



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

**MEMORANDUM**

Date: 09-DEC-2005

Subject: Propazine. Revised Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision Document (TRED) and a Proposal To Reinstate Food/Feed Use on Grain Sorghum (PP#7F4837).

PP#: 7F4837  
DP Number: 323273  
Chemical Class: Chloro Triazine Herbicide  
40 CFR §180: 243  
PC Code: 080808

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This document was originally prepared under contract by Dynamac Corporation (20440 Century Boulevard, Suite 100; Germantown, MD 20874; submitted 07/13/2005). The document has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies. This document supercedes "Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision Document (TRED) and a Proposal To Reinstate Food/Feed Use on Grain Sorghum (PP#7F4837)," D308537, dated 8/31/05.

## Executive Summary

Propazine (6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine) is a member of the chloro triazine class of herbicides. Other members of this pesticide class include atrazine, cyanazine, and simazine. Propazine is a selective herbicide that can be applied before planting, at planting, and after crop emergence for the preemergence control of annual broadleaf weeds. Currently, the only registered uses are for weed control of ornamental plants grown in containers under greenhouse conditions. There are presently no registered food/feed uses of propazine.

Propazine was previously registered for use on sorghum. The 5/19/87 Propazine Residue Chemistry Chapter along with the 12/88 Propazine Reregistration Standard (Guidance Document) identified several data deficiencies for the reregistration of propazine. Ciba-Geigy, which was then the basic manufacturer of propazine, elected to cancel its registrations of propazine. Another petitioner, Griffin Corporation, is now supporting the previously cancelled uses of propazine on grain sorghum and has submitted residue chemistry data which have been evaluated by HED and summarized in this Chapter as a "new active ingredient."

The use of propazine on grain sorghum will be supported at a maximum single application rate of 1.2 lb ai/A with a preharvest interval (PHI) of 60 days. Following HED review of the proposed use directions and the submitted residue field trial data, the following label amendments are required for sorghum: (i) a maximum of one preemergence application per growing season; (ii) a maximum seasonal rate of 1.2 lb ai/A; (iii) a PHI of 70 days for sorghum forage; and (iv) a PHI of 90 days for sorghum grain and stover. In addition, the following label restrictions should be added for rotational crops: (i) do not rotate to leafy vegetables; (ii) do not rotate to root crops or cereals (small grains) at less than a 120-day plantback interval (PBI); (iii) rotation to all other crops should be restricted to a 12-month PBI.

The EPA's Office of Pesticide Programs (OPP) has determined that atrazine, propazine, simazine, and degradants, diaminochlorotriazine (DACT), desisopropyl *s*-atrazine (DIA), and desethyl *s*-atrazine (DEA) should be considered as a Common Mechanism Group due to their ability to suppress the pituitary LH surge and produce consequent effects on reproductive function and reproductive development. For purposes of a cumulative risk assessment and as part of the tolerance reassessment process for these pesticides, they should be considered as a Common Mechanism Group (OPP Office Director Memo on Grouping Triazines, 3/31/2002).

Tolerances are currently established [40 CFR §180.243] for residues of propazine *per se* in/on sorghum commodities (forage, grain, stover, and sweet sorghum) at 0.25 ppm. There are no tolerances established for propazine residues in livestock commodities. The Federal Register (Vol. 70, No. 119, June 22, 2005) has recently announced that Griffin Corporation has filed a petition, PP#7F4837, to amend 40 CFR §180.243, by establishing tolerances for residues of propazine and its two chlorometabolites: 2-amino-4-chloro, 6-isopropylamino-*s*-triazine (G-30033) and 2,4-diamino-6-chloro-*s*-triazine (G-28273) in/on sorghum stover, forage, and grain at 0.25 ppm.

For the purpose of consistency in nomenclature, the chlorometabolites that are included in the proposed tolerance expression will be referred to in this Residue Chapter by their company code

designation. G-30033 will be used for 2-amino-4-chloro, 6-isopropylamino-s-triazine; it is noted that some study submissions also refer to the metabolite G-30033 as desethyl atrazine (DEA) or atrazine desethyl. G-28273 will be used for 2,4-diamino-6-chloro-s-triazine; some study submissions also refer to the metabolite G-28273 as diamino atrazine (DAA) or atrazine desethyl-desisopropyl.

The nature of propazine residues in sorghum is adequately understood. Total radioactive residues (TRR) were 0.126, 0.133 and 2.344 ppm in/on sorghum forage, grain and fodder (stover), respectively, following one preemergence application of [<sup>14</sup>C]propazine at 1.96 lb ai/A (1.6x the proposed single application rate). The parent propazine was identified at a range of <0.001-0.011 ppm (0.5-0.8% TRR) in sorghum matrices. The chlorometabolites G-30033 and G-28273 were not detected in grain but were identified as minor residue components in forage (8.7% TRR, 0.011 ppm) and stover (3.9% TRR, <0.091 ppm). Several free hydroxymetabolites (propazine 2-hydroxy; atrazine des-ethyl 2-hydroxy; and ammeline) were identified at slightly higher combined levels in forage (22.2% TRR, 0.028 ppm), grain (12.6% TRR, <0.016 ppm), and stover (8.2% TRR, <0.193 ppm).

The submitted sorghum metabolism study indicates that propazine is rapidly and extensively metabolized in sorghum via: (i) N-dealkylation; (ii) replacement of chlorine by hydroxy; and (iii) glutathione conjugation. The results suggest that the metabolism of propazine in sorghum is similar to published and available plant metabolism studies for other triazine herbicides. Consistent with the HED Metabolism Assessment Review Committee (MARC) decision memoranda on atrazine (PC Code: 080803) dated 11/15/2000 (D270177) and 2/10/2003 (D288715), the residues of concern in plants for tolerance reassessment are the parent plus the chlorometabolites G-30033 and G-28273.

The nature of propazine residues in ruminants is understood. In a goat metabolism study where [<sup>14</sup>C]propazine was administered orally to a lactating goat at 9.9 ppm (~35x the estimated dietary burden of 0.29 ppm) in the diet for seven consecutive days, TRR were 0.080-0.238 ppm in milk, 1.123 ppm in liver, 1.041 ppm in kidney, 0.209 ppm in muscle, and 0.160 ppm in fat. The parent propazine was not detected in goat milk or tissues. The chlorometabolite G-28273 was the principal residue identified in milk (63.4% TRR, 0.141 ppm), fat (50.4% TRR, 0.080 ppm), muscle (26.1% TRR, 0.054 ppm), and liver (2.7% TRR, 0.031 ppm). The metabolite G-30033 was identified in milk (9.4% TRR, 0.021 ppm) but not in tissues. The remaining radioactivity in goat milk and tissues was characterized to be comprised of up to six unknown metabolites. Although each unknown accounted for <7% TRR in milk, several unknowns were present at significant levels in goat tissues. None of these unknown residues co-chromatographed with the 17 reference standards including standards of known chloro- and hydroxy-metabolites of triazine herbicides. When the study is evaluated according to OPPTS GLN 860.1300, the goat metabolism data are classified as scientifically unacceptable because of insufficient characterization of radioactive residues in goat matrices particularly in kidney, liver, and muscle. However, the Memorandum of Understanding between HED and Griffin Corporation for Propazine (see 1/11/96 memo of M. Metzger) stated that if the available goat metabolism studies adequately and separately determine residues of each chlorometabolite, each hydroxymetabolite, and TRR for each commodity for which data are required, then further identification work for the metabolism study in which parent propazine was fed should not be required.

Another goat metabolism study was performed using a radiolabeled hydroxymetabolite of propazine as the test substance. TRR were 0.025-0.029 ppm in milk, 0.006 ppm in muscle, 0.001 ppm in fat (renal and omental), 0.110 ppm in kidney, and 0.036 ppm in liver taken/collected from a lactating goat administered orally with [U-<sup>14</sup>C]2-hydroxypropazine at 10.9 ppm in the diet for three consecutive days. Residue characterization was not conducted in muscle and fat tissues because of low radioactivity (<0.010 ppm). The test substance, 2-hydroxypropazine, was the major residue identified in all matrices accounting for 63.5% TRR (0.069 ppm) in kidney, 77.2% TRR (0.028 ppm) in liver, and 65.0-69.4% TRR (0.017-0.020 ppm) in milk. The only other metabolite identified was desisopropyl hydroxypropazine, which was detected in minor amounts in all matrices: 2.9% TRR (0.003 ppm) in kidney, 3.6% TRR (0.001 ppm) in liver and 8.2-8.5% TRR (0.002 ppm) in milk.

The nature of propazine residues in poultry is understood. TRR were 0.019-0.448 ppm in whole egg, 0.010-0.669 ppm in egg yolk, 0.024-0.327 ppm in egg white, 1.196 ppm in liver, 0.961 ppm in composite muscle, and 0.172 ppm in composite fat taken/collected from laying hens orally administered with [<sup>14</sup>C]propazine at 20.3 ppm (~102x the dietary burden MTDB of 0.2 ppm) in the diet for 14 consecutive days. The parent propazine was not identified in poultry eggs or tissues. The only residue component identified was G-28273 which was quantitated in poultry matrices as follows: liver (4.3% TRR, 0.171 ppm), muscle (18.3% TRR, 0.212 ppm), fat (48.1% TRR, 0.083 ppm), egg yolk (35.3% TRR, 0.236 ppm), and egg white (51.9% TRR, 0.170 ppm). Seven unknown compounds were detected in select matrices some of which were observed at >10% TRR. The petitioner characterized these unknown metabolites to be relatively more polar than propazine based on the chromatographic profiles.

Consistent with the HED MARC decision memoranda on atrazine (PC Code: 080803) dated 11/15/2000 (D270177) and 2/10/2003 (D288715), the residues of concern in livestock for tolerance reassessment are the parent plus the chlorometabolites G-30033 and G-28273. The results suggest a Category 3 situation with regard to the need for livestock commodity tolerances as per 40 CFR §180.6(a)(3). There is no expectation of finite residues of propazine and its chlorometabolites in livestock commodities as a result of the proposed use on sorghum. Thus, livestock feeding studies are not needed, and tolerances need not be established for meat, milk, poultry, and eggs.

An adequate enforcement method for plants is currently not available and is required for propazine and its two chlorometabolites (G-30033 and G-28273). Currently, the Pesticide Analytical Manual (PAM) Vol. II lists Method IV (AG-281) for the determination of only the chlorometabolite G-28273 in crops and livestock tissues. Samples of sorghum forage, grain, and stover, that were collected from the sorghum field trials, were analyzed for residues of propazine and its chlorometabolites by Corning Hazelton analytical method CHW 6641-106 (Method I, Rev. 1). The method determines residues of propazine and G-30033 by gas chromatography/mass-selective detector (GC/MSD), while residues of G-28273 are determined by GC/nitrogen-phosphorus detector (NPD). The limit of quantitation (LOQ) for each analyte in all sorghum matrices is 0.05 ppm. Overall, the method is adequate for data collection based on acceptable concurrent method recovery data. HED is recommending that the data-collection method (CHW 6641-106, Method I, Rev. 1) be subjected to an independent laboratory validation (ILV) as per GLN 860.1340. If the ILV is successful, then the method will be subjected to

further validation by Agency chemists at Analytical Chemistry Laboratory (ACL)/Biological and Economics Analysis Division (BEAD). At this time, livestock enforcement methods are not required for the reinstatement of propazine uses on sorghum since there is no expectation of finite secondary residues in livestock commodities.

According to FDA's PAM Volume I, Appendix II, propazine is completely recovered using Section 302 (Protocol D), partially recovered using Section 303 (Protocol E), and not recovered using Section 304 (Protocol F). There are no multiresidue methods recovery data for the chlorometabolites G-30033 and G-28273, and these data are required. To fulfill this requirement, the petitioner is required to follow the directions for the protocols found in PAM Vol. I, Appendix II under paragraph (d)(1) of OPPTS GLN 860.1360, starting with the decision tree for multiresidue methods testing and the accompanying guidance found in the suggestions for producing quality data.

No storage stability data were submitted to support the sorghum field trials and limited field rotational crop trials. However, the petitioner has indicated that a storage stability study has been initiated and will be submitted in a separate report upon completion. Samples from the sorghum field trials were stored frozen for 25.7-26.6 months prior to residue analysis. The maximum frozen storage intervals of samples from the limited field rotational crop trials were 129 days (4.2 months) for lettuce, 79 days (2.6 months) for mustard leaves, 100 days (3.3 months) for radish tops and roots, 79 days (2.6 months) for turnip tops and roots, 141 days (4.6 months) for wheat forage, 125 days (4.1 months) for wheat hay, and 89 days (2.9 months) for wheat grain and straw. The submitted plant and livestock metabolism studies are supported by adequate storage stability data. The chromatographic profiles of residues appeared stable following re-analysis of select matrices.

Pending submission of supporting storage stability data and label revision, the proposed use of propazine is supported by adequate residue data. Following a single preemergence broadcast application of a representative FIC formulation of propazine at 1.47-2.43 lb ai/A (1.2-2.0x the proposed single application rate), the results of the sorghum field trials indicate the following: In **sorghum forage** harvested at a PHI range of 69-117 days, residues of propazine and G-30033 were each less than the LOQ (<0.05 ppm) in/on 26 treated samples. Residues of G-28273 ranged 0.050-0.087 ppm in/on four treated forage samples but were <0.05 ppm in/on 22 treated samples. In **sorghum grain and stover** harvested at a PHI range of 86-152 days, residues of propazine, G-30033, and G-28273 were each <0.05 ppm in/on 26 treated samples. These data support the proposed tolerance of 0.25 ppm each for the combined residues of propazine and its two chlorometabolites (G-30033 and G-28273) in/on sorghum stover, forage, and grain. Residue data on the aspirated grain fractions of sorghum are not required since the proposed use of propazine on grain sorghum is for preemergence or preplant application.

A sorghum processing study is not required at this time but may be needed at a later date.

The nature of propazine residues in rotational crops is adequately understood. The study was initiated by applying [<sup>14</sup>C]propazine to bare sandy loam soil at 2.39 lb ai/A (~2.0x the proposed single application rate for sorghum). Lettuce, turnip, and spring wheat were then planted in the treated soil as rotational crops at PBIs of 29, 120, and 365 days. At the 29-PBI, TRR were 1.298

ppm for wheat forage, 5.787 ppm for wheat straw, and 1.680 ppm for wheat grain heads. At the 120-day PBI, TRR were 0.103 ppm for lettuce, 0.179 ppm for turnip tops, 0.057 ppm for turnip roots, 0.355 ppm for wheat forage, 1.987 ppm for wheat straw, and 0.928 ppm for wheat grain heads. At the 365-day PBI, TRR were 0.209 ppm for lettuce, 0.450 ppm for wheat forage, 1.028 ppm for wheat straw, and 0.245 ppm for wheat grain heads. Propazine was identified (<1-43% TRR) in all rotational crop matrices from all PBIs, but appears to decrease with longer PBIs. In addition to the parent, the following metabolites were identified: atrazine des-ethyl (G-30033); propazine 2-hydroxy (GS-11526); and atrazine des-ethyl 2-hydroxy (GS-17794). Quantitative data pertaining to the level of metabolite identification is presented in the topical section for OPPTS 860.1850. The primary metabolic products in rotational crops are similar to those found in the sorghum metabolism study. The propazine residues of concern in rotational crops for the purposes of tolerance establishment and risk assessment are consistent with the HED MARC decision memoranda on atrazine (PC Code: 080803) dated 11/15/2000 (D270177) and 2/10/2003 (D288715), the residues of concern in plants for tolerance reassessment are the parent plus the chlorometabolites G-30033 and G

Two limited field rotational crop trials with propazine were conducted in NC and TX. At each site, a 4 lb/gal flowable concentrate formulation of propazine was applied as a preemergence ground spray to grain sorghum, the primary crop, at a nominal rate of 1.2 lb ai/A (1.0x the proposed single application rate). The primary crop was removed (by cutting) from the plots approximately 90 days after the test substance application. The following rotational crops were then planted at each field site: radish or turnip (a root vegetable), lettuce or mustard (a leafy vegetable), and winter or spring wheat (a cereal grain). The PBIs used in the study were 94, 127, and 242/280 days for the NC field site and 97, 120, 195, and 239 days for the TX field site.

The results of the NC trial indicate that residues of propazine, G-30033, and G-28273 were each below the LOQ of 0.0500 ppm in/on all samples of rotational crop commodities (mustard leaves, turnip tops/roots, and spring/winter wheat forage, hay, straw, and grain) at all PBIs (94, 127, and 242/280 days). The results of the TX trial indicate that residues of propazine, G-30033, and G-28273 were each below the LOQ of 0.0500 ppm in/on the following rotational crop commodities and PBIs: (i) lettuce leaves at a 97-day PBI; (ii) radish root at PBIs of 97 and 239 days; (iii) wheat forage at PBIs of 120 and 195 days; (iv) wheat hay, straw, and grain at PBIs of 97, 120, and 195 days. A few rotational crop commodities from the TX trial showed quantifiable residues including: (i) lettuce leaves at the 239-day PBI (propazine was detected at 0.0505-0.0510 ppm, G-30033 at 0.137-0.139 ppm, and G-28273 at 0.139 ppm); (ii) radish tops at the 97-day PBI (propazine was detected at 0.051-0.052 ppm); and (iii) wheat forage at the 97-day PBI (G-30033 was detected at 0.102-0.107 ppm).

Analytical standards for propazine are currently available at the National Pesticide Standards Repository. However, standards for the chlorometabolites G-30033 and G-28273 are not available and are required.

## Regulatory Recommendations and Residue Chemistry Deficiencies

HED has examined the residue chemistry database for propazine and identified the residue chemistry deficiencies listed below before the use of propazine on grain sorghum can be reinstated.

- For consistency of the proposed use pattern with the submitted field trial data, the following label amendments are required for sorghum: (i) a maximum of one preemergence application per growing season; (ii) a maximum seasonal rate of 1.2 lb ai/A; (iii) a PHI of 70 days for sorghum forage; and (iv) a PHI of 90 days for sorghum grain and stover.
- A plant enforcement method is required. HED is recommending that the data-collection method (CHW 6641-106, Method 1, Rev. 1) be subjected to an ILV as per GLN 860.1340. If the ILV is successful, the method will be further validated by Agency chemists at ACL/BEAD.
- There are no multiresidue methods recovery data for the chlorometabolites G-30033 and G-28273, and these data are required. To fulfill this requirement, the petitioner is required to follow the directions for the protocols found in PAM Vol. I, Appendix II under paragraph (d)(1) of OPPTS GLN 860.1360, starting with the decision tree for multiresidue methods testing and the accompanying guidance found in the suggestions for producing quality data.
- The results of an ongoing storage stability study need to be submitted upon completion to support the storage conditions and intervals of samples collected from the sorghum field trials and limited field rotational crop trials.
- Rotational crops

### Lettuce (leafy crop):

Lettuce showed non-detectable residues or residues below the LOQ (0.05 ppm) at the NC study for parent plus the chloro metabolites at all PBIs (94, 127, and 280 days). TX study showed that residues were below the LOQ at 97 days but lettuce leaves at the 239-day PBI showed that propazine was detected at 0.0505-0.0510 ppm, G-30033 at 0.137-0.139 ppm, and G-28273 at 0.139 ppm. It is clear from these data that the label should specify that there should be no rotation to any leafy vegetable.

### Radish Tops (root vegetable) and wheat (cereal):

The NC study showed non-detectable residues or residues below the LOQ (0.05 ppm) at the NC study for parent plus the chloro metabolites at all PBIs (94, 127, and 280 days) for the root and cereal crops. The TX study showed that residues were below the LOQ for the root and cereal crops except for two sites that showed the following: radish tops at the 97-day PBI (propazine was detected at 0.051-0.052 ppm); and wheat forage at the 97-

day PBI (G-30033 was detected at 0.102-0.107 ppm). Therefore, the label should specify the following: "Do not rotate to root or cereal crops at PBIs less than 120 days".

In summary, the following label restrictions should be added for rotational crops:

"Do not rotate to leafy vegetables. Do not rotate to root crops or cereals (small grains) at less than a 120-day PBI."

In addition, the label needs to specify that rotation to all other crops should be restricted to a 12-month PBI.

The registrant needs to submit a revised Section B reflecting the above restrictions.

Alternatively, if the registrant wants to propose a set of field accumulation in rotational crop studies to establish shorter PBIs, then the crops selected for these field trials should be selected on the basis of those crop rotations that the registrant intends to support. HED may be contacted to discuss possible reduced sets of field trials to fulfill these requirements. When the required field rotational crop studies are submitted, appropriate PBIs and tolerances for inadvertent residues of propazine and its chlorometabolites will be determined.

