

Storage Stability Data (1995; MRID 43861517)

Samples from the submitted corn field trials were promptly frozen after harvest, shipped via freezer truck to American Cyanamid where the samples were homogenized with dry ice, and shipped frozen to the analytical laboratory for analysis (Centre Analytical Laboratories, CAL, State College, PA). Samples were held at -25 to -5 °C at CAL until analysis. The storage intervals between harvest and analysis were 255-816 days (~8-27 months) for forage, 218-650 days (~7-21 months) for silage, 192-581 days (~6-19 months) for grain, and 192-581 days (~6-19 months) for fodder.

Samples from the abbreviated corn processing study were promptly frozen after harvest, shipped via freezer truck to American Cyanamid where the samples were homogenized with dry ice, and shipped frozen to CAL for analysis. Samples were held at -25 to -5 °C at CAL until analysis. Information pertaining to the date and location where the grain samples were processed was not included; therefore the exact intervals from processing to analysis could not be determined. The estimated storage interval between harvest and analysis was 674 days (~22 months) for corn oil and meal.

The petitioner submitted interim data depicting the stability of imazapyr residues in/on field corn commodities. Samples of field corn grain, forage, and fodder were fortified with imazapyr at 1.0 ppm. The fortified and unfortified samples were then stored frozen (-26 to -5 °C) and analyzed after 9 and 12 months of storage. The study protocol indicates that additional samples representing 18 and 24 months of freezer stability are also to be analyzed. Samples were analyzed using Method M 2468 described in the "Residues Analytical Methods" section. Apparent residues of imazapyr were below the LOQ (<0.05 ppm) in/on each of two unfortified samples of field corn grain, forage, and fodder. The interim results of the storage stability study are presented in Table 12.

Table 12. Storage stability and concurrent method recoveries (fresh fortification recovery) of imazapyr residues from samples of field corn grain, forage, and fodder fortified with imazapyr at 1.0 ppm and stored frozen at -26 to -5 °C.

Field Corn Commodity	Storage Period (Months)	Fresh Fortification Recovery (%)	Apparent Recovery in Stored Samples (%)	Corrected Recovery in Stored Samples (%)
Grain	9	92	81, 93	88, 101
	12	105	95, 104	90, 99
Forage	9	98	76, 79	78, 81
	12	89	94, 97	106, 109
Fodder	9	106	73, 79	69, 75
	12	91	83, 101	91, 111

Conclusion

Additional storage stability data are required as follows:

a. Data reflecting residue analyses at zero time for the on-going storage stability study are needed to establish the baseline residue levels present at the time samples were placed into storage.

b. The petitioner must submit the final report for the on-going storage stability study reflecting storage of field corn commodities for up to 24 months.

c. Information pertaining to the date and location where the grain samples were processed was not included. These data must be submitted so that the exact intervals from processing to analysis can be determined for corn oil and meal.

Magnitude of the Residue in Plants

Field corn forage, fodder, and grain (1995; MRID 43861518)

Nineteen field trials were conducted during the 1993 and 1994 growing seasons in IA(2), IL(2), IN(2), MI(2), MN, MO, NC, NE(2), OH(2), PA, SD, TX, and WI depicting the magnitude of imazapyr residues in/on field corn forage, stover (fodder), and grain. Field corn plants that were at the 4- to 5-leaf stage were treated with a single early postemergence broadcast application of either Arsenal® 2 ASU (2 lb ae/gal) or Arsenal® 20 WP at the rate of 0.024 lb ae/A (1.7x the maximum proposed single/seasonal application rate). Arsenal® 2 ASU was applied in 11 studies. Arsenal® 20 WP was applied in 8 studies. The application was made with a non-ionic surfactant and nitrogen fertilizer in 18-22 gal/A of water using ground equipment. Samples of field corn forage, fodder, and grain were collected at the following posttreatment intervals (PTIs): 0, 7, 30, 45, and 60 days for forage; and 103-149

33

days for grain and fodder. Samples of silage were additionally collected at 80- to 90-day PTIs. It is noted that the Livestock Feeds Table (Table II of PAG Subdivision O, issued 9/95) does not recognize silage as a RAC of field corn; these silage data are nevertheless presented in this document and may be useful for risk assessment purposes. One untreated control and one composite treated sample were collected from each test location. All samples were frozen immediately after collection and remained frozen until analyzed for imazapyr residues. Supporting storage stability data are addressed in the "Storage Stability" section of this document. Residues were determined by Method M 2468 described in the "Residue Analytical Methods" section of this document. The validated LOQ of the method was 0.05 ppm for all commodities of field corn.