- Analytical standards for propazine are currently available at the National Pesticide Standards Repository. However, standards for the chlorometabolites G-30033 and G-28273 are not available and are required.
- The tolerances established under 40 CFR §180.243 are currently defined for residues of propazine *per se*. Griffin Corporation has filed a petition, PP#7F4837, to amend 40 CFR §180.243, by establishing tolerances for residues of propazine and its two chlorometabolites: 2-amino-4-chloro, 6-isopropylamino-s-triazine (G-30033) and 2,4-diamino-6-chloro-s-triazine (G-28273) in/on sorghum stover, forage, and grain at 0.25 ppm. The results of a sorghum metabolism study indicate that the proposed tolerance expression for plants is appropriate. Therefore, HED is recommending the revision of the residue definition under 40 CFR §180.243 to specify tolerances for the combined residues of propazine and the chlorometabolites G-30033 and G-28273. Also, HED recommends that the designation "(N)" be deleted from the 40 CFR for all tolerance level entries and that the chemical name of propazine be revised to "6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine."
- Tolerances for propazine residues of concern in meat, milk, poultry, and eggs are not required for the purpose of this petition only. The results of the reviewed ruminant and poultry metabolism studies suggest a Category 3 situation with regard to the need for livestock commodity tolerances as per 40 CFR §180.6(a)(3). There is no expectation of finite residues of propazine and its chlorometabolites in livestock commodities as a result of the proposed use on sorghum. Thus,

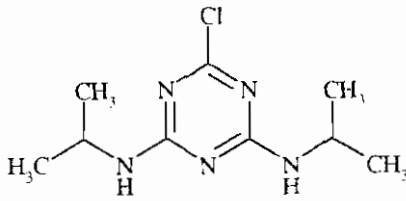


livestock feeding studies are not needed, and tolerances need not be established for meat, milk, poultry, and eggs.

- The established tolerance for sweet sorghum should be revoked unless propazine use on sweet sorghum is proposed and supporting residue data are submitted.

## Background

The PC Code and nomenclature of propazine as well as the physicochemical properties, are presented in the tables below:

Propazine Nomenclature.	
PC Code 006308	
Chemical structure	
Common name	Propazine
Molecular Formula	C <sub>9</sub> H <sub>16</sub> N <sub>5</sub> Cl
Molecular Weight	229.7
IUPAC name	6-chloro- <i>N,N'</i> -di-isopropyl-1,3,5-triazine-2,4-diamine
CAS name	2-chloro-4,6-bis(isopropylamino)-1,3,5-triazine OR 6-chloro- <i>N,N'</i> -bis(1-methylethyl)-1,3,5-triazine-2,4-diamine
CAS #	139-40-2

Physicochemical Properties of Propazine.		
Parameter	Value	Reference
Melting point	217.7 °C	RD D219079, 9/26/95, S. Malak
pH	5.66	
Density, bulk density, or specific gravity	0.46 g/mL	
Water solubility	3.8 ppm at 25 °C	
Solvent solubility (at 25 °C)	14,252 ppm in acetone 4,696 ppm in 1-octanol	
Vapor pressure	2.9 x 10 <sup>-8</sup> mm Hg at 20 °C  2.98 x 10 <sup>-7</sup> Torr at 45 °C	Product Chemistry Chapter of the Propazine Reregistration Standard, 5/19/87  RD D219079, 9/26/95, S. Malak

Physicochemical Properties of Propazine.		
Parameter	Value	Reference
Dissociation constant. pK	Not applicable; practically insoluble in water.	RD D219079, 9/26/95, S. Malak
Octanol/water partition coefficient	P = 1234.7 Log P = 3.08	
UV/visible absorption spectrum	Not available	

### 860.1200 Directions for Use

SRRD issued on June 30, 2004 a Propazine Use Closure Memo which details the food and nonfood uses for the Reregistration Eligibility Decision (RED) risk assessments. The risk assessments for propazine will be based on the use sites and usage data in BEAD's LUIS report, documents presented in the June 21<sup>st</sup> SMART meeting, and the product labels. Information on food/feed use patterns that will be supported is presented in Table 1. A tabular summary of the adequacy of the chemistry science guideline topics, for the purpose of tolerance reassessment, is presented in Table 2.

Following HED review of the proposed use directions and the submitted field trial data, the following label amendments are required for grain sorghum: (i) a maximum of one preemergence application per growing season; (ii) a maximum seasonal rate of 1.2 lb ai/A; (iii) a PHI of 70 days for sorghum forage; and (iv) a PHI of 90 days for sorghum grain and stover.

In addition, the following label restrictions should be added for rotational crops:

“Do not rotate to leafy vegetables. Do not rotate to root crops or cereals (small grains) at less than a 120-day PBI.”

In addition, the label needs to specify that rotation to all other crops should be restricted to a 12-month PBI.

**Table I. Food/Feed Use Patterns Summary for Propazine**

LIMITATIONS						
SITE NAME	Maximum Single Application Rate	Maximum Seasonal Rate	Maximum Number of Application Per cc & Year	MRI	REI	PHI/PGI/PSI Use Limitations
<b>SORGHUM</b>	70 day PHI for sorghum forage 90 day PHI for sorghum grain and stover. Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark Do not apply through any type of irrigation system. Do not contaminate water by cleaning of equipment or disposal of equipment wash waters. Do not contaminate water, food, or feed by storage or disposal Do not make more than one preemergence application per growing season.					
<b>Preemergence</b> Ground Actual	1.2 lb ai/A	1.2 lb ai/A	1/cc (NS)	NS	24 hr	
<b>Preplant</b> Ground Actual	1.2 lb ai/A	1.2 lb ai/A	1/cc (NS)	NS	24 hr	
<b>HEADER ABBREVIATIONS</b>						
Site Name - The site name refers to the entity (crop, building, surface or article) where a pesticide is applied and/or which is being protected						
Limitations - Precautionary statements related to the use of the product(s).						
Application Timing - The timing of pesticide application and is the primary application sort (not aggregated).						
Application Type - The type of pesticide application (aggregated).						
Application Equipment - The equipment used to apply pesticide (aggregated).						
Max. Single Appl. Rate to a Single Site - Maximum Dose for a single application to a single site. System calculated.						
Max. # Apps/cc & yr - Maximum Number of Applications per crop cycle and per year.						
MRI - Minimum Retreatment Interval (days) (at any rate). The minimum interval between pesticide application (days).						
REI - ReEntry Interval - The minimum amount of time that must elapse before workers can reenter a treated area						
PHI/PGI/PSI Use Limitations (May not apply to all Reg.#s) - Preharvest/Pregrazing/Pre-slaughter Interval use limitations pertinent to the application.						
Current As Of: - The label data for the listed products in this report is current of this date.						
<b>ABBREVIATIONS</b>						
NS - Not Specified (on label)						

Table 2. Residue Chemistry Summary for Tolerance Reassessment of Propazine.			
GLN Data Requirements	Current Tolerances (ppm) [40 CFR §180.243]	Additional Data Needed?	MRID Nos. <sup>1</sup>
860.1200: Directions for Use	N/A = Not Applicable	Yes <sup>2</sup>	See Table 1
860.1300: Nature of the Residue - Plants	N/A	No	00024330 00024436 00024728 00087881 00111694 44184813 <sup>3</sup> 44184814 <sup>4</sup> 44287315 <sup>5</sup>
860.1300: Nature of the Residue - Livestock	N/A	No	00087890 44184815 <sup>3</sup> 44184816 <sup>4</sup> 44184817 <sup>3</sup>
860.1340: Residue Analytical Method			
- Plant Commodities	N/A	Yes <sup>4</sup>	00041371 00068044 00087887 00112982 00118949 00119532
- Livestock Commodities	N/A	No	00080630 00087889 00112982 00140830
860.1360: Multiresidue Method	N/A	Yes <sup>5</sup>	PAM Vol. 1
860.1380: Storage Stability Data			
- Plant Commodities	N/A	Yes <sup>6</sup>	
- Livestock Commodities	N/A	No	
860.1400: Magnitude of the Residue - Water, Fish, and Irrigated Crops	N/A	N/A	
860.1460: Magnitude of the Residue - Food Handling	N/A	N/A	
860.1480: Magnitude of the Residue - Meat, Milk, Poultry, Eggs			
- Milk and the Fat, Meat, and Meat Byproducts of Cattle, Goats, Hogs, Horses, and Sheep	None established	No	00093525 00140830
- Eggs and the Fat, Meat, and Meat Byproducts of Poultry	None established	No	00087885
860.1500: Crop Field Trials			
Cereal Grains (Crop Group 15)			
- Sorghum grain	0.25	No	00016607 00016990 00016991 00016992 00026271 00044427 00047878 00063246 00065582 00068044 00087880 00087884 00105170 00111672 00111693 00118949 44287316 <sup>5</sup>
- Sorghum sweet	0.25	Yes <sup>7</sup>	

Table 2. Residue Chemistry Summary for Tolerance Reassessment of Propazine.			
GLN Data Requirements	Current Tolerances (ppm) [40 CFR §180.243]	Additional Data Needed?	MRID Nos.
Forage, Fodder, and Straw of Cereal Grains (Crop Group 16)			
- Sorghum forage and stover	0.25 each for sorghum forage and stover	No	00016607 00016990 00016992 00026271 00044427 00047878 00063246 00065582 00068044 00087880 00087884 00105170 00111672 44287316 <sup>3</sup>
860.1520: Processed Food/Feed			
- Sorghum	None established	No	
860.1650: Submittal of Analytical Reference Standards	N/A	Yes <sup>8</sup>	
860.1850: Confined Accumulation in Rotational Crops	N/A	No	44184810 <sup>5</sup>
860.1900: Field Accumulation in Rotational Crops	N/A	Yes <sup>9</sup>	44184811 <sup>7</sup>

- References were reviewed in the 5/19/87 Residue Chemistry Chapter of the Propazine Registration Standard. All other references were reviewed as noted.
- Based on the submitted residue data, the following label amendments are required for sorghum: (i) a maximum of one preemergence application per growing season; (ii) a maximum seasonal rate of 1.2 lb ai/A; (iii) a PHI of 70 days for sorghum forage; and (iv) a PHI of 90 days for sorghum grain and stover.
- DP Barcode D310517, 8/31/05, J. Morales and G. Kramer.
- A plant enforcement method is required. HED is recommending that the data-collection method (CHW 6641-106, Method 1, Rev. 1) be subjected to an ILV as per GLN 860.1340. If the ILV is successful, the method will be further validated by Agency chemists at ACL/BEAD.
- There are no multiresidue methods recovery data for the chlorometabolites G-30033 and G-28273, and these data are required. To fulfill this requirement, the petitioner is required to follow the directions for the protocols found in PAM Vol 1, Appendix II under paragraph (d)(1) of OPPTS GLN 860.1360, starting with the decision tree for multiresidue methods testing and the accompanying guidance found in the suggestions for producing quality data.
- The results of an ongoing storage stability study need to be submitted upon completion to support the storage conditions and intervals of samples collected from the sorghum field trials and limited field rotational crop trials.
- The established tolerance for sweet sorghum should be revoked unless propazine use on sweet sorghum is proposed and supporting residue data are submitted.
- Analytical standards for propazine are currently available at the National Pesticide Standards Repository. However, standards for the chlorometabolites G-30033 and G-28273 are not available and are required.

9. A set of field accumulation in rotational crop studies is required because in the confined and limited rotational crop study propazine and its chlorometabolites were identified in various rotational crops and intervals and quantified at levels greater than 0.01 ppm. Based upon these limited field trials, restrictions of not less than one year for a plant back for propazine are needed on the end-use product labels. Crops selected for these field trials should be selected on the basis of those crop rotations that the registrant intends to support. HED may be contacted to discuss possible reduced sets of field trials to fulfill these requirements. When the required field rotational crop studies are submitted, appropriate PBIs and tolerances for inadvertent residues of propazine and its chlorometabolites will be determined.

## SUMMARY OF SCIENCE FINDINGS

### 860.1300 Nature of the Residue - Plants

The nature of propazine residues in sorghum is adequately understood. The submitted sorghum metabolism study indicates that propazine is rapidly and extensively metabolized in sorghum via: (i) N-dealkylation; (ii) replacement of chlorine by hydroxy; and (iii) glutathione conjugation. The metabolism of propazine in sorghum is similar to published and submitted plant metabolism studies for other triazine herbicides.

Consistent with the HED MARC decision memoranda on atrazine (PC Code: 080803) dated 11/15/2000 (D270177) and 2/10/2003 (D288715), the residues of concern in plants for tolerance reassessment are the parent plus the chlorometabolites G-30033 and G-28273. In accordance with decisions made for atrazine and simazine, all risk assessments should be done using parent plus chlorometabolites as the residues of concern for dietary (food + water) assessments. These decisions supercede the Memorandum of Understanding between HED and Griffin Corporation for Propazine (see 1/11/96 memo of M. Metzger).

Figure 1 depicts chemical structures of propazine and its chloro- and hydroxy-metabolites that were identified in plants and livestock. The Executive Summary of the sorghum metabolism study DER is reproduced in this TRED document and follows Figure 1.

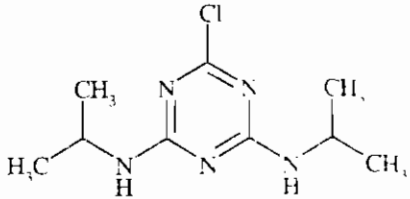
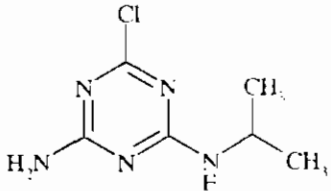
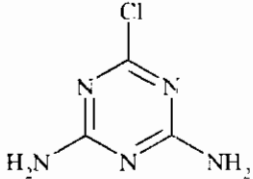
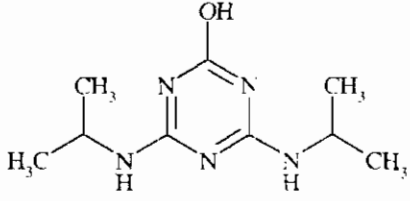
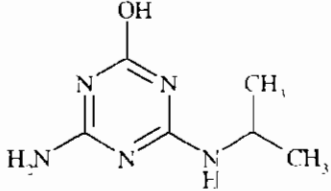
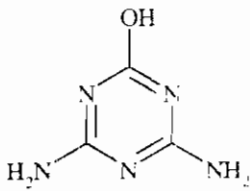
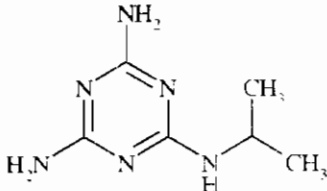
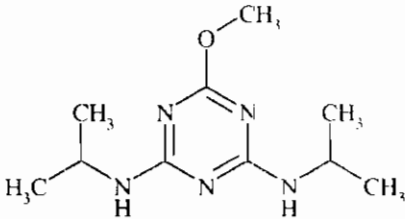
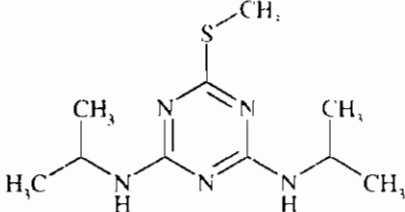
<b>FIGURE 1. Propazine and its Metabolites in Plants and Livestock.</b>		
<b>Common Name (Code)</b> Chemical Name	Substrate	Chemical structure
<b>Propazine</b> (G-30028) 2-chloro-4,6-bis(isopropylamino)-s-triazine	Sorghum forage, grain, and stover  120- and 365-day PBI lettuce; 120-day PBI turnip tops and roots; and 29-, 120- and 365-day PBI wheat forage, grain and straw.	
<b>Propazine des-ethyl</b> (G-30033) 2-amino-4-chloro-6-(1-methylethylamino)-s-triazine <b>OR</b> 2-amino-4-chloro-6-isopropylamino-s-triazine	Sorghum forage and stover  Goat milk  120- and 365-day PBI lettuce; 120-day PBI turnip tops and roots; 29-, 120- and 365-day PBI wheat forage; and 29- and 120-day PBI wheat grain and straw.	
<b>DACT</b> (G-28273) 2,4-diamino-6-chloro-s-triazine	Sorghum stover  Goat milk, liver, muscle, and fat  Poultry liver, muscle, fat, egg yolk, and egg white	
<b>Propazine 2-hydroxy or 2-hydroxypropazine</b> (G-S11526) 2-hydroxy-4,6-bis-(1-methylethylamino)-s-triazine <b>OR</b> 2-hydroxy-4,6-bis(isopropylamino)-s-triazine	Sorghum forage, grain, and stover  Goat kidney, liver, and milk (from the goat metabolism study using [U- <sup>14</sup> C]2-hydroxypropazine as the test substance)  120-day PBI turnip tops, 29-day PBI wheat forage and straw; and 29- and 120-day PBI wheat grain.	
<b>Desisopropyl hydroxypropazine</b> 4-amino-2-hydroxy-6-isopropylamino-triazine	Goat kidney, liver, and milk (from the goat metabolism study using [U- <sup>14</sup> C]2-hydroxypropazine as the test substance)  Sorghum forage, grain, and stover  120- and 365-day PBI lettuce; 120-day PBI turnip tops and roots; and 29-, 120- and 365-day PBI wheat forage, grain and straw	

FIGURE 1. Propazine and its Metabolites in Plants and Livestock.		
Common Name (Code) Chemical Name	Substrate	Chemical structure
<b>Ammeline</b> (GS-17791) 2,4-diamino-6-hydroxy-s-triazine	Sorghum stover	
<b>Triazine-methyl-triamine</b> (CGA-101248) N-(1-methyl)-1,3,5-triazine-2,4,6-triamine	Sorghum stover	
<b>Prometon</b> (G-31435) 2-methoxy-4,6-bis(1-methylethylamino)-s-triazine	Sorghum stover	
<b>Propazine-2-methyl-sulfinyl</b> (GS-16141) 2,4-bis(1-methylethylamino)-6-methylsulfinyl-s-triazine	Sorghum stover	

### Sorghum

44287315.der.wpd (Includes MRIDs 44184813 and 44184814)

Griffin Corporation has submitted a sorghum metabolism study with propazine under greenhouse conditions. Four days after sorghum was seeded in test plots, [<sup>14</sup>C]propazine (labeled uniformly in the triazine ring, specific activity of 49.42 mCi/mole) was applied as one broadcast spray directed to the soil of test plots at target rates of 2.4 and 4.8 lb ai/A; the achieved application rates were verified at 1.96 and 3.91 lb ai/A, respectively. Sorghum forage samples were harvested 45 days after treatment, while grain and stover samples were harvested 124 days posttreatment. The in-life phase was conducted by PTRL East, Inc. (Richmond, KY), and the analytical phase was conducted by PTRL West, Inc. (Richmond, CA).

TRR were 0.126, 0.133 and 2.344 ppm in/on sorghum forage, grain and fodder (stover), respectively, following one application of [<sup>14</sup>C]propazine at 1.96 lb ai/A. At the treatment rate of 3.91 lb ai/A, the TRR were 0.084, 0.132 and 2.678 ppm in the forage, grain and stover,



respectively. Samples which received the treatment rate of 1.96 lb ai/A were selected for residue characterization and identification.

Residues in/on treated sorghum matrices were extracted using a series of solvent systems. Solvent extraction with methanol and methanol/water released 67.6% of TRR in forage and 53.4% of TRR in stover. For grain, extraction with methanol and methanol/water released 39.7% of TRR, and hydrolysis with 6 N HCl further released 34.1% of TRR. Additional radioactivity was released in sorghum matrices by: (i) methanol/0.1 N HCl for grain; (ii) 0.1 N HCl; and (iii) 3 N KOH. Nonextractable residues following extraction/hydrolysis accounted for 4.8%, 6.0% and 12.1% TRR in the forage, grain and stover, respectively. The accountabilities were 101.6%, 103.8% and 97.4% in forage, grain and stover, respectively. Residues were identified and quantitated primarily by C18 and SCX high-performance liquid chromatography (HPLC) co-chromatography with confirmatory analysis by HPLC and/or thin-layer chromatography (TLC) co-chromatography. These methods successfully identified the predominant residues in sorghum forage, grain and stover.

In **forage**, chromatographic analysis of the combined methanol and methanol/water extracts (subsample B) identified the parent propazine as a trace component at 0.8% TRR (0.001 ppm). The chlorometabolite, atrazine des-ethyl (G-30033), was identified at 8.7% TRR (0.011 ppm) along with the following hydroxymetabolites: propazine 2-hydroxy (GS-11526) at 13.5% TRR (0.017 ppm) and atrazine des-ethyl 2-hydroxy (GS-17794) at 8.7% TRR (0.011 ppm).

In **grain**, chromatographic analysis of the combined methanol and methanol/water extracts (subsample A) also showed trace amounts of the parent propazine at 0.8% TRR (<0.001 ppm). Other residue components include atrazine des-ethyl 2-hydroxy (GS-17794) at 10.3% TRR (0.013 ppm) and propazine 2-hydroxy (GS-11526) at 2.3% TRR (<0.003 ppm).

In **stover (fodder)**, chromatographic analysis of the chloroform layer of the combined methanol and methanol/water extracts (subsample D) resolved propazine at 0.5% TRR (0.011 ppm). All other residue components were identified at <10% TRR. Atrazine des-ethyl (G-30033) and prometon (G-31435) accounted for 1.7% TRR (<0.039 ppm) and 1.6% TRR (0.037 ppm), respectively. Propazine 2-hydroxy (GS-11526), atrazine des-ethyl 2-hydroxy (GS-17794), and GS-16141 accounted for 2.7% TRR (0.064 ppm), 3.3% TRR (0.077 ppm), and 3.4% TRR (0.080 ppm), respectively (quantified in the 6 N HCl extracts and combined methanol and methanol/water extracts of subsample A). Ammeline (GS-17791) and atrazine des-ethyl des-isopropyl (G-28273) both accounted for 2.2% TRR (<0.052 ppm; quantified in the combined methanol and methanol/water extracts of subsample A). The ammeline (GS-17791) and atrazine des-ethyl des-isopropyl (G-28273) peaks, overlapping in all HPLC methods employed in the study, accounted for an additional 3.7% TRR (0.086 ppm). CGA-101248 accounted for 2.7% TRR (0.064 ppm; quantified in the combined methanol and methanol/water extracts of subsample A).

The remaining radioactivity in sorghum matrices was characterized as unassigned or diffuse radioactivity, accounting for 35.7% TRR (0.045 ppm, ~27 peaks) in forage, 27.1% TRR (0.036 ppm, ~10 peaks) in grain, and 46.1% TRR (1.081 ppm, ~49 peaks) in stover. In forage, ~18% TRR was characterized based on acid hydrolysis (0.1 N HCl and 6 N HCl), and 11.2% TRR was

characterized following base hydrolysis. In grain, 2.1% TRR was characterized based on acidic methanol extraction, approximately 42% TRR was characterized based on acid hydrolysis (0.1 N HCl and 6 N HCl), and 13.6% TRR was characterized following base hydrolysis. In stover, 16.1% TRR was characterized based on acid hydrolysis with 0.1 N HCl, and 2.8% TRR was characterized following base hydrolysis. In forage and grain, the dichloromethane partitioning of the hydrolysates of the 6 N HCl and 3 N KOH extractions, which were found to contain ~10% TRR, indicated that the radioactivity compounds were highly polar, water-soluble materials, not organic. These hydrolysates could not be analyzed by HPLC due to their viscosity after concentration.

An additional subsample of sorghum stover (subsample B) was subjected to a different extraction scheme after the initial extraction with methanol and methanol/water in order to maximize the release of radiocarbon by using increasingly harsh extractions to break down the plant constituents into various classes of organic materials. Solvent extraction with methanol and methanol/water released the majority of the TRR (66.5%). Additional radioactivity was released in sorghum stover by: (i) phosphate buffer (6.5% TRR, 0.152 ppm); (ii)  $\alpha$ -amylase (4.0% TRR, 0.095 ppm); (iii) pronase (2.7% TRR, 0.062 ppm); (iv) pectin (3.1% TRR, 0.072 ppm); (v) lignin (1.8% TRR, 0.043 ppm); (vi) hemicellulose (5.0% TRR, 0.116 ppm); and (vii) cellulose (4.2% TRR, 0.099 ppm). Nonextractable residues following extraction/hydrolysis accounted for 1.4% TRR. No metabolites were identified in the HPLC analyses of the exhaustive/enzymatic extractions.

Sorghum forage samples were stored frozen for ~8 months prior to extraction, while the grain and stover samples were stored frozen for 5 months prior to extraction. The time intervals between extractions and analyses of the test sorghum matrices were not provided. Methanol and methanol/water extraction conducted 24 months after the original extraction date indicated no loss of radioactivity. Subsequent chloroform partitioning of the combined methanol extracts, performed two months after extraction, also yielded a metabolic profile similar to that of the initial chloroform partitioning. No additional storage stability data are required to support the study.

Based on the results of the sorghum metabolism study, propazine is rapidly and extensively metabolized in sorghum via: (i) N-dealkylation; (ii) replacement of chlorine by hydroxy; and (iii) glutathione conjugation. The results of the study were similar to other published results of triazine herbicides.

#### **860.1300 Nature of the Residue - Livestock**

The nature of propazine residues in livestock is adequately understood based on adequate metabolism studies with goats and hens. Propazine metabolism in livestock is similar to that in plants, involving dealkylation and conjugation, with the triazine ring remaining intact.

Consistent with the HED MARC decision memoranda on atrazine (PC Code: 080803) dated 11/15/2000 (D270177) and 2/10/2003 (D288715), the residues of concern in livestock for tolerance reassessment are the parent plus the chlorometabolites G-30033 and G-28273. In accordance with decisions made for atrazine and simazine, all risk assessments should be done

using parent plus chlorometabolites as the residues of concern for dietary (food + water) assessments. These decisions supercede the Memorandum of Understanding between HED and Griffin Corporation for Propazine (see 1/11/96 memo of M. Metzger).

The Executive Summaries of the livestock metabolism study DERs are reproduced below.

#### Goat. [<sup>14</sup>C]propazine as the test substance

44184815.der.wpk

Griffin Corporation has submitted a goat metabolism study with propazine. The test substance, [<sup>14</sup>C]propazine (labeled uniformly in the triazine ring, specific activity of 49.42 mCi/mmol), was administered orally to a single lactating goat at 9.9 ppm in the diet. The goat was dosed once per day for seven consecutive days. Milk was collected twice daily throughout the study, and tissues (muscle, fat, liver, and kidney) were collected at sacrifice. The in-life and analytical phases of the study were conducted by PTRL East, Inc. (Richmond, KY).

TRR were 0.080-0.238 ppm in milk, 1.123 ppm in liver, 1.041 ppm in kidney, 0.209 ppm in muscle, and 0.160 ppm in fat. Radioactivity was highest in liver and kidney, and lowest in fat. Residues in milk were generally highest in samples collected 8 hours after dosing and appeared to have reached a plateau after two days of dosing. The study reported that a large portion of the administered dose was excreted, with urine and feces (including cage washes and solids) accounting for a total of ~74% of the administered dose.

Radioactive residues in goat milk and tissues were adequately extracted using water and a combination of organic solvents. Enzyme hydrolysis was also used to release bound residues in muscle and fat tissues only. In milk, ~91% of TRR was retained in the aqueous fraction with hexane extraction. In tissues, ~86-98% of TRR was extractable with water, and additional minor amounts (<3% TRR) were sequentially extracted with acetonitrile (ACN)/water, ACN, and hexane. Nonextractable residues after solvent extraction and enzyme hydrolysis were 18.9% TRR (0.042 ppm) for milk, 10.8% TRR (0.113 ppm) for kidney, 6.1% TRR (0.068 ppm) for liver, 5.9% TRR (0.012 ppm) for muscle, and 7.2% TRR (0.012 ppm) for fat. These data suggest that further attempts should have been made to release the nonextractable/bound residues in kidney and liver.

Residues in extracts and hydrolysates were subjected to HPLC analysis. Metabolites were identified by comparison of retention times or co-chromatography with 17 reference standards including standards of known chloro- and hydroxy-metabolites of triazine herbicides. The identities of metabolites were confirmed by TLC co-chromatography.

Approximately 73% of TRR was identified in goat milk, 50% TRR in fat, 26% TRR in muscle, and <3% TRR in kidney and liver. The parent propazine was not detected in goat milk or tissues. Atrazine-desethyl-desisopropyl (G-28273) was the principal residue component identified in milk (63.4% TRR, 0.141 ppm), fat (50.4% TRR, 0.080 ppm), muscle (26.1% TRR, 0.054 ppm), and liver (2.7% TRR, 0.031 ppm). The metabolite atrazine-desethyl (G-30033) was only identified in milk (9.4% TRR, 0.021 ppm).

The remaining radioactivity in goat milk and tissues was characterized to be comprised of up to six unknown metabolites. Although each unknown accounted for <7% TRR in milk, several unknowns were present at significant levels in goat tissues. None of these unknown residues co-chromatographed with propazine, propazine-2-hydroxy, ammelide or any other reference standards used in the study. Region G was the major unknown component in kidney (59.5% TRR, 0.619 ppm) and liver (76.1% TRR, 0.855 ppm) but was present at lower levels in muscle (5.8% TRR, 0.012 ppm) and fat (15.6% TRR, 0.025 ppm). Region G was characterized by the petitioner as stable to glucuronidase, sulfatase, and 3 N HCl hydrolysis. Based on the metabolism of other triazine herbicides, the petitioner proposed that the unknown may be an acid stable glutathione conjugate of propazine or one of its biotransformations.

Another unknown, Region A, was quantitated at >10% TRR in muscle (19.9% TRR, 0.042 ppm), fat (10.3% TRR, 0.016 ppm), and kidney (10.2% TRR, 0.106 ppm). Region E was detected in kidney as a significant residue at 21.2% TRR (0.221 ppm). Acid and enzyme hydrolysis was conducted on the pronase hydrolysate of the aqueous extract of kidney to further characterize unknown residues. However, no discussion of the results and no chromatograms for the acid and enzyme hydrolysates were presented.

Milk samples were stored frozen for <6 months and tissues for ~7 months. Adequate storage stability data were submitted demonstrating the stability of the metabolic profile in goat kidney and liver for up to ~23 months.

Based on the results of the study, propazine is metabolized in goats via sequential dealkylation of the isopropyl alkyl groups with excretion in the urine, primarily as the di-dealkylated metabolite (atrazine-desetnyl-desisopropyl or G-28273). A water-soluble hydrolytically-stable conjugate of propazine or one of its metabolites may also be formed, which is the major metabolite in goat tissues.

#### Goat, [<sup>14</sup>C]hydroxypropazine as the test substance

44184817.der.wp.l

Griffin Corporation has submitted a goat metabolism study with [<sup>14</sup>C]hydroxypropazine. The test substance, [U-<sup>14</sup>C]2-hydroxypropazine (specific activity 55.9 mCi/mmol), was administered orally to a single goat at 10.9 ppm in the diet. The goat was dosed once per day for three consecutive days. Milk was collected twice daily throughout the study, and tissues (muscle, fat, liver, and kidney) were collected at sacrifice. The in-life and analytical phases of the study were conducted by Corning Hazelton, Inc. (Madison, WI).

TRR were 0.025-0.029 ppm in milk, 0.006 ppm in muscle, 0.001 ppm in fat (renal and omental), 0.110 ppm in kidney, and 0.036 ppm in liver. Radioactivity was highest in kidney and lowest in fat. Residues in milk were at relatively constant levels during dosing.

Muscle and fat tissues were not extracted because of low radioactivity (<0.010 ppm). In milk, ~88-91% of TRR was retained in the aqueous fraction following hexane extraction, and the nonextractable residues were <7% TRR (0.001-0.002 ppm). The majority of radioactivity was

extracted from kidney and liver with methanol/water, with ~40-43% TRR being retained in the aqueous fraction. In liver, 66% TRR (0.024 ppm) remained in the organic fraction, leaving <8% TRR (0.003 ppm) as nonextractable residues. In kidney, only ~34% TRR (0.038 ppm) remained in the organic fraction, and nonextractable residues were <0.05 ppm (26.5% TRR, 0.029 ppm). Accountabilities were ~93-114%. Residues were identified by HPLC analysis, using 2D-TLC, a second HPLC method, and/or cation exchange chromatography for confirmation. These methods successfully identified the predominant residues in goat matrices. No supporting storage stability data are required because milk and tissue samples from the subject goat metabolism study were stored frozen and analyzed within 6 months of collection.

Approximately 66-81% TRR were identified in goat milk, kidney, and liver. The test substance, hydroxypropazine, was found to be the major residue in all matrices, accounting for 63.5% TRR (0.069 ppm) in kidney, 77.2% TRR (0.028 ppm) in liver, and 65.0-69.4% TRR (0.017-0.020 ppm) in milk. The only other metabolite identified was desisopropyl hydroxypropazine, which was detected in minor amounts in all matrices: 2.9% TRR (0.003 ppm) in kidney, 3.6% TRR (0.001 ppm) in liver and 8.2-8.5% TRR (0.002 ppm) in milk. The remaining radioactivity was attributed to unknowns accounting for 10.3% TRR in kidney, 24.7% TRR in liver, and ~14.8% TRR in milk; no individual peak unknown was present at >0.003 ppm.

Based on the results of the study, the petitioner concluded that hydroxypropazine is metabolized in goats by N-dealkylation to yield desisopropyl hydroxypropazine. Furthermore, the petitioner stated that hydroxypropazine, the polar metabolite of propazine, is likely rapidly excreted by lactating livestock with little deposition into tissues.

### Poultry

44184816 der.wpc

Griffin Corporation has submitted a study investigating the metabolism of [<sup>14</sup>C]propazine (labeled uniformly in the triazine ring; specific activity of 49.42 mCi/mmol) in laying hens. The test substance was orally administered to five hens at 20.3 ppm in the diet. The hens were dosed once per day for 14 consecutive days. Eggs were collected twice daily, and tissues (liver, fat, and muscle) were collected at sacrifice. The in-life and analytical phases of the study were conducted by PTRL East, Inc.

TRR were 0.019-0.448 ppm in whole egg, 0.010-0.669 ppm in egg yolk, 0.024-0.327 ppm in egg white, 1.196 ppm in liver, 0.961 ppm in composite muscle, and 0.172 ppm in composite fat. Residues in eggs appeared to plateau after 9 days of dosing. The study reported that a large portion of the administered dose was excreted, ~77% in the collected excreta and ~5% in the cage wash.

Approximately 72-104% of TRR in poultry liver, egg yolk, and egg white were readily extracted using water. For muscle and fat, water extraction only released ~42-45% of TRR. Subsequent extraction with ACN/water released <5% of the radioactivity from all matrices; additional extractions with organic solvents released <2% of the radioactivity. Nonextractable residues remaining after these solvent extractions measured 15.9% TRR (0.191 ppm) in liver, 50.6% TRR

(0.587 ppm) in muscle, 103.6% TRR (0.178 ppm) in fat, 22.6% TRR (0.151 ppm) in egg yolk, and 0.3% TRR (0.001 ppm) in egg white. The nonextractable residues of all of these matrices, except egg white, were subjected to protease hydrolysis. The nonextractable residues remaining after protease hydrolysis measured 0.5% TRR (0.006 ppm) in liver, 3.9% TRR (0.045 ppm) in muscle, 34.2% TRR (0.059 ppm) in fat and 0.5% TRR (0.003 ppm) in egg yolk. The accountabilities ranged ~92-105% for all hen matrices, except fat (~132%).

Residues in extracts and hydrolysates were characterized primarily by HPLC analysis. Residue components were identified by co-chromatography and/or retention time comparison with 17 reference standards which included several putative chloro- and hydroxy-metabolites of triazine herbicides. TLC analysis was performed as a confirmatory technique.

Characterization of the radioactive residues in hen tissues and egg samples by HPLC indicated the presence of at least eight metabolites. The parent propazine was not detected in any extracts and/or hydrolysates. The only residue component identified was atrazine-desethyl-desisopropyl (G-28273) which was quantitated in poultry matrices as follows: liver (4.3% TRR, 0.171 ppm), muscle (18.3% TRR, 0.212 ppm), fat (48.1% TRR, 0.083 ppm), egg yolk (35.3% TRR, 0.236 ppm), and egg white (51.9% TRR, 0.170 ppm). Seven unknown compounds were found in the matrices: A (RT 4.0-5.5 min.), B (RT 6.0-7.0 min.), C (RT 9.0-9.5 min.), E (RT 14.0 min.), F (RT 15.0-16.5 min.), G (RT 17.0-18.0 min.) and H (RT 25.0-26.0 min.). Compounds A, B, C, G and H were observed at >10% TRR in various matrices. HED would have preferred that additional attempts, such as LC/MS analysis, were made to identify these compounds. However, the petitioner characterized these unknown metabolites to be relatively more polar than propazine based on the chromatographic profiles.

Samples were stored frozen for up to 4 months prior to residue characterization. To demonstrate the stability of frozen samples while in storage, the extracts of liver tissue and egg white were reanalyzed by HPLC after approximately 19 months of sample collection. The results of these analyses indicate that metabolite profiles were stable in liver extracts during frozen storage. In the case of the egg white extracts, reanalysis indicated that a conjugated form of atrazine-desethyl-desisopropyl degraded to atrazine-desethyl-desisopropyl during frozen storage.

Based on the study results, all of the metabolites which were observed in the study were more polar than propazine, indicating that propazine is readily metabolized in the laying hen to more polar metabolites. Propazine was metabolized via dealkylation of the two isopropyl alkyl group, generating atrazine-desethyl-desisopropyl as a major metabolite. Further degradation to the multiple polar metabolites was suggested to occur via oxidation and/or conjugation.

### **860.1340 Residue Analytical Methods**

#### Plant commodities

An adequate enforcement method is currently not available and is required for propazine and its two chlorometabolites (G-30033 and G-28273), the terminal residues of concern for tolerance establishment. Currently, PAM Vol. II lists Method IV (AG-281) for determination of only the chlorometabolite G-28273 in crops and livestock tissues. G-28273 is extracted from crops and

livestock tissues by blending the finely chopped material or tissue with methanol:water (9:1; v:v). The tissue extract is washed with hexane to remove oily materials. The methanol/water extract is then taken to dryness, and G-28273 is separated from co-extractives by partition column chromatography using a pH 7.0 buffer as the stationary phase and hexane, hexane:ethyl ether (9:1; v:v), and ethyl ether as the sequential mobile phases. The G-28273 is eluted from the column with ethyl ether. The ethyl ether eluate is evaporated to dryness, and the residue is dissolved in absolute ethanol for determination of G-28273 by GC with Dohrmann microcoulometric detection in the chloride-specific mode or Coulson electrolytic conductivity detection in the nitrogen-specific mode. The detection limit is 0.1 ppm.

Samples of sorghum forage, grain, and stover, that were collected from the sorghum field trials, were analyzed for residues of propazine and its chlorometabolites by a Corning Hazelton analytical method entitled "Determination of Propazine, Desethyl Atrazine (DEA), and Diamino Atrazine (DAA) in Forage, Grain, and Stover using Capillary Gas Chromatography with Mass-Selective Detection and Nitrogen-Phosphorous Detection," dated 10/16/96. Briefly, a representative sample is soxhlet-extracted with acetone, concentrated by rotary evaporation, and diluted with acetone. An aliquot is extracted with ethyl acetate and saturated sodium chloride. The organic layer is reserved, and the water layer is re-extracted. The organic layers are combined and evaporated to dryness. Residues are redissolved in water and cleaned up on a Chem-Elut column. Residues are eluted with 15% ethyl acetate/hexane for isolation of propazine and DEA (G-30033, Fraction A). The eluate is evaporated to dryness, redissolved in ethyl acetate, and analyzed for propazine and G-30033 using GC/MSD. A second aliquot is taken for isolation of G-28273. The aliquot is evaporated to dryness and redissolved in water. The water solution is centrifuged and cleaned up on a Chem-Elut column. Residues of DAA are eluted with 50% ethyl acetate/hexane (fraction B). The eluate is evaporated to dryness, redissolved in acetone, and cleaned up on a LC-SCX column. Residues are eluted with 1 N ammonium hydroxide:methanol (1:3, v:v). The eluate is mixed with phosphate buffer (pH 6.5) and ethyl acetate. The organic layer is reserved, and the water layer is re-extracted. The organic layers are combined and evaporated to dryness. Residues are redissolved in ethyl acetate and analyzed for G-28273 using GC/NPD. The LOQ for each analyte in all RACs is 0.05 ppm. This method has been deemed adequate for data collection based on acceptable concurrent method recovery data.

HED recommends that the data-collection method (CHW 6641-106, Method 1, Rev. 1) be subjected to an ILV as per GLN 860.1340. If the ILV is successful, then the method will be subjected to further validation by Agency chemists at ACL/BEAD.

### Livestock commodities

At this time, livestock enforcement methods are not required for the reinstatement of propazine uses on sorghum since there is no expectation of finite secondary residues in livestock commodities (See Section 860.1480 Meat, Milk, Poultry, and eggs).

### **860.1360 Multiresidue Methods**

According to FDA's PAM Volume I, Appendix II, propazine is completely recovered using Section 302 (Protocol D), partially recovered using Section 303 (Protocol E), and not recovered

using Section 304 (Protocol F). There are no multiresidue methods recovery data for G-30033 and G-28273, and these data are required. To fulfill this requirement, the petitioner is required to follow the directions for the protocols found in PAM Vol. I, Appendix II under paragraph (d)(1) of OPPTS GLN 860.1360, starting with the decision tree for multiresidue methods testing and the accompanying guidance found in the suggestions for producing quality data.

### **860.1380 Storage Stability**

#### Plant commodities

Samples from the conducted sorghum field trials and limited field rotational crop trials are not supported by storage stability data. However, the petitioner has indicated that a storage stability study has been initiated and will be submitted in a separate report upon completion. Samples from the sorghum field trials were stored frozen for 25.7-26.6 months prior to residue analysis. The maximum frozen storage intervals of samples from the limited field rotational crop trials were 129 days (4.2 months) for lettuce, 79 days (2.6 months) for mustard leaves, 100 days (3.3 months) for radish tops and roots, 79 days (2.6 months) for turnip tops and roots, 141 days (4.6 months) for wheat forage, 125 days (4.1 months) for wheat hay, and 89 days (2.9 months) for wheat grain and straw. The submitted plant and livestock metabolism studies are supported by adequate storage stability data. The chromatographic profiles of residues appeared stable following re-analysis of select matrices.

#### Livestock commodities

Storage stability data for livestock commodities are not required since livestock feeding studies are not needed; there is no expectation of finite secondary residues in livestock commodities.

### **860.1400 Water, Fish, and Irrigated Crops**

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

### **860.1460 Food Handling**

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

### **860.1480 Meat, Milk, Poultry, and Eggs**

Sorghum grain, forage, and stover, and soybean meal as a source of protein are the livestock feed items included in the *maximum theoretical dietary burden (MTDB)* given below. Following tolerance reassessment, the maximum theoretical dietary burden of propazine has been calculated (see Table 3) as follows: 0.29 ppm for beef cattle and dairy cattle, 0.16 ppm for swine, and 0.14 ppm for poultry.