Apparent residues of imazapyr were below the LOQ (<0.05 ppm) in/on the following untreated field corn RACs: forage (n=94), silage (n=38), fodder (n=19), and grain (n=19). The uncorrected residues of imazapyr in/on treated samples are presented in Table 13.

Table 13. Residues of imazapyr in/on field corn RACs following a single early postemergence broadcast application of either Arsenal® 2 ASU (2 lb ae/gal) or a 20% WP formulation of imazapyr at 0.024 lb ae/A (1.7x the maximum proposed single/seasonal application rate).

Formulation	PTI [a] (days)	Trial Sites	Uncorrected Residues of Imazapyr (ppm) [b]
Arsenal® 2 ASU (2 lb ae/gal)	**Forage**		
	0	IA, IL, IN, MI, MO, NC, NE, OH, PA, SD, and WI	1.59-5.88 (n=11)
	7-8	IA, IL, IN, MI, MO, NC, NE, OH, PA, SD, and WI	<0.05-0.171 (n=11)
	29-31	IA, IL, IN, MI, MO, NC, NE, OH, PA, SD, and WI	<0.05 (n=11)
	43-46	IA, IL, MI, MO, NC, NE, OH, PA, SD, and WI	<0.05 (n=10)
	59-62	IA, IL, IN, MI, MO, NC, NE, OH, PA, SD, and WI	<0.05 (n=11)
	Silage		
	80-82	IA, IL, IN, MI, MO, NC, NE, OH, PA, SD, and WI	<0.05 (n=11)
	90-105	IA, IL, IN, MI, MO, NC, NE, OH, PA, SD, and WI	<0.05 (n=11)
	Grain		
	103-149	IA, IL, IN, MI, MO, NC, NE, OH, PA, SD, and WI	<0.05 (n=11)
	Fodder		
	103-149	IA, IL, IN, MI, MO, NC, NE, OH, PA, SD, and WI	<0.05 (n=11)
20% WP formulation	**Forage**		
	0	IA, IL, IN, MI, MN, NE, OH, and TX	1.68-5.43 (n=8)
	6-8	IA, IL, IN, MI, MN, NE, OH, and TX	<0.05-0.127 (n=8)
	30-32	IA, IL, IN, MI, MN, NE, OH, and TX	<0.05 (n=8)
	44-48	IA, IL, IN, MI, MN, NE, OH, and TX	<0.05 (n=8)
	60-61	IA, IL, IN, MI, MN, NE, OH, and TX	<0.05 (n=8)
	Silage		
	79-81	IA, IL, IN, MI, MN, NE, OH, and TX	<0.05 (n=8)
	89-98	IA, IL, IN, MI, MN, NE, OH, and TX	<0.05 (n=8)
	Grain		
	110-146	IA, IL, IN, MI, MN, NE, OH, and TX	<0.05 (n=8)
	Fodder		
	110-146	IA, IL, IN, MI, MN, NE, OH, and TX	<0.05 (n=8)

[a] Posttreatment interval.
[b] The number (n) of samples represented by the range is listed in parentheses.

35

Conclusion

The geographic representation and number of conducted field trials are adequate for establishment of pesticide residue tolerances. A total of 19 trials reflecting the proposed maximum use pattern was conducted in IA, IL, IN, MI, MN, MO, NC, NE, OH, PA, SD, TX, and WI. These test states encompass Regions 1, 2, 5, 6, and 7.

The submitted residue data for field corn indicate that residues of imazapyr *per se* were below the LOQ (<0.05 ppm) in/on field corn forage samples harvested 29-62 days and in/on grain and fodder samples harvested 103-149 days following a single early postemergence broadcast application of either Arsenal® 2 ASU (2 lb ae/gal) or Arsenal® 20 WP at the rate of 0.024 lb ae/A (1.7x the maximum proposed single/seasonal application rate). These field trial data indicate that residues of imazapyr in/on field corn forage, fodder, and grain resulting from application of Arsenal® 2 ASU or Arsenal® 20 WP will not exceed the proposed tolerances of 0.05 ppm, the limit of quantitation (LOQ) of the proposed enforcement method.