<b>Table 3. Calculation of Maximum Dietary Burdens of Propazine to Livestock.</b>				
Feedstuff	% Dry Matter <sup>1</sup>	% Diet <sup>1</sup>	Estimated Tolerance (ppm)	Dietary Contribution (ppm) <sup>2</sup>
<b>Dairy &amp; Beef Cattle</b>				
Soybean meal	89	15	0	0
Sorghum grain	86	35	0.15	0.061
Sorghum forage	35	35	0.20	0.200
Sorghum stover	88	15	0.15	0.025
<b>TOTAL BURDEN</b>	--	100	--	<b>0.29</b>
<b>Swine</b>				
Sorghum grain	86	90	0.15	0.157
<b>TOTAL BURDEN</b>	--	90	--	<b>0.157</b>
<b>Poultry</b>				
Sorghum grain	86	80	0.15	0.140
<b>TOTAL BURDEN</b>	--	80	--	<b>0.140</b>

<sup>1</sup> Table 1 (OPPTS Guideline 860.1000) & personnel communication B. Schneider.

<sup>2</sup> Contribution = (tolerance / % DM) x % diet for beef and dairy cattle; contribution = (tolerance x % diet) for poultry and swine

In a goat metabolism study where [<sup>14</sup>C]propazine was administered orally to a single lactating goat at 9.9 ppm in the diet (~35X the MTDB of 0.286 ppm), the parent propazine was not detected in goat milk or tissues. The metabolite G-28273 was the principal residue identified in milk (63.4% TRR, 0.141 ppm), fat (50.4% TRR, 0.080 ppm), muscle (26.1% TRR, 0.054 ppm), and liver (2.7% TRR, 0.031 ppm). The metabolite G-30033 was only identified in milk (9.4% TRR, 0.021 ppm). When the residue level in milk, which shows the highest residue from the study, is interpolated to 1x of the MTDB, the anticipated residue of G-28273 is about 0.004 ppm. In fat, the anticipated residue is 0.0023 ppm, in meat it is 0.0015 ppm, and in liver it is 0.00089 ppm.

In a poultry metabolism study where [<sup>14</sup>C]propazine was administered at 20.3 ppm in the diet, the parent propazine was not identified in eggs and tissues. The only residue identified was G-28273 which was quantitated in poultry matrices as follows: liver (4.3% TRR, 0.171 ppm), muscle (18.3% TRR, 0.212 ppm), fat (48.1% TRR, 0.083 ppm), egg yolk (35.3% TRR, 0.236 ppm), and egg white (51.9% TRR, 0.170 ppm). When the residue level in egg yolk, which shows the highest residue from the study, is interpolated to 1x of the MTDB, the expected residue of G-28273 is about 0.002 ppm

Although there are no submitted feeding studies, the results of livestock metabolism studies suggest a Category 3 situation with regard to the need for livestock commodity tolerances as per 40 CFR §180.6(a)(3). Based on the metabolism study results in the goat, there is no expectation of finite residues of propazine and its chlorometabolites in livestock commodities as a result of the proposed use on grain sorghum.

In addition to the results of the metabolism study, the team considered the additional information regarding the likelihood that forage from grain sorghum will be fed to dairy cattle. (Personnel communication from B. Schneider)

1) Grain (which has non-detectable residues of propazine) from grain sorghum is the livestock feed commodity, not the forage. The grain and stover are most likely utilized as a livestock feed, not the forage

2) It is more likely the forage from grain sorghum would be fed to beef cattle because dairy cattle are not raised where grain sorghum is grown, thus limiting their likelihood of being fed forage from grain sorghum, and reducing the likelihood of residue transfer on forages of grain sorghum to milk; i.e., the areas where dairy cattle are raised in the South and grain sorghum production are not similar. Most grain sorghum is grown near areas where beef cattle are raised.

3) It is unlikely that forage from grain sorghum would be harvested for livestock feed use because that would mean harvesting the forage from the plant before the grain actually had a chance to mature, which would defeat the purpose of growing the plant for grain, and

4) There are specific forage sorghums grown for livestock feed; i.e., although grain from grain sorghum is used for an livestock feed, forage from grain sorghum is typically not grown and used as an livestock feed.

Based on the above practical considerations regarding the likelihood that forage from sorghum grown for grain; i.e., it is not very likely that forage from grain sorghum will be fed to dairy and beef cattle, the team concluded that for the petition for **grain sorghum, only**, livestock feeding studies are not needed, and tolerances need not be established for meat, milk, poultry, and eggs. However, if in the future, the registrant petitions for propazine uses on additional livestock feed items, livestock feeding studies conducted in accordance with OPPTS Guideline 860.1480 (Meat, Milk, Poultry, Eggs) will be required as a part of that petition.

### 860.1500 Crop Field Trials

Pending submission of supporting storage stability data and label revision, the proposed use of propazine is supported by adequate residue data. Following a single preemergence broadcast application of a representative FIC formulation of propazine at 1.47-2.43 lb ai/A (1.2-2.0x the proposed single application rate), the results of the sorghum field trials indicate the following: In **sorghum forage** harvested at a PHI range of 69-117 days, residues of propazine and G-30033 were each less than the LOQ (<0.05 ppm) in/on 26 treated samples. Residues of G-28273 ranged 0.050-0.087 ppm in/on four treated forage samples but were <0.05 ppm in/on 22 treated samples. In **sorghum grain and stover** harvested at a PHI range of 86-152 days, residues of propazine, G-30033, and G-28273 were each <0.05 ppm in/on 26 treated samples. These data support the proposed tolerance of 0.25 ppm each for the combined residues of propazine and its two chlorometabolites (G-30033 and G-28273) in/on sorghum stover, forage, and grain. Residue data on the aspirated grain fractions of sorghum are not required since the proposed use of propazine on grain sorghum is for preemergence or preplant application.

The Executive Summary of the sorghum field study DER is reproduced below.

### Sorghum grain, forage and stover

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Griffin Corporation has submitted field trial data on sorghum with propazine. A total of 13 sorghum trials were conducted in Regions 2 (GA; 1 trial), 4 (AR and MO; 2 trials), 5 (IL, KS, and NE; 3 trials), 6 (OK and TX; 4 trials), 7 (SD; 1 trial), and 8 (CO and TX; 2 trials) during the 1994 growing season. Geographic representation of residue data is adequate since the number and locations of field trials are in accordance with OPPTS Guideline 860.1500.

The field study was designed to include three plots at each field trial site. Plot 1 was untreated to provide control samples. Two additional plots each received a single preemergence broadcast application of the 4 lb/gal flowable-concentrate (FIC) formulation at low rates (Treatment Plot 2) or high rates (Treatment Plot 3). Nominal "low rates" of ~0.75, 1.5, or 2.4 lb ai/A were applied in plots with soil described as coarse-, medium-, or fine-textured, respectively. Nominal "high rates" of ~1.5, 3.0, or 4.8 lb ai/A were also applied in plots with soil described as coarse-, medium-, or fine-textured, respectively. Soil analysis was not conducted before application of the propazine test substance, and the principal study investigator 'estimated' the soil texture designation by direct examination and by using available information sources; the target application rates for each soil texture were based on these estimates. Application was made in 10-17 gal/A of water using ground equipment. Samples of sorghum forage (whole green plants) were collected at the late or hard dough stage at a 69- to 117-day PHI, and samples of sorghum grain and stover were collected at normal harvest for each test location with a PHI range of 85/86 to 152 days.

Following treatment, soil samples from each treatment plot were sent to Agvise Laboratories (Northwood, ND) for texture characterization. The results of soil analysis showed discrepancies between the field investigator's "estimates" and the laboratory determinations of soil texture. It was reported that the actual applied rates ranged from 60.4-320% of target rates. Consequently, the study submission only reported residue data from treatment rates bracketing the application rate of 1.2 lb ai/A, which is the maximum single application rate the petitioner wishes to support (see 6/30/2004 Propazine Use Closure Memo) and the rate approved for Section 18 (96-TX-02, dated 1/31/96) use on sorghum for all soil types.

Samples of sorghum forage, grain, and stover were analyzed by a Corning Hazelton analytical method (CHW 6641-106, Method 1, Rev. 1) entitled "Determination of Propazine, Desethyl Atrazine (DEA), and Diamino Atrazine (DAA) in Forage, Grain, and Stover using Capillary Gas Chromatography with Mass-Selective Detection and Nitrogen-Phosphorous Detection," dated 10/16/96. The method determines residues of propazine and the chlorometabolite DEA (aka G-30033) by GC/MSD, while residues of DAA (aka G-28273) are quantitated by GC/NPD. The LOQ for propazine, DEA, and DAA in all sorghum matrices is 0.05 ppm for each analyte. Overall, the method is adequate for data collection based on acceptable concurrent method recovery data.

Samples were stored frozen for 25.7-26.6 months prior to residue analysis. The petitioner stated that a storage stability study has been initiated and will be submitted in a separate report upon completion. In the interim, the petitioner cited the storage stability data submitted in conjunction with a sorghum metabolism study (MRID 44184814). These data indicate that the metabolic profiles of select sorghum extracts are reasonably unchanged after 25 months of freezer storage. The petitioner has also cited the available storage stability data (MRID 41258601) for corn matrices which indicate that residues of DEA and DAA are stable for at least 24 months. A summary of the residue data from the sorghum field trials with propazine is presented below in Table 4.

Commodity	Analyte	Total Applicable Rate (lb ai/A)	PHI (days)	Residue Levels (ppm) <sup>1</sup>						
				n	Min	Max.	HAFT <sup>2</sup>	Median	Mean	Std. Dev
Sorghum forage	Propazine	1.47-2.43	69-117	26	<0.05	<0.05	<0.05	<0.05	<0.05	0.0
	DEA			26	<0.05	<0.05	<0.05	<0.05	<0.05	0.0
	DAA			26	<0.05	0.087	0.078	0.05	0.052	0.008
	Total			26	<0.15	<0.187	<0.178	0.150	0.152	0.008
Sorghum grain	Propazine	1.47-2.43	85-152	26	<0.05	<0.05	<0.05	<0.05	<0.05	0.0
	DEA			26	<0.05	<0.05	<0.05	<0.05	<0.05	0.0
	DAA			26	<0.05	<0.05	<0.05	<0.05	<0.05	0.0
	Total			26	<0.15	<0.15	<0.15	<0.15	<0.15	0.0
Sorghum stover	Propazine	1.47-2.43	86-152	26	<0.05	<0.05	<0.05	<0.05	<0.05	0.0
	DEA			26	<0.05	<0.05	<0.05	<0.05	<0.05	0.0
	DAA			26	<0.05	<0.05	<0.05	<0.05	<0.05	0.0
	Total			26	<0.15	<0.15	<0.15	<0.15	<0.15	0.0

<sup>1</sup> For the determination of minimum, maximum, HAFT, median, mean, and standard deviation values, the LOQ (<0.05 ppm) was used for residues reported as nonquantifiable (NQ).

<sup>2</sup> HAFT = Highest Average Field Trial.

### 860.1520 Processed Food and Feed

Table 1 of OPPTS 860.1000 lists flour as a processed commodity of grain sorghum. At this time, residue data on sorghum flour are not needed since this item is used exclusively in the U.S. as a component for drywall, and not as either human food or a feedstuff. However, because 50% of the worldwide sorghum production goes toward human consumption, data may be needed at a later date.

### 860.1650 Submittal of Analytical Reference Standards

Analytical standards for propazine are currently available at the National Pesticide Standards Repository. However, standards for the chlorometabolites G-30033 and G-28273 are not available and are required. Analytical reference standards of propazine and its chlorometabolites must be supplied and supplies replenished as requested by the Repository. The reference

standards should be sent to the Analytical Chemistry Lab, which is located at Fort Meade, to the attention of either Theresa Cole or Frederic Siegelman at the following address:

USEPA  
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP  
701 Mapes Road  
Fort George G. Meade, MD 20755-5350  
(Note that the mail will be returned if the extended zip code is not used.)

### **860.1850 Confined Accumulation in Rotational Crops**

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The nature of propazine residues in rotational crops is adequately understood. The propazine residues of concern in rotational crops for the purposes of tolerance establishment and risk assessment are consistent with the HED MARC decision memoranda on atrazine (PC Code: 080803) dated 11/15/2000 (D270177) and 2/10/2003 (D288715), the residues of concern in plants for tolerance reassessment are the parent plus the chlorometabolites G-30033 and G-28273. In accordance with decisions made for atrazine and simazine, all risk assessments should be done using parent plus chlorometabolites as the residues of concern for dietary (food + water) assessments. These decisions supercede the Memorandum of Understanding between HED and Griffin Corporation for Propazine (see 1/11/96 memo of M. Metzger).

The Executive Summary of the submitted confined rotational crop study DER is reproduced below.

Griffin Corporation has submitted a confined rotational crop study with propazine. The radiolabeled test substance, [<sup>14</sup>C]propazine (labeled uniformly in the triazine ring, specific activity of 49.42 mCi/mmole), was mixed with formulation blank and applied to bare sandy loam soil in three planting containers at 2.39 lb ai/A. Lettuce, turnip, and spring wheat were planted in the treated soil as rotational crops at PBIs of 29, 120, and 365 days. The in-life phase was conducted by PTRL East, Inc. (Richmond, KY), and the analytical phase was conducted by PTRL West, Inc. (Richmond, CA).

Severe phytotoxicity occurred with the 29-day PBI lettuce and turnip and 365-day PBI turnip crops, and samples were not collected. It was noted that chlorosis was also observed on the tips of immature wheat from the 29-day PBI. The petitioner attributes the better survival of the 120-day PBI crops to the growing environment, because the 29- and 365-day PBI rotations were initiated and mostly maintained outdoors, while the 120-day PBI rotation was conducted entirely in the greenhouse creating a less stressful condition.

TRR accumulated at  $\geq 0.01$  ppm in/on all rotated crops planted 29, 120 or 365 days following treatment. TRR were highest in wheat straw, grain, and forage. Generally, TRR decreased in wheat crop matrices with increased PBIs; however, the TRR actually increased from the 120-day to 365-day PBI in wheat forage and lettuce. At the 29-day PBI, residues were 1.298, 1.680, and 5.787 ppm in wheat forage, grain, and straw, respectively; lettuce and turnips were not sampled

at this plantback interval. At the 120-day PBI, residues were 0.355, 0.928, and 1.987 ppm in wheat forage, grain, and straw, respectively, and 0.057-0.179 ppm in lettuce, turnip tops, and turnip roots. At the 365-day PBI, residues were 0.450, 0.245, and 1.028 ppm in wheat forage, grain, and straw, respectively, and 0.209 ppm in lettuce; turnips were not sampled at this plantback interval.

Extraction with methanol and methanol/water released the majority of the TRR (65-99% TRR) from rotational lettuce, turnip tops and roots, and wheat forage; the majority of the radioactivity was released with the initial methanol extraction. Extraction with methanol and methanol/water was variable in wheat grain and straw: ~50-79% TRR from 29- and 120-day PBI grain and straw and ~16-18% TRR from 365-day PBI grain and straw. Subsequent acid extraction, mild and strong acid hydrolysis, and/or base hydrolysis released ~7-21% TRR in lettuce, ~11-18% TRR in turnip tops and roots, ~14-26% TRR in wheat forage, ~23-61% TRR in wheat grain, and ~19-55% TRR in wheat straw; the majority of the radioactivity in mature wheat matrices (grain and straw) was tightly bound and mostly released with strong acid and base hydrolysis. Nonextractable residues remaining following extraction/hydrolysis accounted for  $\leq 8\%$  TRR in all rotational crop matrices, except for 365-day PBI wheat straw which had 13% TRR (0.135 ppm) as nonextractable residues. A separate subsample was extracted with methanol and methanol/water and partitioned with chloroform to aid in identifying and quantitating residues. The extraction procedures extracted sufficient residues from rotational crop matrices from all PBIs. Accountabilities were ~74-114%.

The petitioner did not provide the dates of sample extraction and analysis; however, based on the study initiation and completion dates, samples may have been stored for up to ~2 years. Re-analysis of the methanol/water extract of 120-day PBI wheat grain indicated that propazine had degraded (from 0.117 ppm to 0.042 ppm) to more polar compounds within 4 months of frozen storage. Re-analysis of the methanol/water extract of 120-day PBI wheat straw indicated a slight decrease in propazine and a corresponding increase in the metabolites, especially atrazine des-ethyl 2-hydroxy within 4 months of frozen storage.

Total identified residues ranged 27-88% TRR in all rotated crop commodities, except in 365-day PBI wheat grain and straw for which only 4-5% TRR was identified. Propazine and the hydroxymetabolite, atrazine des-ethyl 2-hydroxy (GS-17794), were identified in all rotational crop matrices from all plantback intervals. The chlorometabolite atrazine des-ethyl (G-30033) was identified at significant levels in 120-day turnip tops, and 29- and 120-day PBI forage but was a minor component in 120- and 365-day PBI lettuce, 120-day PBI turnip roots, 365-day PBI wheat forage, 29- and 120-day PBI wheat grain and straw; atrazine des-ethyl (G-30033) was not detected in 365-day PBI wheat grain and straw. Another hydroxymetabolite, propazine 2-hydroxy (GS-11526), was identified only in 120-day PBI turnip tops, 29-day PBI wheat forage, 29- and 120-day PBI wheat grain, and 29-day PBI wheat straw. Since propazine 2-hydroxy (GS-11526) was detected only in the earlier plantback intervals, it is likely metabolized further to such compounds such as atrazine des-ethyl 2-hydroxy (GS-17794), which was present at all plantback intervals. Additional minor amounts of propazine, atrazine des-ethyl (G-30033), propazine 2-hydroxy (GS-11526), and/or atrazine des-ethyl 2-hydroxy (GS-17794) were identified in the acid and/or base hydrolysates of wheat forage, grain, and straw. The remaining radioactivity was mostly polar in nature and did not co-elute with any of the reference standards; most individual

peaks were present at <10% TRR or <0.05 ppm. Unknowns from several acid or base hydrolysates could not be further identified because of large matrix co-extractives.

Based on the results of the confined rotational crop study, the petitioner concluded that the primary metabolic products in rotational crops were similar to those found in a sorghum metabolism study (refer to the DER for MRIDs 44184813, 44184814, and 44287315). Propazine metabolism in plants involves N-dealkylation, hydrolysis, and conjugation with glutathione. The petitioner further states that the study results confirm literature concerning the metabolism of other triazine herbicides, except that propazine and chloro-residues were detected in wheat grain in the subject study and chloro-residues are typically not seen in grain with chloro-s-triazine herbicides.

### **860.1900 Field Accumulation in Rotational Crops**

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Two limited field rotational crop trials with propazine were conducted in NC and TX. At each site, a 4 lb/gal flowable concentrate formulation of propazine was applied as a preemergence ground spray to grain sorghum, the primary crop, at a nominal rate of 1.2 lb ai/A (1.0x the proposed single application rate). The primary crop was removed (by cutting) from the plots and approximately 90 days after the test substance application. The following rotational crops were then planted at each field site: radish or turnip (a root vegetable), lettuce or mustard (a leafy vegetable), and winter or spring wheat (a cereal grain). The PBI used in the study were 94, 127, and 242/280 days for the NC field site and 97, 120, 195, and 239 days for the TX field site.

The results of the NC trial indicate that residues of propazine, G-30033, and G-28273 were each below the LOQ of 0.0500 ppm in/on all samples of rotational crop commodities (mustard leaves, turnip tops/roots, and spring/winter wheat forage, hay, straw, and grain) at all tested PBIs (94, 127, and 242/280 days). The results of the TX trial indicate that residues of propazine, G-30033, and G-28273 were each below the LOQ of 0.0500 ppm in/on the following rotational crop commodities and PBIs: (i) lettuce leaves at a 97-day PBI; (ii) radish root at PBIs of 97 and 239 days; (iii) wheat forage at PBIs of 120 and 195 days; (iv) wheat hay, straw, and grain at PBIs of 97, 120, and 195 days. A few rotational crop commodities from the TX trial, however, showed quantifiable residues including: (i) lettuce leaves at the 239-day PBI (propazine was detected at 0.0505-0.0510 ppm, G-30033 at 0.137-0.139 ppm, and G-28273 at 0.139 ppm); (ii) radish tops at the 97-day PBI (propazine was detected at 0.051-0.052 ppm); and (iii) wheat forage at the 97-day PBI (G-30033 was detected at 0.102-0.107 ppm).

In summary, the following label restrictions should be added for rotational crops:

“Do not rotate to leafy vegetables. Do not rotate to root crops or cereals (small grains) at less than a 120-day PBI.”

In addition, the label needs to specify that rotation to all other crops should be restricted to a 12-month PBI.

If shorter or different PBIs are desired by the registrant, then extensive field rotational trial data, as described under OPPTS 860.1900, to determine appropriate tolerances for inadvertent residues of propazine and its chlorometabolites should be submitted.

The Executive Summary of the limited field rotational crop trial DER is reproduced below.

Griffin Corporation has submitted a limited field rotational crop study with propazine. Two trials were conducted in Regions 2 (NC) and 8 (TX). At each trial site, a 4 lb/gal FIC formulation of propazine was applied as a preemergence ground spray to grain sorghum, the primary crop, at a nominal rate of 1.2 lb ai/A. The test substance was applied either on the day of planting (NC) or five days after planting (TX).

The primary crop was to be removed (by cutting) from the plots prior to 90 days after the test substance application since the target PBIs the petitioner initially intended to investigate were 90, 120, and 180 or 210/240 days. However, due to unusually cold and wet weather, the actual plantback intervals used in the study were 94, 127, and 242/280 days for the NC field site and 97, 120, 195, and 239 days for the TX field site. The following rotational crops were planted at the plantback intervals listed above for each field site: radish or turnip (a root vegetable), lettuce or mustard (a leafy vegetable), and winter or spring wheat (a cereal grain). The rotational crops were allowed to grow according to good agricultural practices. It was reported that extremely cold weather during the winter months impacted the development and yield of some crops at both test sites. Samples of radish (roots and tops), turnip (roots and tops), leaf lettuce (leaves), mustard (leaves), wheat (forage, hay, grain, and straw) were collected at appropriate crop growth stage or at maturity.

A GC/MSD method (CHW 6641-101, Method 1) was used for the analysis of harvested crop commodities for residues of propazine and its two chlorometabolites: 2-amino-4-chloro-6-isopropylamino-s-triazine (desethyl atrazine or DEA; aka G-30033) and 2,4-diamino-6-chloro-s-triazine (diamino atrazine or DAA; aka G-28273). The LOQ for propazine, DEA, and DAA in all RACs is 0.0500 ppm for each analyte. The efficiency of the method was verified by fortifying aliquots of control matrix with propazine and its chlorometabolite DAA, each at 0.05, 0.1, and 0.2 ppm and with the chlorometabolite DEA at 0.0575, 0.115, 0.230 ppm. Average method recoveries ranged 86.8-106% for propazine, 83.3-110% for DEA, and 76.7-98.6% for DAA. The method is adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen prior to residue analysis. The maximum storage intervals, from harvest to analysis, were 129 days (4.2 months) for lettuce, 79 days (2.6 months) for mustard leaves, 100 days (3.3 months) for radish tops and roots, 79 days (2.6 months) for turnip tops and roots, 141 days (4.6 months) for wheat forage, 125 days (4.1 months) for wheat hay, and 89 days (2.9 months) for wheat grain and straw. No supporting storage stability data were included in the subject study. In a separate submission for a residue field study on sorghum (MRID 44287316), it was reported that a storage stability study has been initiated and will be submitted in a separate report. It was also reported in a sorghum metabolism study (MRID 44287315) that the metabolic profiles of sorghum extracts did not change 24 months after the initial chromatographic analysis.



The results of the NC trial indicate that residues of propazine, DEA (G-30033), and DAA (G-28273) were each below the LOQ of 0.0500 ppm in/on all samples of rotational crop commodities (mustard leaves, turnip tops/roots, and spring/winter wheat forage, hay, straw, and grain) at all PBIs (94, 127, and 242/280 days).

The results of the TX trial indicate that residues of propazine, DEA (G-30033), and DAA (G-28273) were each below the LOQ of 0.0500 ppm in/on the following rotational crop commodities and plantback intervals: (i) lettuce leaves at a 97-day PBI; (ii) radish root at PBIs of 97 and 239 days; (iii) wheat forage at PBIs of 120 and 195 days; (iv) wheat hay, straw, and grain at PBIs of 97, 120, and 195 days. A few rotational crop commodities showed quantifiable residues including: (i) lettuce leaves at the 239-day PBI which bore residues of propazine (0.0505-0.0510 ppm), DEA (0.137-0.139 ppm), and DAA (0.139 ppm); (ii) radish tops at the 97-day PBI which bore quantifiable residues of propazine (0.051-0.052 ppm) but nondetectable (< LOQ) residues of DEA and DAA; and (iii) wheat forage at the 97-day PBI which bore quantifiable residues of DEA (0.102-0.107 ppm) but nondetectable (< LOQ) residues of propazine and DAA.

The discrepancies of results from the two test locations were attributed by the petitioner to be mainly due the fact that the rotational crops in TX were planted on 10/9/95 which is much later than normal (crops would not typically be planted for commercial production at this time of the year), and the environmental conditions were adverse for plant growth especially for lettuce and radishes.

## **TOLERANCE REASSESSMENT SUMMARY**

The tolerances established under 40 CFR §180.243 are currently defined for residues of propazine *per se*. The Federal Register (Vol. 70, No. 119, June 22, 2005) has recently announced that Griffin Corporation has filed a petition, PP#7F4837, to amend 40 CFR §180.243, by establishing tolerances for residues of propazine and its two chlorometabolites: 2-amino-4-chloro, 6-isopropylamino-s-triazine (G-30033) and 2,4-diamino-6-chloro-s-triazine (G-28273) in/on sorghum stover, forage, and grain at 0.25 ppm. The results of a sorghum metabolism study indicate that the proposed tolerance expression for plants is appropriate. Therefore, HED is recommending the revision of the residue definition under 40 CFR §180.243 to specify tolerances for the combined residues of propazine and the chlorometabolites G-30033 and G-28273.

Tolerances for propazine residues of concern in meat, milk, poultry, and eggs are not required for the purpose of this grain sorghum petition only. The results of the reviewed ruminant and poultry metabolism studies suggest a Category 3 situation with regard to the need for livestock commodity tolerances as per 40 CFR §180.6(a)(3). There is no expectation of finite residues of propazine and its chlorometabolites in livestock commodities as a result of the proposed use on grain sorghum. Thus, livestock feeding studies are not needed, and tolerances need not be established for meat, milk, poultry, and eggs.

This decision was supported by HED Science Advisory Council for Chemistry (ChemSAC) (meeting date 11/30/05) based on the practical considerations regarding the likelihood that forage from sorghum grown for grain; i.e., it is not very likely that forage from grain sorghum will be fed to dairy and beef cattle. However, if in the future, the registrant petitions for propazine uses on additional livestock feed items, then livestock feeding studies conducted in accordance with OPPTS Guideline 860.1480 (Meat, Milk, Poultry, Eggs) will be required as a part of that petition.

The reassessed tolerance levels of 0.15 ppm on sorghum stover and grain and 0.20 ppm on forage for the combined residues of propazine and the chlorometabolites G-30033 and G-28273 are supported by adequate data pending submission of supporting storage stability data and label revision. Following a single preemergence broadcast application of a representative FIC formulation of propazine at 1.47-2.43 lb ai/A (1.2-2.0x the proposed single application rate), the results of the sorghum field trials indicate the following: In **sorghum forage** harvested at a PHI range of 69-117 days, residues of propazine and G-30033 were each less than the LOQ (<0.05 ppm) in/on 26 treated samples. Residues of G-28273 ranged 0.050-0.087 ppm in/on four treated forage samples but were <0.05 ppm in/on 22 treated samples. In **sorghum grain and stover** harvested at a PHI range of 86-152 days, residues of propazine, G-30033, and G-28273 were each <0.05 ppm in/on 26 treated samples.

These field trial residue data were used to reassess the existing tolerances for sorghum, *grain*, *grain*; sorghum, *grain*, *stover*; and sorghum, *grain*, *forage*. Specifically, the tolerance maximum residue limit (MRL) harmonization spreadsheet was used with the residue data from the field trials to calculate reassessed tolerances. The residue data used are described in "Magnitude of the Residue of Propazine (2-Chloro-4,6-bis (isopropylamino)-s-triazine) and its Metabolites in/on Grain Sorghum Forage, Grain, and Stover Harvested After Preemergence Ground Application of Milo-Pro 4L Herbicide", 1997. (MRID 44287316).

The established tolerance for sweet sorghum should be revoked unless propazine use on sweet sorghum is proposed and supporting residue data are submitted.

HED recommends that the designation "(N)" be deleted from the 40 CFR for all tolerance level entries and that the chemical name of propazine be revised to "6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine." A summary of propazine tolerance reassessment is presented in Table 5.

**Table 5. Tolerance Reassessment Summary for Propazine.**

Commodity	Current Tolerance Listed in 40 CFR §180.243 (ppm)	Reassessed Tolerance (ppm)	Comments [ <i>Correct Commodity Definition</i> ]
Sorghum, forage	0.25 (N)	0.20	Sorghum, grain, forage
Sorghum, grain	0.25 (N)	0.15	Sorghum, grain, grain
Sorghum, grain, stover	0.25 (N)	0.15	
Sorghum, sweet	0.25 (N)	Revoke	No registered uses on sweet sorghum.

### Codex/International Harmonization

There is no Canadian tolerance, Mexican tolerance, or Codex MRL for residues of propazine in/on sorghum; therefore, no compatibility questions exist with respect to the Codex MRL.

Attachments:

Attachment 1. International Residue Limit Status

## ATTACHMENT I

INTERNATIONAL RESIDUE LIMIT STATUSCHEMICAL: PropazineCODEX NO.:CODEX STATUS:\_\_\_ No Codex Proposal  
Step 6 or abovePROPOSED U.S. TOLERANCES:Petition No: PP#7F4837Agency Reviewer: José J. MoralesResidue (if Step 8):Residues Proposed For Inclusion in the  
Tolerance Expression: Propazine and its two  
chlorometabolites G-30033 and G-28273

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>	<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
		Sorghum, stover .....	0.25
		Sorghum, forage .....	0.25
		Sorghum, grain .....	0.25

CANADIAN LIMITS:

\_\_\_ No Canadian limit

Residue:

MEXICAN LIMITS:

\_\_\_ No Mexican limit

Residue:

<u>Crop(s)</u>	<u>Limit (mg/kg)</u>	<u>Crop(s)</u>	<u>Limit (mg/kg)</u>
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NOTES:

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**AGENCY MEMORANDA RELEVANT TO THIS RESIDUE CHEMISTRY CHAPTER**

CB No.	DP Barcode	ID No.	Date	Reviewer	MRID	Topic
	D310517 D308537		8/31/05	J. Morales & G. Kramer	44184813, 44184814, 44287315, 44184815, 44184816, 44184817, 44287316, 44184810, and 44184811	Propazine (080808). Proposed New Use on Grain Sorghum. Pettitone Griffin Corporation. HED Review of Sorghum, Ruminant, and Poultry Metabolism Studies, Sorghum Field Trials; Confined Rotational Crop Study, and Limited Field Accumulation Trials.
17214	D226108 and D226191		5/28/96	J. Abbotts	None	Propazine (080808), Proposed New Use on Sorghum. Registrant Griffin Corporation. Residue Chemistry Requirements.
16780 and 17099	D222623 and D224749		5/14/96	J. Abbotts	None	Propazine (080808). Reregistration Case No. 0230. Registrant Griffin Corporation. Dietary and Drinking Water Health Hazard Assessment
None	None		3/7/96	J. Abbotts	None	Propazine (080808), Reregistration Case No. 0230. Conversations with Registrant Representative
None	None		1/11/96	M. Metzger	None	Propazine. Response to Meeting (8/2/95) Memorandum of Understanding Submitted by Griffin
12729	D196214		3/23/94	J. Herndon	None	Review of the Proposed Protocols for Conducting the Following Studies Using <sup>14</sup> C-Labeled Propazine: Nature of the Residue in Sorghum; Nature of the Residue in Lactating Goats; Nature of the Residue in Laying Hens; and Confined Rotational Crops.
11696	D190115	93TX0014	4/19/93	M. Bradley	None	Section 18 Exemption for Use of Propazine on Sorghum




Primary Evaluator:

  
George F. Kramer, Ph.D., Chemist  
Registration Action Branch 1 (RAB1)  
Health Effects Division (HED) (7509C)

Date: 07-DEC-2005

Approved by:

  
P.V. Shah, Ph.D., Branch Senior  
Scientist/RAB1/HED (7509C)

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This DER was originally prepared under contract by Dynamac Corporation (20440 Century Boulevard, Suite 100; Germantown, MD 20874; submitted 07/13/2005). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

### **STUDY REPORT:**

44184810 Jalali, K.; Saber, A.; Hiler, R. *et al.* (1996) [<sup>14</sup>C]Propazine: A Confined Rotational Crop Study: Lab Project Number: 859E/513W: 859E/513W-1: 859E/104S. Unpublished study prepared by PTRL West, Inc. and PTRL East, Inc. 464 p.

### **EXECUTIVE SUMMARY:**

Griffin Corporation has submitted a confined rotational crop study with propazine. The radiolabeled test substance, [<sup>14</sup>C]propazine (labeled uniformly in the triazine ring, specific activity of 49.42 mCi/mmole), was mixed with formulation blank and applied to bare sandy loam soil in three planting containers at 2.39 lb ai/A. Lettuce, turnip, and spring wheat were planted in the treated soil as rotational crops at plantback intervals (PBIs) of 29, 120, and 365 days. The in-life phase was conducted by PTRL East, Inc. (Richmond, KY), and the analytical phase was conducted by PTRL West, Inc. (Richmond, CA).

Severe phytotoxicity occurred with the 29-day PBI lettuce and turnip and 365-day PBI turnip crops, and samples were not collected. It was noted that chlorosis was also observed on the tips of immature wheat from the 29-day PBI. The petitioner attributes the better survival of the 120-day PBI crops to the growing environment, because the 29- and 365-day PBI rotations were initiated and mostly maintained outdoors, while the 120-day PBI rotation was conducted entirely in the greenhouse creating a less stressful condition.

Total radioactive residues (TRR) accumulated at  $\geq 0.01$  ppm in/on all rotated crops planted 29, 120 or 365 days following treatment. TRR were highest in wheat straw, grain, and forage. Generally, TRR decreased in wheat crop matrices with increased PBIs; however, the TRR actually increased from the 120-day to 365-day PBI in wheat forage and lettuce. At the 29-day PBI, residues were 1.298, 1.680, and 5.787 ppm in wheat forage, grain, and straw, respectively; lettuce and turnips were not sampled at this plantback interval. At the 120-day PBI, residues were 0.355, 0.928, and 1.987 ppm in wheat forage, grain, and straw, respectively, and 0.057-0.179 ppm in lettuce, turnip tops, and turnip roots. At the 365-day PBI, residues were 0.450,



0.245, and 1.028 ppm in wheat forage, grain, and straw, respectively, and 0.209 ppm in lettuce; turnips were not sampled at this plantback interval.

Extraction with methanol and methanol/water released the majority of the TRR (65-99% TRR) from rotational lettuce, turnip tops and roots, and wheat forage; the majority of the radioactivity was released with the initial methanol extraction. Extraction with methanol and methanol/water was variable in wheat grain and straw: ~50-79% TRR from 29- and 120-day PBI grain and straw and ~16-18% TRR from 365-day PBI grain and straw. Subsequent acid extraction, mild and strong acid hydrolysis, and/or base hydrolysis released ~7-21% TRR in lettuce, ~11-18% TRR in turnip tops and roots, ~14-26% TRR in wheat forage, ~23-61% TRR in wheat grain, and ~19-55% TRR in wheat straw; the majority of the radioactivity in mature wheat matrices (grain and straw) was tightly bound and mostly released with strong acid and base hydrolysis. Nonextractable residues remaining following extraction/hydrolysis accounted for ≤8% TRR in all rotational crop matrices, except for 365-day PBI wheat straw which had 13% TRR (0.135 ppm) as nonextractable residues. A separate subsample was extracted with methanol and methanol/water and partitioned with chloroform to aid in identifying and quantitating residues. The extraction procedures extracted sufficient residues from rotational crop matrices from all PBIs. Accountabilities were ~74-114%.

The petitioner did not provide the dates of sample extraction and analysis; however, based on the study initiation and completion dates, samples may have been stored for up to ~2 years. Re-analysis of the methanol/water extract of 120-day PBI wheat grain indicated that propazine had degraded (from 0.117 ppm to 0.042 ppm) to more polar compounds within 4 months of frozen storage. Re-analysis of the methanol/water extract of 120-day PBI wheat straw indicated a slight decrease in propazine and a corresponding increase in the metabolites, especially atrazine des-ethyl 2-hydroxy within 4 months of frozen storage.

Total identified residues ranged 27-88% TRR in all rotated crop commodities, except in 365-day PBI wheat grain and straw for which only 4-5% TRR was identified. Propazine and the hydroxymetabolite, atrazine des-ethyl 2-hydroxy (GS-17794), were identified in all rotational crop matrices from all plantback intervals. The chlorometabolite atrazine des-ethyl (G-30033) was identified at significant levels in 120-day turnip tops, and 29- and 120-day PBI forage but was a minor component in 120- and 365-day PBI lettuce, 120-day PBI turnip roots, 365-day PBI wheat forage, 29- and 120-day PBI wheat grain and straw; atrazine des-ethyl (G-30033) was not detected in 365-day PBI wheat grain and straw. Another hydroxymetabolite, propazine 2-hydroxy (GS-11526), was identified only in 120-day PBI turnip tops, 29-day PBI wheat forage, 29- and 120-day PBI wheat grain, and 29-day PBI wheat straw. Since propazine 2-hydroxy (GS-11526) was detected only in the earlier plantback intervals, it is likely metabolized further to such compounds such as atrazine des-ethyl 2-hydroxy (GS-17794), which was present at all plantback intervals. Additional minor amounts of propazine, atrazine des-ethyl (G-30033), propazine 2-hydroxy (GS-11526), and/or atrazine des-ethyl 2-hydroxy (GS-17794) were identified in the acid and/or base hydrolysates of wheat forage, grain, and straw. The remaining radioactivity was mostly polar in nature and did not co-elute with any of the reference standards; most individual



peaks were present at <10% TRR or <0.05 ppm. Unknowns from several acid or base hydrolysates could not be further identified because of large matrix co-extractives.

Based on the results of the confined rotational crop study, the petitioner concluded that the primary metabolic products in rotational crops were similar to those found in a sorghum metabolism study (refer to the DER for MRIDs 44184813, 44184814, and 44287315). Propazine metabolism in plants involves N-dealkylation, hydrolysis, and conjugation with glutathione. The petitioner further states that the study results confirm literature concerning the metabolism of other triazine herbicides, except that propazine and chloro-residues were detected in wheat grain in the subject study and chloro-residues are typically not seen in grain with chloro-s-triazine herbicides.

### **STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:**

Under the conditions and parameters used in the study, the confined rotational crop residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision (TRED) Document for propazine.

### **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.

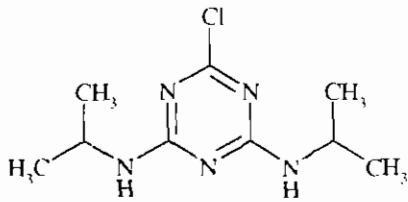
### **A. BACKGROUND INFORMATION**

Propazine (6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine) is a member of the chloro triazine class of herbicides. Other members of this pesticide class include atrazine, cyanazine, and simazine. Propazine is a selective herbicide that can be applied before planting, at planting, and after crop emergence for the preemergence control of annual broadleaf weeds. Currently, the only registered uses are for weed control of ornamental plants grown in containers under greenhouse conditions. There are presently no registered food/feed uses of propazine.

Propazine was previously registered for use on sorghum. The 5/19/87 Propazine Residue Chemistry Chapter along with the 12/88 Propazine Reregistration Standard (Guidance Document) identified several data deficiencies for the reregistration of propazine. Ciba-Geigy, which was then the basic manufacturer of propazine, elected to cancel its registrations of propazine. Another registrant, Griffin Corporation, is now supporting the previously-cancelled uses of propazine on grain sorghum. The structure and nomenclature of propazine are presented in Table A.1. The physicochemical properties of propazine are listed in Table A.2.



**TABLE A.1. Propazine Nomenclature**

PC Code 006308	
Chemical structure	
Common name	Propazine
Molecular Formula	C <sub>9</sub> H <sub>16</sub> N <sub>5</sub> Cl
Molecular Weight	229.7
IUPAC name	6-chloro- <i>N,N'</i> -diisopropyl-1,3,5-triazine-2,4-diamine
CAS name	6-chloro- <i>N,N'</i> -bis(1-methylethyl)-1,3,5-triazine-2,4-diamine
CAS #	139-40-2

**TABLE A.2. Physicochemical Properties of Propazine**

Parameter	Value	Reference
Melting point	217.7 °C	RD D219079, 9/26/95, S. Malak
pH	5.66	
Density, bulk density, or specific gravity	0.46 g/mL	
Water solubility	3.8 ppm at 25 °C	
Solvent solubility (at 25 °C)	14,252 ppm in acetone 4,696 ppm in 1-octanol	
Vapor pressure	2.9 x 10 <sup>-8</sup> mm Hg at 20 °C  2.98 x 10 <sup>-5</sup> Torr at 45 °C	Product Chemistry Chapter of the Propazine Reregistration Standard. 5/19/87  RD D219079, 9/26/95, S. Malak
Dissociation constant, pK	Not applicable; practically insoluble in water.	RD D219079, 9/26/95, S. Malak
Octanol/water partition coefficient	P = 1234.7 Log P = 3.08	



## B. EXPERIMENTAL DESIGN

### B.1. Test Site and Crop Information

Testing Environment and location	Soil characteristics <sup>1</sup>						
	Type	% Sand	% Silt	% Clay	%OM	pH	CEC (meq/100 g)
Planting containers (2.5x3.0x2.25 feet) at PTRL East (Richmond, KY)	Sandy loam <sup>2</sup>	72.3	19.3	8.3	2.83	6.99	5.8

<sup>1</sup> %OM = % Organic Matter, CEC = Cation Exchange Capacity.