Refer to the Product Chemistry section of this review for additional issues on the formulation proposed for use.

The petitioner is requested to submit a revised Section F to separately propose tolerances for the correct field corn RACs as follows:

corn, field, stover (fodder).....0.05 ppm
corn, field, forage.....0.05 ppm
corn, field, grain.....0.05 ppm

The proposed use would allow use of a nonionic surfactant or crop oil. All of the residue studies included nonionic surfactant. Since no residue data have been submitted in which crop oil was applied, either a revised Section B/label must be submitted which deletes references to crop oil or additional residue data in which crop oil is included must be submitted.

No residue data for field corn aspirated grain fractions (grain dust) were submitted with this petition. Because the proposed use is an early season use (before corn is 12 inches in height) and residues of imazapyr were below the LOQ in/on field corn grain following treatment at 1.7x, no residue data on aspirated grain fractions are required for the purposes of this petition.

Magnitude of the Residue in Processed Food/Feed

Field corn grain (1995; MRID 43861518)

An abbreviated processing study was conducted using field corn grain samples harvested from a NE field trial following a single broadcast postemergence application of a 2 lb ae/gal

ammonium salt formulation with urea at 0.24 lb ae/A (17x the maximum proposed single/seasonal application rate). At the analytical laboratory (CAL, State College, PA) the harvested grain samples were extracted twice with hexane in a blender. The hexane extracts were evaporated to yield a corn oil sample, and the remaining residue after extraction was designated corn meal. Residues in/on treated and untreated field corn grain and its processed commodities were determined using Method M-2468. The results of the abbreviated processing study are presented in Table 14. Apparent residues of imazapyr were below the LOQ (<0.05 ppm) in/on one sample of untreated field corn grain and in each of the duplicate samples of meal and oil processed from untreated grain.

Table 14. Residues of imazapyr in meal and oil following an abbreviated processing study using field corn grain samples that were treated at 17x.

Substrate	Uncorrected Imazapyr Residues (ppm) [a]	Concentration/Reduction Factor
Grain	0.0995	--
Meal	0.113, 0.118	1.1x, 1.2x
Oil	<0.05, <0.05	<0.5x

Conclusion

The abbreviated field corn processing study indicates that residues of imazapyr did not concentrate in oil but concentrated slightly in meal (1.1-1.2x) processed/extracted from field corn grain bearing detectable residues and treated at 17x the maximum proposed single/seasonal application rate. CBTS recognizes that obtaining samples with significant residues with an early season herbicide is difficult, and considers the submitted abbreviated processing study to be adequate in demonstrating that residues of imazapyr will not significantly concentrate in the processed commodities of field corn at the proposed use pattern. For the purposes of this petition request, no Section 409 tolerances are required for imazapyr residues in the processed commodities of field corn.

Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

No studies pertaining to magnitude of the residue in meat, milk, poultry, and eggs were submitted with this petition. Since several raw agricultural and processed commodities of field corn may be utilized as animal feed items, the maximum theoretical dietary burdens of imazapyr to beef and dairy cattle were calculated. The dietary burdens for beef and dairy cattle are presented in Table 15, and are estimated to be 0.084 ppm and 0.092 ppm, respectively. For poultry, the estimated dietary burden is 0.04 ppm (based on 80% corn grain in the diet and the 0.05 ppm proposed tolerance).

Table 15. Calculation of maximum theoretical dietary burden of imazapyr to beef and dairy cattle.

Field Corn Feed Item	% Dry Matter	Estimated Tolerance (ppm)	Beef Cattle		Dairy Cattle	
			% in Diet	Dietary Burden (ppm)	% in Diet	Dietary Burden (ppm)
Grain	88	0.05	60	0.034	40	0.023
Forage	40	0.05	40	0.050	50	0.063
Fodder	83	0.05	--	--	10	0.006
Total			**100**	**0.084**	**100**	**0.092**