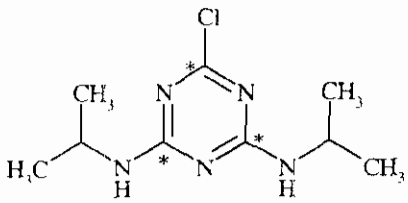
<sup>2</sup> Same soil as used for an aerobic soil metabolism study (PTRL East Project No. 865E)

Nine planting containers were used for the study; three containers were used for each plantback rotation (1 for control, 1 for wheat, and 1 for lettuce and turnips). Typically, planting containers were kept outdoors in a fenced screenhouse area, except the 29- and 120-day planting containers which were moved to a greenhouse with the onset of cold weather and kept there for the duration of the study. The crops were watered, fertilized, hand weeded, and sprayed with maintenance chemicals as needed. A listing of the daily temperature and rainfall recordings during the course of the study was included in the submission. No unusual weather conditions were reported.

Crop, crop group	Variety	Plantback intervals (days)	Growth stage at harvest	Harvested RAC	Harvesting procedure
Lettuce, Vegetable, leafy, except brassica, group 4	Bibb	29, 120, 365	Mature, 53-55 days after planting (DAP)	Leaves	Cut at the soil level using a razor blade
Turnip, Vegetable, root and tuber, group 1, and Vegetable, leaves of root and tuber, group 2	Purple Top Globe	29, 120, 365	Mature, 53-55 DAP	Tops and roots	Foliage was first cut at the soil level using a razor blade, and roots were pulled from the ground and rinsed with water to remove adhering soil.
Spring wheat, Grain, cereal, group 15, and Grain, cereal, forage, fodder, and straw, group 16	Amdon Hard Red	29, 120, 365	Boot stage, 53-55 DAP	Forage	Actual harvest procedures were not discussed. Wheat heads were separated from the straw
			Mature, tiller browning, 133-144 DAP	Straw and grain	



## B.2. Test Materials

Chemical structure	
Radiolabel position	[ring-U- <sup>14</sup> C]propazine
Lot No.	812B-13
Purity	99.9% radiochemical purity (HPLC)
Specific activity	49.42 mCi/mmol; 21.440 dpm/μg (isotopically diluted test substance)

## B.3. Study Use Pattern

Chemical name	[ <sup>14</sup> C]propazine
Application method	The radiolabeled test material was mixed with nonlabeled propazine, and Milo Pro 4L formulation blank, and diluted with water for broadcast spray application to the bare soil.
Application rate	2.39 lb ai/A
Number of applications	One
Timing of applications	Applications were made 29 days prior to the first planting rotation.
PHI (days)	Not applicable

## B.4. Identification/Characterization of Residues

### B.4.1. Sample Handling and Preparation

All rotated crop samples were placed in Ziploc™ bags and stored in a cooler with dry ice at harvest. The samples were frozen and shipped from PTRL East, Inc. to the initial facility (PTRL South, Inc.; Greensboro, NC) within 13 days of harvest, where they were then shipped to PTRL West, Inc. (Richmond, CA) for analysis, or samples were directly shipped to PTRL West. All samples were stored frozen (<0 °C) throughout the study. Samples were cut into small pieces when possible, and homogenized with dry ice.

All rotational crop commodities from all PBIs were subjected to extraction procedures, except for 29-day PBI lettuce and turnips, and 365-day PBI turnips which could not be collected due to severe phytotoxicity. Subsamples of rotational crop commodities were initially extracted with methanol and methanol:water (1:1, v:v). Various subsamples were then extracted with 0.1% HCl, and/or subjected to acid and/or base hydrolysis for 4-6 hours. The specific procedures for





each crop matrix following initial extraction with methanol and methanol/water is outlined below.

The methanol extract of 120- and 365-day PBI lettuce (subsample A) was reserved for high-performance liquid chromatography (HPLC) analysis. Nonextractable residues were then further extracted with 0.1% HCl and hydrolyzed with 6 N HCl at reflux. The 365-day PBI lettuce nonextractable residues were also hydrolyzed with 3 N NaOH at reflux following acid hydrolysis.

The methanol extract of 120-day PBI turnip tops and roots (subsample A) was reserved for HPLC analysis. Nonextractable residues of turnip tops were then further extracted with 0.1% HCl and sequentially hydrolyzed with 0.1 N HCl, 6 N HCl at 80 °C and 3 N NaOH at reflux. Nonextractable residues of turnip roots were further extracted with 0.1% HCl and hydrolyzed with 6 N HCl at reflux.

The methanol extract of 29- and 365-day PBI wheat forage (subsample A) was analyzed by HPLC. To further characterize radioactivity, the methanol extract of 29-day PBI forage was fractionated on a SCX (strong cation-exchange) solid-phase extraction (SPE) column; the major fraction, which was retained on the column and eluted with 0.15 M NaCl:acetonitrile (ACN) (2:1; v:v; pH 11), was reserved for HPLC analysis. The methanol and methanol/water extracts of 120-day PBI wheat forage (subsample A) were combined for HPLC analysis. Nonextractable residues of 29- and 120-day PBI forage were further extracted with 0.1% HCl. Nonextractable residues of forage (all PBIs) were then sequentially hydrolyzed with 0.1 N HCl, 6 N HCl at 80 °C and 3 N NaOH at reflux.

The methanol and methanol/water extracts of wheat grain heads (all PBIs; subsample A) were respectively combined and analyzed by HPLC. To further characterize radioactivity, the extracts of 29- and 120-day PBI grain heads were fractionated on a SCX SPE column; the major two fractions, which were retained on the column and eluted with 0.15 M NaCl:acetonitrile (ACN) (2:1; v:v; pH 11), were reserved for HPLC analysis. Nonextractable residues of 29-day PBI grain heads were further extracted with 0.1% HCl. Nonextractable residues of grain heads (all PBIs) were then sequentially hydrolyzed with 0.1 N HCl, 6 N HCl at reflux and 3 N NaOH at reflux.

The methanol and methanol/water extracts of wheat straw (all PBIs; subsample A) were respectively combined and analyzed by HPLC. To further characterize radioactivity, the extract of 29-day PBI straw were fractionated on a SCX SPE column; the major fractions eluted were reserved for HPLC analysis. Nonextractable residues of 29-day PBI straw were further extracted with 0.1% HCl. Nonextractable residues of straw (all PBIs) were then sequentially hydrolyzed with 0.1 N HCl, 6 N HCl at reflux and 3 N NaOH at reflux.

To investigate the incorporation pattern of residues into various plant components, an alternate extraction scheme was also conducted on 29-day PBI wheat straw, because it bore the highest TRR level. A subsample of 29-day PBI straw was extracted with methanol and methanol/water as described previously and the extracts were combined for HPLC analysis. The nonextractable residues were then sequentially subjected to the following: (i) phosphate buffer (pH 7)



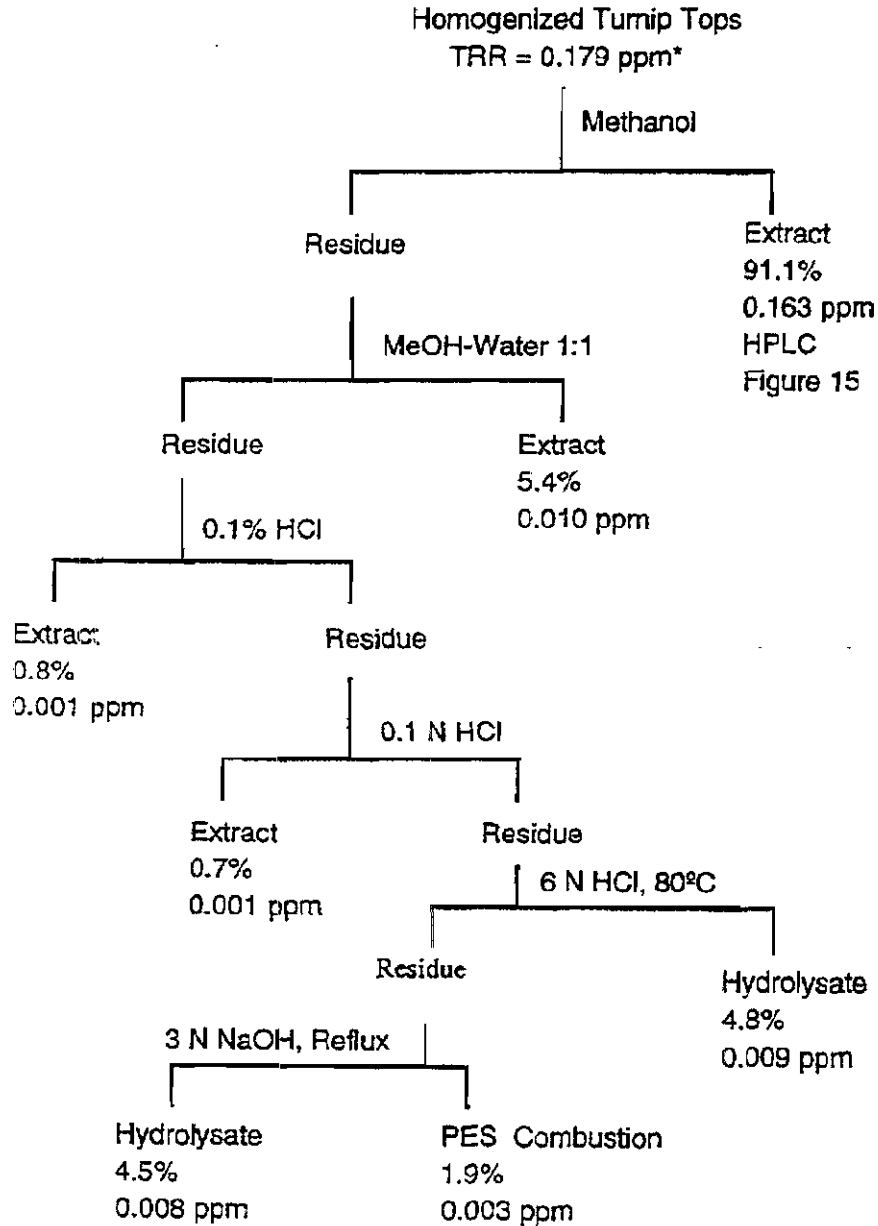
extraction: (ii) starch digestion with  $\alpha$ -Amylase in a water bath at 30 °C for 20 hours; (iii) protein digestion with Pronase E in a water bath at 25 °C for 20 hours; (iv) pectin extraction with 0.05 M EDTA:0.05 M sodium acetate (1:1, v:v; pH 4.5) incubated at 70 °C for 22 hours; (v) lignin extraction with acetic acid and sodium chloride (added four times) in a water bath incubated at 70 °C for a total of 5 hours; (vi) hemicellulose extraction with aqueous potassium hydroxide in a water bath at 25 °C for 40 minutes, followed by shaking with HCl; and (vii) cellulose extraction with sulfuric acid at room temperature for 4 hours, followed by neutralization with aqueous potassium hydroxide. Each extract/hydrolysate was analyzed by HPLC.

A separate subsample (designated subsample B or C) of each of the rotated crop matrices, was also subjected to methanol and methanol/water extraction as described above, and the combined extracts were partitioned with chloroform to selectively remove chlorometabolites. The aqueous and chloroform phases were separated and analyzed by HPLC. For 365-day PBI wheat straw, the combined methanol/water extracts were concentrated and filtered which resulted in two layers (aqueous and organic), and the aqueous layer was analyzed by HPLC.

The extraction procedures for the rotational crop matrices are summarized in the flow charts below, which were copied without alteration from MRID 44184810. We note that a flowchart was included for each crop and each extraction procedure; however, only the flowcharts for 120-day PBI turnip tops and 29-day PBI wheat straw are presented herein as representative of all possible extraction steps.

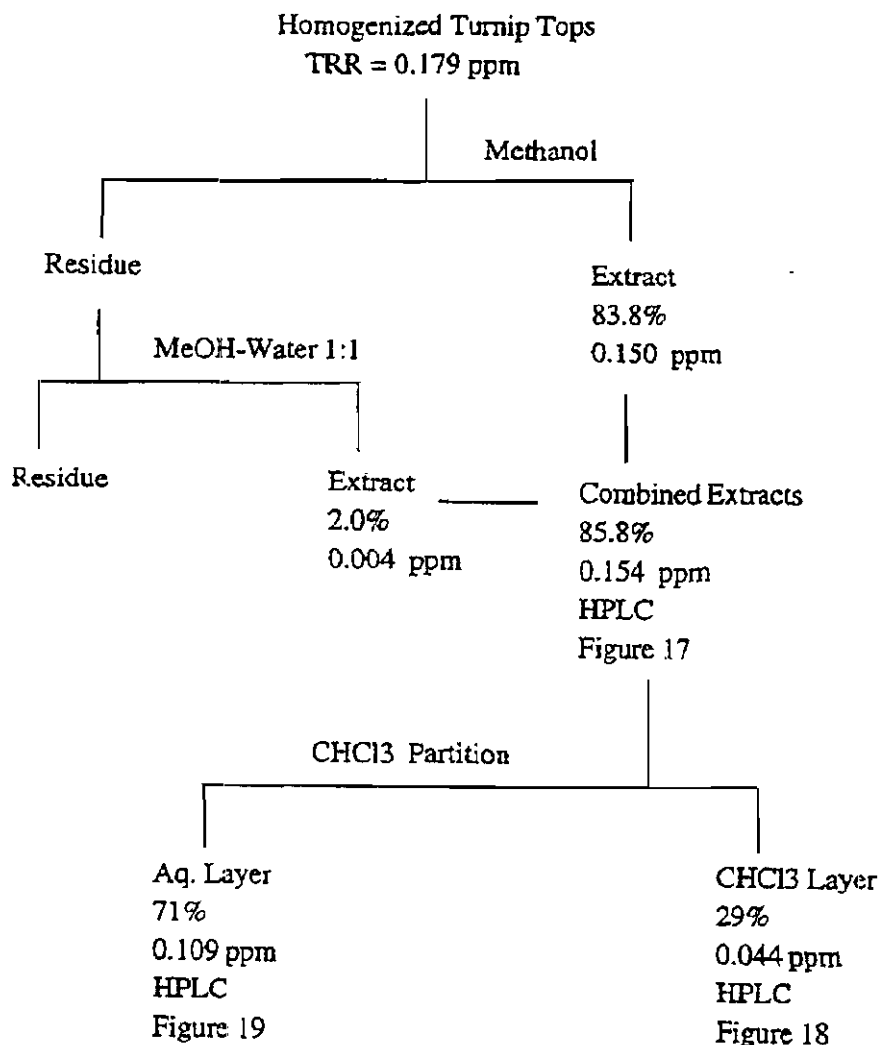


### Extraction Procedure for 120-Day PBI Turnip Tops (Subsample A)



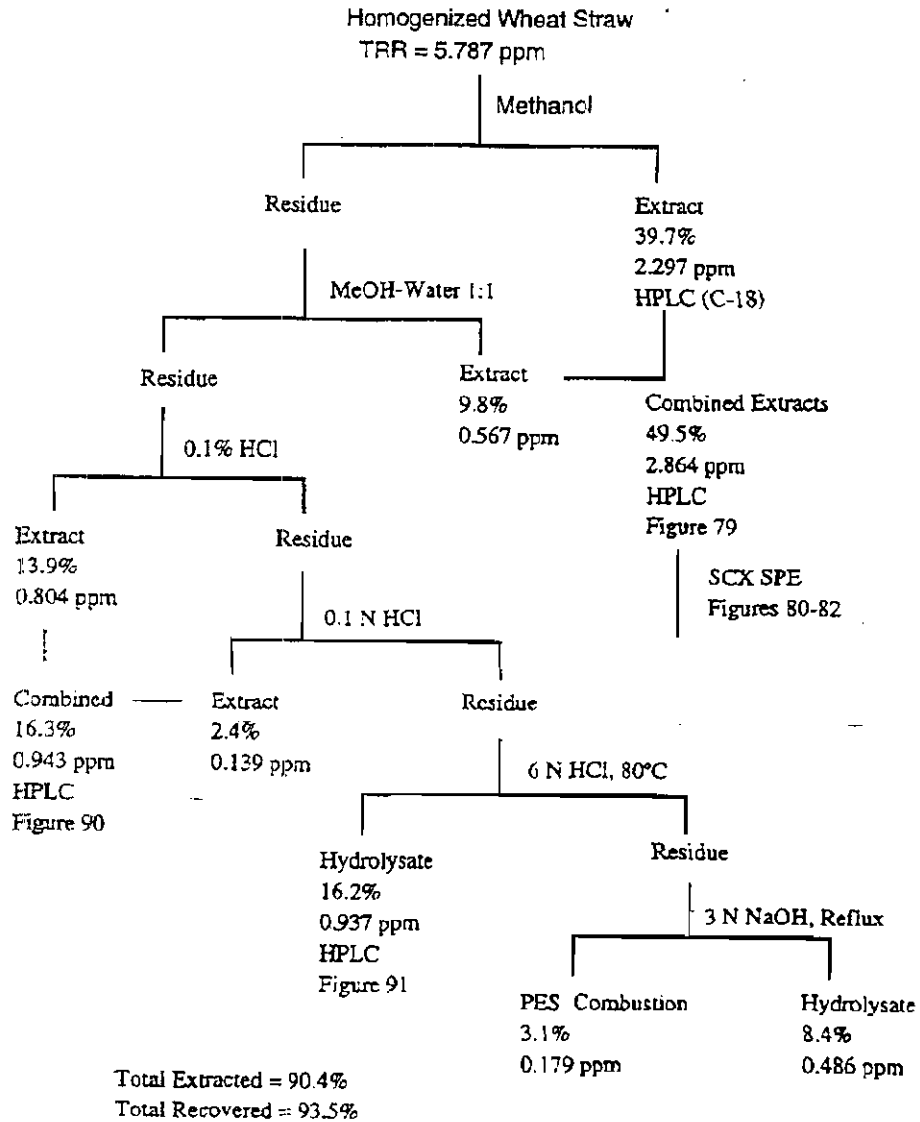


### Extraction Procedure for 120-Day PBI Turnip Tops (Subsample C)



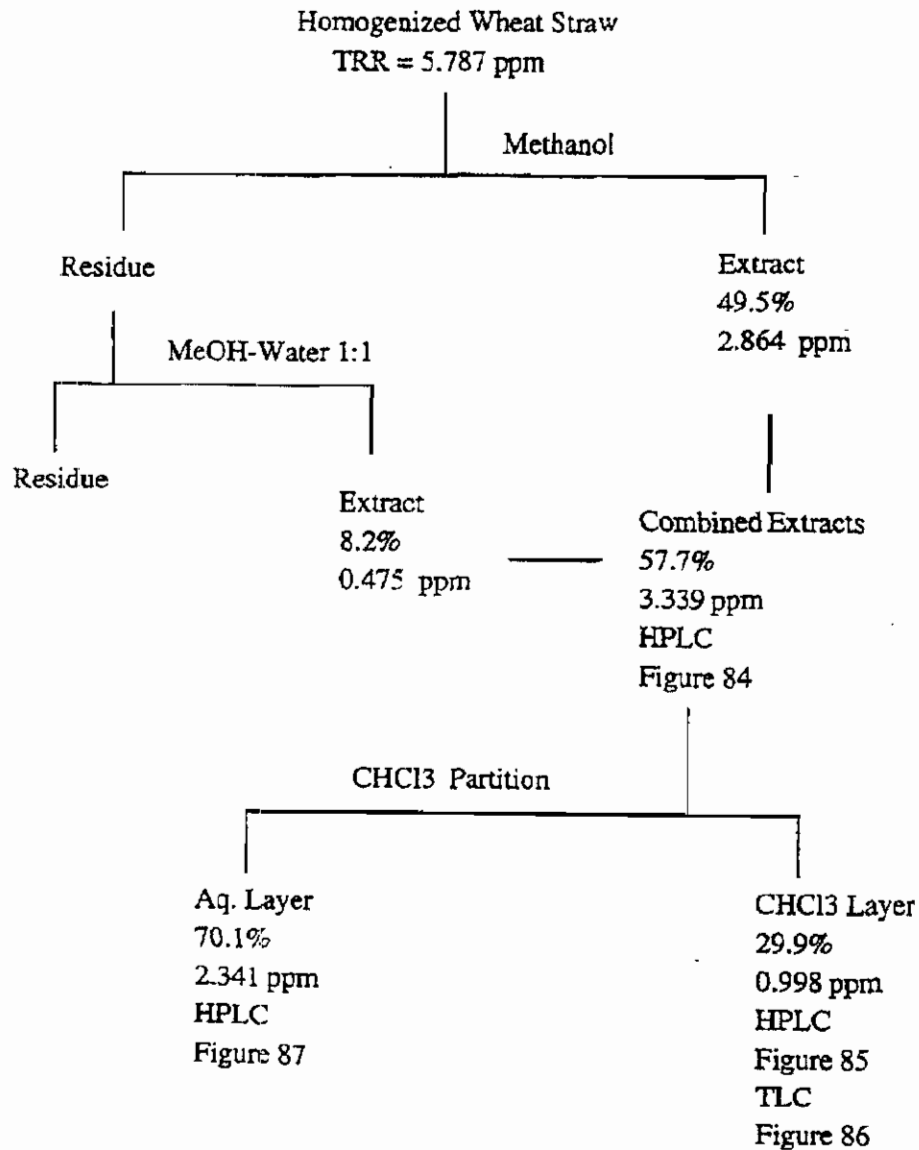


**Extraction Procedure for 29-Day PBI Wheat Straw (Subsample A)**





### Extraction Procedure for 29-Day PBI Wheat Straw (Subsample C)





#### **B.4.2. Analytical Methodology**

TRR in rotational crop matrices were determined by combustion/liquid-scintillation counting (LSC). Extracts and hydrolysates were radioassayed by LSC and nonextractable residues were radioassayed by combustion/LSC. The limit of detection (LOD) for LSC determinations using a 0.5 g sample with a background of 30 dpm, was calculated as 0.0010 ppm.