Conclusion

In consideration of the exaggerated feeding levels utilized in the animal metabolism studies which resulted in nondetectable radioactive residues (<0.01 or <0.05 ppm depending on the matrix) in goat muscle, goat liver, and goat fat, and all poultry matrices along with small amounts of radioactive residues in milk and goat kidney, there is no reasonable expectation that finite imazapyr residues will occur in meat, milk, poultry, and eggs (Category 3 of 40 CFR §180.6) as a result of the proposed use pattern on field corn. Residues of imazapyr were also below the validated LOQ (<0.05 ppm) in/on field corn forage, grain, and fodder following application of imazapyr at 1.7x. Therefore, animal feeding studies or tolerances for meat, milk, poultry, and eggs are not required for purposes of this petition request. However, CBTS reserves the right to request animal feeding studies if additional uses on crops with livestock feed items are proposed for registration in the future.

Confined Rotational Crop Study (1994; MRID 43861502)

American Cyanamid submitted data pertaining to residues of [^{14}C]imazapyr in rotational crops. The field phase of this study was conducted by AASI (Lucama, NC), and the analytical phase was conducted by American Cyanamid (Princeton, NJ). The radiolabelled test substance, [6-pyridine-^{14}C]imazapyr (specific activity 43.6 µCi/mg, radiochemical purity 98.6%), was dissolved in acetone to a final specific activity of 20.8 µCi/mg; [6-pyridine-^{13}C]imazapyr was added as a mass marker. The radioactive test substance was formulated with nonlabelled imazapyr, water, and a non-ionic spreader, and applied as an ammonium salt formulation to IMI-corn™ plants at the 6-leaf stage as a single broadcast foliar application at 0.025 lb ae/A (1.8x the proposed maximum use rate) 22 days after planting. Applications were made in 51.4 gal/A using ground equipment. The test plots contained sandy loam soil (55% sand, 27% silt, 18% clay, 1.7% organic matter, pH 5.9, cation exchange capacity 8.6 meq/100 g).

Field corn plants were harvested at maturity (86 days after treatment; DAT) by cutting at the soil line. The test plots remained fallow until rotational crops were planted. Subplots of the treated and control plots were planted with winter wheat at 120 DAT, with radishes, lettuce, and soybeans at 271 DAT, and with radishes and lettuce at 420 DAT. Immature and mature

matrices of each rotational crop were harvested at the intervals listed in Table 16. On collection, radishes were separated into roots and tops, mature wheat was separated into straw and heads, and soybeans were separated into straw and pods. Samples were frozen immediately after harvest and were stored at ≤-2 °C for 1-10 days, after which they were shipped frozen by overnight delivery to the analytical laboratory.

Total radioactive residue (TRR)

At the analytical laboratory, wheat grain was separated from chaff and soybean seeds were separated from pods. Samples were ground frozen with dry ice and stored at ~-20 °C until analysis. All analyses were completed within 9 to 38 days of sampling.
Triplicate subsamples of each rotational crop commodity were combusted and radioassayed by LSS. The limit of detection for the radioassay was 0.002 ppm for all crop and soil samples. Sample calculations were submitted. The TRR in rotational crops are presented in Table 16. Radioactive residues in all treated and control rotational crop matrices were <0.002 ppm.

Table 16. Total radioactive residues (TRR) in rotational crops planted following a field corn crop treated with a single broadcast application of [^{14}C]imazapyr at 0.025 lb ae/A (1.8x).

Commodity	Harvest Interval (days) [a]	TRR (expressed as ppm [^{14}C]imazapyr acid equivalents)		
		120 DAT [b]	271 DAT	420 DAT
Radish tops (immature)	35, 24 [c]	--	<0.002	<0.002
Radish roots (immature)	35, 24	--	<0.002	<0.002
Radish tops (mature)	50, 41	--	<0.002	<0.002
Radish roots (mature)	50, 41	--	<0.002	<0.002
Lettuce (immature)	45	--	<0.002	<0.002
Lettuce (mature)	57	--	<0.002	<0.002
Wheat forage	158	<0.002	--	--
Wheat straw	217	<0.002	--	--
Wheat grain	217	<0.002	--	--
Soybean forage	85	--	<0.002	--
Soybean hay/hulls	213	--	<0.002	--
Soybean seed	213	--	<0.002	--

[a] Interval between planting and harvest of rotational crop.
[b] DAT = Days after treatment (interval between treatment of the primary crop and planting of the rotational crop).
[c] First number is harvest interval for 271 DAT samples and the second number is the harvest interval for 420 DAT samples.