Extracts and hydrolysates of rotational crop matrices were subjected to reverse-phase and cation-exchange HPLC analyses for identification and quantification of residues. HPLC analyses were conducted on systems equipped with a ultraviolet (UV) detector. Radiolabeled compounds were detected by radioassaying fractions which were collected every 30 seconds; HPLC radiochromatograms were reconstructed using a radiochromatograph program. The following column/mobile phase combinations were used: (Method I) analytical C18 column with a gradient mobile phase of 0.1% phosphoric acid and ACN with 0.1% phosphoric acid; (Method II) analytical cation-exchange column with a gradient mobile phase of 0.1 N phosphoric acid:0.05 M sodium chloride (1:1, v:v; pH 3.5) and 0.15 M sodium chloride:ACN (2:1, v:v). The LOD for the reconstructed HPLC radiochromatograms was based on the limit of detection for the LSC data, i.e., 2x background.

Confirmation of the identification of the test material and its metabolites was performed using thin-layer chromatography (TLC) analyses. TLC analyses were conducted using silica gel F254 plates and two solvent systems: chloroform:methanol:formic acid:water (75:10:1:1, v:v:v:v) and butanol:acetic acid:water (6:1:1, v:v:v). For 1D TLC analyses, one of the solvent systems was used; for 2D TLC analyses, both solvent systems were used.

### **C. RESULTS AND DISCUSSION**

The storage conditions for rotational crop samples are presented in Table C.1. The petitioner did not provide the dates of sample extraction and analysis; however, based on the study initiation and completion dates samples may have been stored for up to ~2 years. Re-analysis of the methanol/water extract of 120-day PBI wheat grain indicated that propazine had degraded (from 0.117 ppm to 0.042 ppm) to more polar compounds with 4 months frozen storage. Re-analysis of the methanol/water extract of 120-day PBI wheat straw indicated a slight decrease in propazine and a corresponding increase in the metabolites, especially atrazine des-ethyl 2-hydroxy with 4 months frozen storage. To supplement the storage stability data from this study, HED will rely on the additional data submitted from the sorghum metabolism study.

TRR in rotational crops are reported in Table C.2.1. Severe phytotoxicity occurred with the 29-day PBI lettuce and turnip and 365-day PBI turnip crops, and samples were not collected. It was noted that chlorosis was also observed on the tips of immature wheat from the 29-day PBI. The petitioner attributes the better survival of the 120-day PBI crops to the growing environment, because the 29- and 365-day PBI rotations were initiated and mostly maintained outdoors, while



the 120-day PBI rotation was conducted entirely in the greenhouse creating a less stressful condition.

TRR accumulated at  $\geq 0.01$  ppm in all rotated crops planted 29, 120 or 365 days following a single application of [ $^{14}\text{C}$ ]propazine to bare soil at a total rate of 2.39 lb ai/A. TRR were highest in wheat straw, grain, and forage. Generally TRR decreased in wheat crop matrices with increased PBIs; however, TRR actually increased from the 120-day to 365-day PBI in wheat forage and lettuce. At the 29-day PBI, residues were 1.298, 1.680, and 5.787 ppm in wheat forage, grain, and straw, respectively; lettuce and turnips were not sampled at this plantback interval. At the 120-day PBI, residues were 0.355, 0.928, and 1.987 ppm in wheat forage, grain, and straw, respectively, and 0.057-0.179 ppm in lettuce, turnip tops, and turnip roots. At the 365-day PBI, residues were 0.450, 0.245, and 1.028 ppm in wheat forage, grain, and straw, respectively, and 0.209 ppm in lettuce; turnips were not sampled at this plantback interval.

The extraction profiles and distribution of the radioactivity in rotational crop matrices are presented in Tables C.2.2.1 through C.2.2.5. Extraction with methanol and methanol/water released the majority of the TRR (65-99% TRR) from rotational lettuce, turnip tops and roots, and wheat forage; the majority of the radioactivity was released with the initial methanol extraction. Extraction with methanol and methanol/water was variable in wheat grain and straw: ~50-79% TRR from 29- and 120-day PBI grain and straw and ~16-18% TRR from 365-day PBI grain and straw. Subsequent acid extraction, mild and strong acid hydrolysis, and/or base hydrolysis released ~7-21% TRR in lettuce, ~11-18% TRR in turnip tops and roots, ~14-26% TRR in wheat forage, ~23-61% TRR in wheat grain, and ~19-55% TRR in wheat straw; the majority of the radioactivity in mature wheat matrices (grain and straw) was tightly bound and released with strong acid and base hydrolysis. Nonextractable residues remaining following extraction/hydrolysis accounted for  $\leq 8\%$  TRR in all rotational crop matrices, except for 365-day PBI wheat straw (13.1% TRR, 0.135 ppm nonextractable). A separate subsample was extracted with methanol and methanol/water and partitioned with chloroform to aid in identifying and quantitating residues. The extraction procedures extracted sufficient residues from rotational crop matrices from all PBIs. Accountabilities were ~74-114%.

The characterization and identification of residues in rotational crop matrices are summarized in Tables C.2.3.1 through C.2.3.5. Total identified residues ranged 27-88% TRR in all rotated crop commodities, except in 365-day PBI grain and straw for which only 4-5% TRR was identified. Propazine was identified in all rotational crop matrices from all plantback intervals, but appears to decrease with the longer plantback intervals: 20% and 11% TRR in 120- and 365-day PBI lettuce; 43% and 11% TRR in 120-day PBI turnip tops and roots; 39%, 33%, and 13% TRR in 29-, 120-, and 365-day PBI wheat forage, respectively; 15%, 13%, <1% TRR in 29-, 120-, and 365-day PBI wheat grain, respectively; and 16%, 21%, and <1% TRR in 29-, 120-, and 365-day PBI wheat straw, respectively. Atrazine des-ethyl, another chloro-residue, was identified at significant levels (11-15% TRR) in 120-day turnip tops, and 29- and 120-day PBI forage. Atrazine des-ethyl was identified at minor levels (<10% TRR) in 120- and 365-day PBI lettuce, 120-day PBI turnip roots, 365-day PBI wheat forage, 29- and 120-day PBI wheat grain and straw; atrazine des-ethyl was not detected in 365-day PBI wheat grain and straw.





The hydroxymetabolite, atrazine des-ethyl 2-hydroxy, was also present in all rotational crop matrices from all plantback intervals. Atrazine des-ethyl 2-hydroxy was a significant residue identified in lettuce, turnip tops and roots, and wheat forage (all plantback intervals), and in 29-day PBI wheat grain and 120-day PBI straw, at 18-42% TRR. Atrazine des-ethyl 2-hydroxy was identified as a minor residue (<7% TRR) in 120- and 365-day PBI wheat grain, and 29- and 365-day PBI wheat straw. Another hydroxymetabolite, propazine 2-hydroxy, was identified only in 120-day PBI turnip tops (7% TRR), 29-day PBI wheat forage (11% TRR), 29- and 120-day PBI wheat grain (1.3% TRR), and 29-day PBI wheat straw (3% TRR). Since propazine 2-hydroxy was detected only in the earlier plantback intervals, it is likely metabolized further to such compounds such as atrazine des-ethyl 2-hydroxy, which was present at all plantback intervals. The remaining radioactivity was mostly polar in nature and did not co-elute with any of the reference standards; unknowns from several acid or base hydrolysates could not be further identified because of large matrix co-extractives. Most individual peaks were present at <10% TRR or <0.05 ppm.

The distribution of radioactivity in Subsample B of 29-day PBI wheat straw following an alternate extraction scheme designed to investigate the incorporation of radioactivity to various plant components is presented below. These data were copied without alteration from MRID 44184810. The extractability indicates that the majority of the radioactivity was not tightly bound and HPLC analysis of each extract demonstrated that the metabolic profiles were similar to those observed in various extracts of other subsamples of wheat straw.

Extract	% of TRR (ppm)	HPLC Shown in Figure #
Methanol-Water	82.9 (4.796)	106
Phosphate Buffer	6.5 (0.375)	107
Starch Digestion	2.4 (0.140)	108
Protein Digestion	1.9 (0.112)	109
Pectin Extraction	2.3 (0.135)	110
Lignin Extraction	2.0 (0.117)	111
Hemicellulose Extraction	6.1 (0.355)	112
Cellulose Extraction	2.3 (0.131)	113
Post-Extraction Solids	1.0 (0.060)	NA

### C.1. Storage Stability

Samples of rotated crop matrices were stored frozen (<0 °C) prior to analysis. The petitioner did not provide the dates of sample extraction and analysis; however, based on the study initiation and completion dates samples may have been stored for up to ~2 years. To demonstrate storage stability of incurred residues “over the course of the analytical phase of the study,” the petitioner re-analyzed the methanol/water extracts of 120-day PBI wheat grain and straw 4 months after the



initial analyses. For wheat grain, the stored extract chromatogram indicated that propazine had degraded (from 0.117 ppm to 0.042 ppm) to more polar compounds. For wheat straw, the stored extract chromatogram indicated a slight decrease in propazine with a corresponding increase in the metabolites, especially atrazine des-ethyl 2-hydroxy.

To supplement the storage stability data from this study, HED will rely on the additional data submitted from the sorghum metabolism study. In this sorghum study, methanol and methanol:water extraction conducted 24 months after the original extraction date indicated no loss of radiocarbon. In addition, subsequent chloroform partitioning of the combined methanol extracts, performed two months after extraction, yielded a metabolic profile similar to that of the initial chloroform partitioning.

Matrix (RAC or Extract)	Plantback interval (days)	Storage Temp. (°C)	Actual Storage Duration	Interval of Demonstrated Storage Stability
Lettuce	120, 365	<0	Analysis dates not provided; ~2 years based on study completion date.	None provided
Turnip tops	120			
Turnip roots	120			
Wheat forage	29, 120, 365			
Wheat straw	29, 120, 365			
Wheat grain	29, 120, 365			~4 months for the methanol/water extract of wheat grain and straw

## C.2. Identification, Characterization, and Distribution of Residues

Matrix	TRR (ppm)		
	29-day Plantback interval	120-day Plantback interval	365-day Plantback interval
Lettuce	Not sampled (NS)	0.103	0.209
Turnip tops	NS	0.179	NS
Turnip roots	NS	0.057	NS
Wheat forage	1.298	0.355	0.450
Wheat straw	5.787	1.987	1.028
Wheat grain heads	1.680	0.928	0.245



**TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Rotational Lettuce Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A. <sup>1</sup>**

Metabolite Fraction	120-day PBI Lettuce				365-day PBI Lettuce			
	TRR = 0.103 ppm				TRR = 0.209 ppm			
	Subsample A		Subsample B		Subsample A		Subsample B	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Methanol	73.3	0.075	116.0	0.119	62.8	0.131	55.1	0.115
Propazine	20.4	0.021			10.5	0.022		
Atrazine des-ethyl	9.7	0.010			7.7	0.016		
Atrazine des-ethyl 2-hydroxy	--	--			24.4	0.051		
Unknowns	42.7 <sup>2</sup>	0.044			20.1 <sup>3</sup>	0.042		
Methanol/water	4.5	0.005	2.9	0.003	1.8	0.004	1.7	0.003
-Combined MeOH&MeOH/water			118.9	0.122			56.8	0.118
Organic (chloroform)			36.9	0.038			17.2	0.036
Propazine			13.5	0.014			5.7	0.012
Atrazine des-ethyl			19.4	0.020			9.6	0.020
Unknowns			4.4	0.005			1.9	0.004
Aqueous			81.6	0.084			39.2	0.082
Atrazine des-ethyl 2-hydroxy			41.7	0.043			--	--
Unknowns			40.1 <sup>4</sup>	0.041			34.4 <sup>5</sup>	0.072
0.1% HCl extract	1.9	0.002						
Nonextractable	20.4	0.021	NR	NR	NR	NR	NR	NR
6N HCl hydrolysate	19.2	0.020			3.9	0.008		
3N NaOH hydrolysate					3.2	0.007		
Nonextractable	NR	NR			1.9	0.004		

<sup>1</sup> Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question  
 NR = Not reported *italicized* ppm values for metabolites were calculated by the study reviewer from the area percent reported on the chromatogram and *italicized* % TRR values were calculated by the study reviewer using the ppm values.

<sup>2</sup> Eight peaks, each present at  $\leq 10.7\%$  TRR ( $\leq 0.011$  ppm).

<sup>3</sup> Sixteen peaks, each present at  $\leq 5.3\%$  TRR ( $\leq 0.011$  ppm)

<sup>4</sup> Ten peaks, each present at  $\leq 19.4\%$  TRR ( $\leq 0.020$  ppm).

<sup>5</sup> Single broad solvent front band; further isolation was not possible due to large matrix co-extractives.



**TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Rotational Turnips Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A.<sup>1</sup>**

Metabolite Fraction	120-day PBI Turnip Tops				120-day PBI Turnip Roots			
	TRR = 0.179 ppm				TRR = 0.057 ppm			
	Subsample A		Subsample C		Subsample A		Subsample C	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Methanol	91.1	0.163	83.8	0.150	65.8	0.037	73.1	0.042
Propazine	<i>43.0</i>	0.077			<i>10.5</i>	0.006		
Atrazine des-ethyl	<i>12.3</i>	0.022			--	--		
Atrazine des-ethyl 2-hydroxy	--	--			<i>35.1</i>	0.020		
Unknowns	<i>35.2<sup>2</sup></i>	<i>0.063</i>			<i>21.1</i>	<i>0.012</i>		
Methanol/water	5.4	0.010	2.0	0.004	5.8	0.003	2.2	0.001
-Combined MeOH&MeOH/water			85.8	0.154			75.3	0.043
Organic (chloroform)			24.6	0.044			10.5	0.006
Propazine			<i>15.1</i>	0.027			3.5	0.002
Atrazine des-ethyl			7.9	0.014			5.3	0.003
Unknowns			1.4	0.002			0.7	<0.001
Aqueous			60.9	0.109			64.9	0.037
Propazine 2-hydroxy			7.3	0.013			--	--
Atrazine des-ethyl 2-hydroxy			25.7	0.046			43.9	0.025
Unknowns			27.8 <sup>3</sup>	0.050			20.1	0.012
0.1% HCl extract	0.8	0.001			2.0	0.001		
Nonextractable	NR	NR	NR	NR	22.7	0.013	NR	NR
0.1N HCl hydrolysate	0.7	0.001						
6N HCl hydrolysate	4.8	0.009			15.8	0.009		
3N NaOH hydrolysate	4.5	0.008						
Nonextractable	1.9	0.003			NR	NR		

<sup>1</sup> Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question

NR = Not reported. *Italicized* ppm values for metabolites were calculated by the study reviewer from the area percent reported on the chromatogram and *italicized* % TRR values were calculated by the study reviewer using the ppm values.

<sup>2</sup> Seven peaks, each present at ± 17.2% TRR (<0.031 ppm).

<sup>3</sup> Six peaks, each present at ± 12.6% TRR (< 0.023 ppm).



**TABLE C.2.2.3. Distribution of the Parent and the Metabolites in Rotational Wheat Forage Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A. <sup>1</sup>**

Metabolite Fraction	29-day PBI Forage				120-day PBI Forage				365-day PBI Forage			
	TRR = 1.298 ppm				TRR = 0.355 ppm				TRR = 0.450 ppm			
	Subsample A		Subsample B		Subsample A		Subsample B		Subsample A		Subsample B	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Methanol	96.5	1.253	92.4	1.199	64.6	0.229	82.0	0.291	58.3	0.262	74.6	0.336
Propazine	39.3	0.510							10.2	0.046		
Unknowns	57.2	0.743							48.0 <sup>2</sup>	0.216		
-SCX SPE Fractions	96.5	1.253										
Propazine	33.5	0.435										
Atrazine des-ethyl	10.6	0.137										
Propazine 2-hydroxy	11.4	0.148										
Unknowns	41.0 <sup>3</sup>	0.532										
Methanol/water	2.2	0.029	1.8	0.023	8.1	0.028	3.4	0.012	15.1	0.068	3.8	0.017
-Combined MeOH&MeOH/water			94.2	1.222	72.7	0.257	85.4	0.303			78.4	0.353
Propazine					33.2	0.118						
Atrazine des-ethyl					13.8	0.049						
Unknowns					25.4 <sup>4</sup>	0.090						
Organic (chloroform)			26.0	0.338			42.3	0.150			12.2	0.055
Propazine			11.4	0.148			25.4	0.090			7.8	0.035
Atrazine des-ethyl			12.9	0.168			14.9	0.053			2.9	0.013
Unknowns			1.7	0.022			1.9	0.007			1.6	0.007
Aqueous			68.1	0.884			43.1	0.153			66.2	0.298
Atrazine des-ethyl 2-hydroxy			26.0	0.337			18.3	0.065			34.2	0.154
Unknowns			42.0 <sup>5</sup>	0.545			24.8 <sup>6</sup>	0.088			32.0 <sup>7</sup>	0.144
0.1% HCl extract					3.1	0.011						
Nonextractable	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
0.1 N HCl hydrolysate	3.4	0.044			2.2	0.008			1.9	0.009		
-Combined acid extract and hydrolysate					5.3	0.019						
Atrazine des-ethyl					1.1	0.004						
Atrazine des-ethyl 2-hydroxy					1.4	0.005						
Unknowns					2.5	0.009						
6N HCl hydrolysate	4.7	0.061			11.5	0.040			7.8	0.035		
Atrazine des-ethyl 2-hydroxy					6.5	0.023						
Unknowns					4.8 <sup>8</sup>	0.017						
3N NaOH hydrolysate	5.9	0.077			8.8	0.032			9.4	0.042		



**TABLE C.2.2.3. Distribution of the Parent and the Metabolites in Rotational Wheat Forage Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A. <sup>1</sup>**

Metabolite Fraction	29-day PBI Forage				120-day PBI Forage				365-day PBI Forage			
	TRR = 1.298 ppm				TRR = 0.355 ppm				TRR = 0.450 ppm			
	Subsample A		Subsample B		Subsample A		Subsample B		Subsample A		Subsample B	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Nonextractable	0.8	0.011			1.8	0.006			2.3	0.010		

<sup>1</sup> Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question  
 NR = Not reported. *Italicized* ppm values for metabolites were calculated by the study reviewer from the area percent reported on the chromatogram and *italicized* % TRR values were calculated by the study reviewer using the ppm values.  
<sup>2</sup> Sixteen peaks, each present at  $\leq 20.4\%$  TRR ( $\leq 0.092$  ppm)  
<sup>3</sup> Five peaks, each present at  $\leq 15.6\%$  TRR ( $\leq 0.203$  ppm).  
<sup>4</sup> Fourteen peaks, each present at  $\leq 10.7\%$  TRR ( $\leq 0.038$  ppm).  
<sup>5</sup> Thirteen peaks, each present at  $\leq 8.1\%$  TRR ( $\leq 0.105$  ppm).  
<sup>6</sup> Ten peaks, each present at  $\leq 9.7\%$  TRR ( $\leq 0.034$  ppm).  
<sup>7</sup> Thirteen peaks, each present at  $\leq 7.6\%$  TRR ( $\leq 0.034$  ppm).  
<sup>8</sup> Ten peaks, each present at  $\leq 3.1\%$  TRR ( $\leq 0.011$  ppm). One peak had a similar retention time to propazine 2-hydroxy, however, co-chromatography with reference standards was not possible due to large UV absorption from matrix coextractants.