Storage stability

All samples from the confined rotational crop study were stored frozen for 9-38 days prior to analysis. The petitioner provided the dates of sample collection and final analysis. Because samples were stored for <1.3 months prior to analysis, no storage stability data are required.

Conclusion

The submitted confined rotational crop study is adequate. ^{14}C-Residues were <0.002 ppm in the RACs of wheat from a 4-month plant back interval (PBI) and in the RACs of radishes, lettuce, and soybeans from a 9-month PBI. The proposed label specifies rotational crop PBIs of 4 months for rye and wheat, 8.5 months for field corn, and ≥9.5 months for all other crops. Based on the submitted data, no PBIs longer than 9 months are required. No limited or extensive field rotational crop studies or rotational crop tolerances are required for purposes of this petition. However, a revised Section B/label must be submitted which specifies rotational crop plant back intervals of 4 months for small grains and 9 months for all other crops unless the petitioner states that longer intervals are needed due to phytotoxicity concerns.

MASTER RECORD IDENTIFICATION NUMBERS

Citations for the MRID documents referred to in this review are presented below.

43861502 Zulalian, J. (1995) Imazapyr (CL 243,997): Metabolism of Carbon-14 Labeled CL 243,997 Using Radishes, Soybeans, Lettuce and Winter Wheat as Rotational Crops: Lab Project Number: MET95-003: M93P997NC2: 0462. Unpublished study prepared by American Cyanamid Co. 216 p.

43861503 Zulalian, J. (1995) CL 243,997: Metabolism of Carbon-14 Labeled CL 243,997 in Imidazolinone-Resistant Corn Under Field Conditions: Lab Project Number: MET 95-002: M93P997NC1: 0462. Unpublished study prepared by American Agricultural Services,Inc. 347 p.

43861504 Zdybak, J. (1992) CL 243,997: Carbon-14 Labeled CL 243,997-Derived Residues in Blood, Milk and Edible Tissues of Lactating Goats: Lab Project Number: PD-M 29-34: RPT0025: 89020. Unpublished study prepared by Xenobiotic Labs, Inc. and Biological Test Center. 126 p.

43861505 Tsalta, C. (1995) CL 243,997: Metabolic Fate of (carbon 14)-CL 243,997 in Tissues and Eggs of the Laying Hen: Lab Project Number: MET 95-007: M94A997PT1. Unpublished study prepared by American Cyanamid Co. 170 p.

40

43861506 Fletcher, J. (1995) CL 243,997: Independent Laboratory Validation of GC/MS Method M 2468 for the Determination of CL 243,997 Residues in Corn Grain, Forage and Fodder: Lab Project Number: RES 95-080: M-2468: AR94PT02. Unpublished study prepared by Centre Analytical Labs, Inc. 68 p.

43861508 Piznik, M. (1995) Certification of Limits and Analytical Methods: (AC 513,996): Lab Project Number: F-1325:95FAI-0193-01. Unpublished study prepared by American Cyanamid Co. 48 p.

43861509 Ong, J. (1995) Imazethapyr/Imazapyr 70 DG Herbicide: Physical and Chemical Characteristics: Lab Project Number: F-1341:95PIF-0193-09. Unpublished study prepared by American Cyanamid Co. 22 p.

43861516 Fletcher, J.; Khunachak, A. (1995) CL 243,997: Extractability and Accountability of CL 243,997 Residues in Corn Grain and Plant: Lab Project Number: RES 95-081: AR95PT01. Unpublished study prepared by American Cyanamid Co. 34 p.

43861517 Fletcher, J.; Zheng, S. (1995) CL 243,997: Freezer Storage Stability of Residues of CL 243,997 in Corn Commodities (Grain, Forage, and Fodder): Lab Project Number: RES 95-163: AR94PT01:007-35. Unpublished study prepared by Centre Analytical Labs, Inc. 52 p.

43861518 Mahl, T. (1995) CL 243,997 (Imazapyr): Crop Residue Study with AC 243,997 on Field Corn: Lab Project Number: RED 95-083: RES95-085: RES 95-086. Unpublished study prepared by Agsearch Co.; Centre Analytical Labs, Inc.; and Agvise Labs. 1702 p.

41