**TABLE C.2.2.4. Distribution of the Parent and the Metabolites in Rotational Wheat Grain Heads Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A. <sup>1</sup>**

Metabolite Fraction	29-day PBI Grain				120-day PBI Grain				365-day PBI Grain	
	TRR = 1.680 ppm				TRR = 0.928 ppm				TRR = 0.245 ppm	
	Subsample A		Subsample B		Subsample A		Subsample B		Subsample A	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Methanol	55.9	0.939	51.9	0.872	41.1	0.382	51.3	0.476	12.9	0.032
Methanol/water	22.8	0.383	12.5	0.210	21.5	0.200	12.8	0.119	4.8	0.012
-Combined MeOH&MeOH/water	78.7	1.322	64.4	1.082	62.6	0.582	64.1	0.595	17.7	0.044
Propazine	15.3	0.257			12.6	0.117			0.4	<0.001
Atrazine des-ethyl	6.6	0.111			6.6	0.061			--	--
Propazine 2-hydroxy	5.6	0.094							--	--
Atrazine des-ethyl 2-hydroxy	--	--			--	--			4.9	0.012
Unknowns	51.2	0.860			43.5	0.404			12.5	0.031
SCX SPE Fractions 11-13 or 9-11	51.0	0.857			40.2	0.373				
Propazine	14.8	0.249			8.9	0.083				
Atrazine des-ethyl	5.4	0.090			4.8	0.045				
Atrazine des-ethyl 2-hydroxy	--	--			6.8	0.063				
Unknowns	30.9 <sup>2</sup>	0.518			19.6 <sup>3</sup>	0.182				
SCX SPE Fractions 14-17 or 15-17	25.4	0.426			7.9	0.073				
Propazine	5.0	0.084			--	--				



**TABLE C.2.2.4. Distribution of the Parent and the Metabolites in Rotational Wheat Grain Heads Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A. <sup>1</sup>**

Metabolite Fraction	29-day PBI Grain				120-day PBI Grain				365-day PBI Grain	
	TRR = 1.680 ppm				TRR = 0.928 ppm				TRR = 0.245 ppm	
	Subsample A		Subsample B		Subsample A		Subsample B		Subsample A	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Propazine 2-hydroxy	3.0	0.050			1.7	0.016				
Atrazine des-ethyl 2-hydroxy	--	--			1.8	0.017				
Unknowns	17.4 <sup>4</sup>	0.292			4.3	0.040				
Organic (chloroform)			33.2	0.557			32.0	0.297		
Propazine			7.6	0.128			20.0	0.186		
Atrazine des-ethyl			7.4 <sup>5</sup>	0.124			--	--		
Atrazine des-ethyl 2-hydroxy			11.7	0.197			--	--		
Unknowns			6.5	0.109			12.0 <sup>6</sup>	0.111		
Aqueous			31.3	0.525			32.1	0.298		
Propazine			--	--			2.9	0.027		
Propazine 2-hydroxy			2.7	0.045			--	--		
Atrazine des-ethyl			--	--			4.1	0.038		
Atrazine des-ethyl 2-hydroxy			12.9	0.217			--	--		
Unknowns			15.7 <sup>7</sup>	0.263			25.2 <sup>8</sup>	0.234		
0.1% HCl extract	3.0	0.050								
Nonextractable	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
0.1 N HCl hydrolysate	2.0	0.034			8.9	0.083			2.7	0.007
-Combined acid extract and hydrolysate	5.0	0.084								
Propazine	0.1	<0.001			0.2	0.002				
Atrazine des-ethyl 2-hydroxy	0.4	0.007			1.2	0.011				
Unknowns	4.6	0.077			7.5	0.070				
6N HCl hydrolysate	9.3	0.156			16.6	0.154			35.1 <sup>9</sup>	0.086
Propazine 2-hydroxy	0.4	0.007			--	--				
Unknowns	8.9	0.149			16.6 <sup>10</sup>	0.154				
3N NaOH hydrolysate	9.0	0.151			14.5	0.135			22.9	0.056
Nonextractable	1.1	0.018			5.7	0.053			7.7	0.019

<sup>1</sup> Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question  
 NR = Not reported. *Italicized* ppm values for metabolites were calculated by the study reviewer from the area percent reported on the chromatogram and *italicized* % TRR values were calculated by the study reviewer using the ppm values.

<sup>2</sup> Thirteen peaks, each present at 16.2% TRR (0.272 ppm)

<sup>3</sup> Ten peaks, each present at 8.7% TRR (0.081 ppm)

<sup>4</sup> Sixteen peaks, each present at 4.0% TRR (0.068 ppm)

<sup>5</sup> Doublet band of two peaks (0.064 and 0.060 ppm), theorized as atrazine des-ethyl based on Subsample A.



<sup>6</sup> Eleven peaks, each present at  $\pm 3.1\%$  TRR ( $\pm 0.029$  ppm).

Eleven peaks, each present at  $\pm 5.3\%$  TRR ( $\pm 0.089$  ppm).

<sup>8</sup> Seventeen peaks, each present at  $\pm 11.1\%$  TRR ( $\pm 0.103$  ppm).

<sup>9</sup> HPLC analyses were unsuccessful even following repeated SPE cleanup because of the large amount of solubilized matrix components.

<sup>10</sup> At least nine broad peak bands, each present at  $\pm 5.3\%$  TRR ( $\pm 0.049$  ppm).





TABLE C.2.2.5. Distribution of the Parent and the Metabolites in Rotational Wheat Straw Following Application of [ <sup>14</sup> C]Propazine to Bare Soil at 2.39 lb a/A. <sup>1</sup>												
Metabolite Fraction	29-day PBI Straw				120-day PBI Straw				365-day PBI Straw			
	TRR = 5.787 ppm				TRR = 1.987 ppm				TRR = 1.028 ppm			
	Subsample A		Subsample C		Subsample A		Subsample C		Subsample A		Subsample B	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Methanol	39.7	2.297	49.5	2.864	56.5	1.122	53.1	1.054	12.3	0.126	7.5	0.077
Methanol/water	9.8	0.567	8.2	0.475	12.1	0.240	6.2	0.123	3.3	0.034	4.3	0.044
-Combined MeOH&MeOH/water	49.5	2.864	57.7	3.339	68.6	1.362	59.3	1.177	15.6	0.160	11.8	0.121
Propazine	15.8	0.915			21.3	0.423			--	--		
Unknowns	33.7	1.949			47.3 <sup>2</sup>	0.939			15.6 <sup>3</sup>	0.160		
SCX SPE Fractions 5-9	49.5 <sup>4</sup>	2.864										
Propazine	15.7 (15.9)	0.911 (0.922)										
Atrazine des-ethyl	2.6 (4.1)	0.152 (0.237)										
Propazine 2-hydroxy	3.3 (3.0)	0.193 (0.176)										
Atrazine des-ethyl 2-hydroxy	9.8 (6.6)	0.570 (0.384)										
Unknowns	17.9 <sup>5</sup> (19.8 <sup>6</sup> )	1.037 (1.145)										
Organic			17.2	0.998			25.1	0.499			4.9	0.050
Propazine			9.2	0.533			21.0	0.418				
Atrazine des-ethyl			--	--			2.0	0.040				
Unknowns			8.0 <sup>7</sup>	0.465			2.0	0.040				
Aqueous			40.5	2.341			34.1	0.678			6.9	0.071
Propazine			--	--			--	--			0.3	0.003
Atrazine des-ethyl 2-hydroxy			18.2	1.055 <sup>8</sup>			17.7	0.352			1.5	0.015
Unknowns			22.2 <sup>9</sup>	1.286			16.4 <sup>10</sup>	0.326			5.1	0.053
0.1% HCl extract	13.9	0.804										
Nonextractable	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
0.1 N HCl hydrolysate	2.4	0.139			4.9	0.098			2.7	0.028		
-Combined acid extract and hydrolysate	16.3	0.943										
Propazine	1.1	0.063			--	--			--	--		
Atrazine des-ethyl 2-hydroxy	3.1	0.180			--	--			0.5	0.005		
Unknowns	12.1 <sup>11</sup>	0.701			4.9 <sup>12</sup>	0.098			2.2	0.023		
6N HCl hydrolysate	16.2	0.937			7.5	0.149			29.3 <sup>13</sup>	0.301		



**TABLE C.2.2.5. Distribution of the Parent and the Metabolites in Rotational Wheat Straw Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A.<sup>1</sup>**

Metabolite Fraction	29-day PBI Straw				120-day PBI Straw				365-day PBI Straw			
	TRR = 5.787 ppm				TRR = 1.987 ppm				TRR = 1.028 ppm			
	Subsample A		Subsample C		Subsample A		Subsample C		Subsample A		Subsample B	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Atrazine des-ethyl 2-hydroxy	3.0	0.176			1.0	0.020						
Unknowns	13.1 <sup>14</sup>	0.766			6.5	0.129						
3N NaOH hydrolysate	8.4	0.486			6.1	0.121			23.3 <sup>13</sup>	0.240		
Nonextractable	3.1	0.179			5.4	0.107			13.1	0.135		

<sup>1</sup> Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question  
 NR = Not reported. *italicized* ppm values for metabolites were calculated by the study reviewer from the area percent reported on the chromatogram and *italicized* % TRR values were calculated by the study reviewer using the ppm values.  
<sup>2</sup> Fifteen peaks, each present at ≤ 15.2% TRR (± 0.302 ppm).  
<sup>3</sup> Twelve peaks, each present at 6.1% TRR (± 0.063 ppm); poor column recovery 56.0%.  
<sup>4</sup> Analysis results using C18 HPLC are reported, with analysis results using cation-exchange HPLC reported in parentheses.  
<sup>5</sup> Eleven peaks, each present at ≤ 5.4% TRR (± 0.311 ppm).  
<sup>6</sup> Ten peaks, each present at ≤ 9.9% TRR (± 0.573 ppm).  
<sup>7</sup> Twelve peaks, each present at ≤ 1.5% TRR (± 0.087 ppm) and two broad bands present at 0.080 ppm and 0.183 ppm which eluted in the region typical for atrazine des-ethyl; atrazine des-ethyl is not typically observed in the chloroform fraction. TLC analysis could not resolve propazine and atrazine des-ethyl because of a matrix effect.  
<sup>8</sup> Confirmed by HPLC analysis following SCX SPE fractionation.  
<sup>9</sup> Twelve peaks, each present at ≤ 4.2% TRR (± 0.243 ppm).  
<sup>10</sup> Ten peaks, each present at ≤ 6.6% TRR (± 0.131 ppm).  
<sup>11</sup> Twelve peaks, each present at ≤ 4.3% TRR (± 0.252 ppm).  
<sup>12</sup> One major peak at 3.4% TRR (0.068 ppm) and twelve peaks, each present at ≤ 0.012 ppm.  
<sup>13</sup> Could not be analyzed by HPLC even with C18 and SCX SPE cleanup, because of large amounts of solubilized matrix components.  
<sup>14</sup> Eleven peaks, each present at ≤ 8.6% TRR (± 0.499 ppm), which included a broad band in the region of propazine 2-hydroxy and atrazine des-ethyl. Due to excessive matrix co-chromatography, this sample analysis was not used.



**TABLE C.2.3.1. Summary of Characterization and Identification of Radioactive Residues in Rotational Lettuce Planted 120 and 365 Days Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A.<sup>1</sup>**

Compound	120-day PBI Lettuce		365-day PBI Lettuce	
	TRR = 0.103 ppm		TRR = 0.20 <sup>a</sup> ppm	
	%TRR	ppm	%TRR	ppm
<b>Identified in the Methanol or Methanol/water extract</b>				
Propazine	20.4	0.021	10.5	0.022
Atrazine des-ethyl	9.7	0.010	7.7	0.016
Propazine 2-hydroxy	--	--	--	--
Atrazine des-ethyl 2-hydroxy	41.7	0.043*	24.4	0.051*
<b>Characterized</b>				
0.1% HCl extract	1.9	0.002	--	--
6 N HCl hydrolysate	19.2	0.020	3.9	0.008
3 N NaOH hydrolysate	--	--	3.2	0.007
Total identified	71.8	0.074	42.6	0.089
Total characterized	21.4	0.022	7.1	0.015
Total extractable	99.0	0.102	71.8	0.150
Unextractable (PES) <sup>2</sup>	NR	NR	1.9	0.004
Accountability <sup>3</sup>	>99.0		73.7	

<sup>1</sup> Summary of identified components as presented by the petitioner; ppm values for the components were taken from the analysis of various extracts, SCX fractions, and/or subsamples, and TRR values were calculated by the study reviewer. Components followed by an asterisk were tentatively identified by comparison of the retention times with reference standards using only one method. Characterized residues were taken from the Subsample A workup; see Table C.2.2.1. Unknowns are not included in the table because the petitioner used identified components from different analyses or subsamples.

<sup>2</sup> Residues remaining after exhaustive extractions.

<sup>3</sup> Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) \* 100.



**TABLE C.2.3.2. Summary of Characterization and Identification of Radioactive Residues in Rotational Turnips Planted 120 Days Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A.<sup>1</sup>**

Compound	120-day PBI Turnip Tops		120-day PBI Turnip Roots	
	TRR = 0.179 ppm		TRR = 0.057 ppm	
	%TRR	ppm	%TRR	ppm
<b>Identified in the Methanol or Methanol/water extract</b>				
Propazine	43.0	0.077	10.5	0.006
Atrazine des-ethyl	12.3	0.022	5.3	0.003
Propazine 2-hydroxy	7.3	0.013*	--	--
Atrazine des-ethyl 2-hydroxy	25.7	0.046*	36.8	0.021* <sup>2</sup>
<b>Characterized</b>				
0.1% HCl extract	0.8	0.001	2.0	0.001
0.1 N HCl hydrolysate	0.7	0.001	--	--
6 N HCl hydrolysate	4.8	0.009	15.8	0.009
3 N NaOH hydrolysate	4.5	0.008	--	--
Total identified	88.3	0.158	52.6	0.030
Total characterized	10.8	0.019	17.8	0.010
Total extractable	107.3	0.192	87.7	0.050
Unextractable PES <sup>3</sup>	1.9	0.003	NR	NR
Accountability <sup>4</sup>	109		>87.7	

<sup>1</sup> Summary of identified components as presented by the petitioner. ppm values for the components were taken from the analysis of various extracts, SCX fractions, and/or subsamples, and TRR values were calculated by the study reviewer. Components followed by an asterisk were tentatively identified by comparison of the retention times with reference standards using only one method. Characterized residues were taken from the Subsample A workup; see Table C.2.2.2. Unknowns are not included in the table because the petitioner used identified components from different analyses or subsamples.

<sup>2</sup> Values reported by the petitioner (and presented here) do not agree with the chromatographic data reported in Table C.2.2.2.

<sup>3</sup> Residues remaining after exhaustive extractions.

<sup>4</sup> Accountability = Total extractable + Total unextractable / (TRR from combustion analysis; see TABLE C.2.1) \* 100.



**TABLE C.2.3.3. Summary of Characterization and Identification of Radioactive Residues in Rotational Wheat Forage Planted 29, 120, and 365 Days Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A.<sup>1</sup>**

Compound	29-day PBI Forage		120-day PBI Forage		365-day PBI Forage	
	TRR = 1.298 ppm		TRR = 0.355 ppm		TRR = 0.450 ppm	
	% TRR	ppm	%TRR	ppm	%TRR	ppm
<b>Identified in the Methanol or Methanol/water extract</b>						
Propazine	39.3	0.510	33.2	0.118	12.9	0.058
Atrazine des-ethyl <sup>2</sup>	10.6	0.137	14.9	0.053	2.9	0.013*
Propazine 2-hydroxy	11.4	0.148	--	--	--	--
Atrazine des-ethyl 2-hydroxy	26.0	0.338* <sup>3</sup>	18.3	0.065*	34.2	0.154*
<b>Identified in the 0.1% and 0.1 N HCl extract/hydrolysate</b>						
Atrazine des-ethyl <sup>2</sup>	NA	NA	1.1	0.004*	NA	NA
Atrazine des-ethyl 2-hydroxy	NA	NA	1.4	0.005	NA	NA
<b>Identified in the 6 N HCl hydrolysate</b>						
Atrazine des-ethyl 2-hydroxy	NA	NA	6.5	0.023*	NA	NA
<b>Characterized</b>						
0.1 N HCl hydrolysate	3.4	0.044	--	--	1.9	0.009
6 N HCl hydrolysate	4.7	0.061	--	--	7.8	0.035
3 N NaOH hydrolysate	5.9	0.077	8.8	0.032	9.4	0.042
Total identified	67.3	1.133	75.4	0.268	50.0	0.225
Total characterized	14.0	0.182	8.8	0.032	19.1	0.086
Total extractable	112.8	1.464	98.0	0.348	92.4	0.416
Unextractable (PES) <sup>3</sup>	0.8	0.011	1.8	0.006	2.3	0.010
Accountability <sup>4</sup>	114		99.7		94.7	

<sup>1</sup> Summary of identified components as presented by the petitioner; ppm values for the components were taken from the analysis of various extracts, SCX fractions, and/or subsamples, and TRR values were calculated by the study reviewer. Components followed by an asterisk were tentatively identified by comparison of the retention times with reference standards using only one method. Characterized residues were taken from the Subsample A workup; see Table C.2.2.3. Unknowns are not included in the table because the petitioner used identified components from different analyses or subsamples.

NR = Not reported. NA = Fraction was not analyzed.

<sup>2</sup> Values reported by the petitioner (and presented here) do not agree with the chromatographic data reported in Table C.2.2.3.

<sup>3</sup> Residues remaining after exhaustive extractions.

<sup>4</sup> Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) \* 100.



**TABLE C.2.3.4. Summary of Characterization and Identification of Radioactive Residues in Rotational Wheat Grain Heads Planted 29, 120, and 365 Days Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A.<sup>1</sup>**

Compound	29-day PBI Grain		120-day PBI Grain		365-day PBI Grain	
	TRR = 1.680 ppm		TRR = 0.928 ppm		TRR = 0.245 ppm	
	% TRR	ppm	%TRR	ppm	%TRR	ppm
<b>Identified in the Methanol or Methanol/water extract</b>						
Propazine	15.3	0.257	12.6	0.117	0.4	<0.001
Atrazine des-ethyl	5.4	0.090	4.8	0.045	--	--
Propazine 2-hydroxy	3.0	0.050	1.7	0.016	--	--
Atrazine des-ethyl 2-hydroxy	24.6	0.414*	6.8	0.063*	4.9	0.012
<b>Identified in the 0.1% and 0.1 N HCl extract/hydrolysate</b>						
Propazine	0.1	<0.001	0.2	0.002	NA	NA
Atrazine des-ethyl 2-hydroxy	0.4	0.007*	1.2	0.011*	NA	NA
<b>Identified in the 6 N HCl hydrolysate</b>						
Propazine 2-hydroxy	0.8	0.014* <sup>2</sup>	--	--	--	--
<b>Characterized</b>						
0.1 N HCl hydrolysate	--	--	--	--	2.7	0.007
6 N HCl hydrolysate	--	--	16.6	0.154	35.1	0.086
3 N NaOH hydrolysate	9.0	0.151	14.5	0.135	22.9	0.056
Total identified	49.6	0.832	27.4	0.254	5.3	0.012
Total characterized	9.0	0.151	31.1	0.289	60.7	0.149
Total extractable	102.0	1.713	102.8	0.954	78.8	0.193
Unextractable (PES) <sup>3</sup>	1.1	0.018	5.7	0.053	7.7	0.019
Accountability	103		109		86.5	

<sup>1</sup> Summary of identified components as presented by the petitioner; ppm values for the components were taken from the analysis of various extracts, SCX fractions, and/or subsamples, and TRR values were calculated by the study reviewer. Components followed by an asterisk were tentatively identified by comparison of the retention times with reference standards using only one method. Characterized residues were taken from the Subsample A workup; see Table C.2.2.4. Unknowns are not included in the table because the petitioner used identified components from different analyses or subsamples.

NR = Not reported. NA = Fraction was not analyzed.

<sup>2</sup> Values reported by the petitioner (and presented here) do not agree with the chromatographic data reported in Table C.2.2.4.

<sup>3</sup> Residues remaining after exhaustive extractions.

<sup>4</sup> Accountability = (Total extractable + Total unextractable)/TRR from combustion analysis; see TABLE C.2.1) \* 100



**TABLE C.2.3.5. Summary of Characterization and Identification of Radioactive Residues in Rotational Wheat Straw Planted 29, 120, and 365 Days Following Application of [<sup>14</sup>C]Propazine to Bare Soil at 2.39 lb ai/A.<sup>1</sup>**

Compound	29-day PBI Straw		120-day PBI Straw		365-day PBI Straw	
	TRR = 5.787 ppm		TRR = 1.987 ppm		TRR = 1.028 ppm	
	% TRR	ppm	%TRR	ppm	%TRR	ppm
<b>Identified in the Methanol or Methanol/water extract</b>						
Propazine	15.8	0.915	21.3	0.423	0.6	0.006 <sup>2</sup>
Atrazine des-ethyl	2.6	0.152	2.0	0.040	--	--
Propazine 2-hydroxy	3.0	0.176	--	--	--	--
Atrazine des-ethyl 2-hydroxy	6.6	0.384*	17.7	0.352*	2.4	0.025* <sup>2</sup>
<b>Identified in the 0.1% and/or 0.1 N HCl extract/hydrolysate</b>						
Propazine	1.1	0.063	--	--	--	--
Atrazine des-ethyl 2-hydroxy	3.1	0.180*	--	--	0.5	0.005*
<b>Identified in the 6 N HCl hydrolysate</b>						
Atrazine des-ethyl 2-hydroxy	3.0	0.176*	1.0	0.020*	NA	NA
<b>Characterized</b>						
0.1 N HCl hydrolysate	--	--	4.9	0.098	--	--
6 N HCl hydrolysate	--	--	7.5	0.149	29.3	0.301
3 N NaOH hydrolysate	8.4	0.486	6.1	0.121	23.3	0.240
Total identified	35.4	2.046	42.0	0.835	3.5	0.036
Total characterized	8.4	0.486	18.5	0.368	52.6	0.541
Total extractable	90.4	5.230	87.1	1.730	70.9	0.729
Unextractable (PES) <sup>3</sup>	3.1	0.179	5.4	0.107	13.1	0.135
Accountability <sup>4</sup>	93.5		92.5		84.0	

<sup>1</sup> Summary of identified components as presented by the petitioner; ppm values for the components were taken from the analysis of various extracts, SCX fractions, and/or subsamples, and TRR values were calculated by the study reviewer. Components followed by an asterisk were tentatively identified by comparison of the retention times with reference standards using only one method. Characterized residues were taken from the Subsample A workup; see Table C.2.2.5. Unknowns are not included in the table because the petitioner used identified components from different analyses or subsamples.

NR = Not reported. NA = Fraction was not analyzed.

<sup>2</sup> Values reported by the petitioner (and presented here) do not agree with the chromatographic data reported in Table C.2.2.5.

<sup>3</sup> Residues remaining after exhaustive extractions.

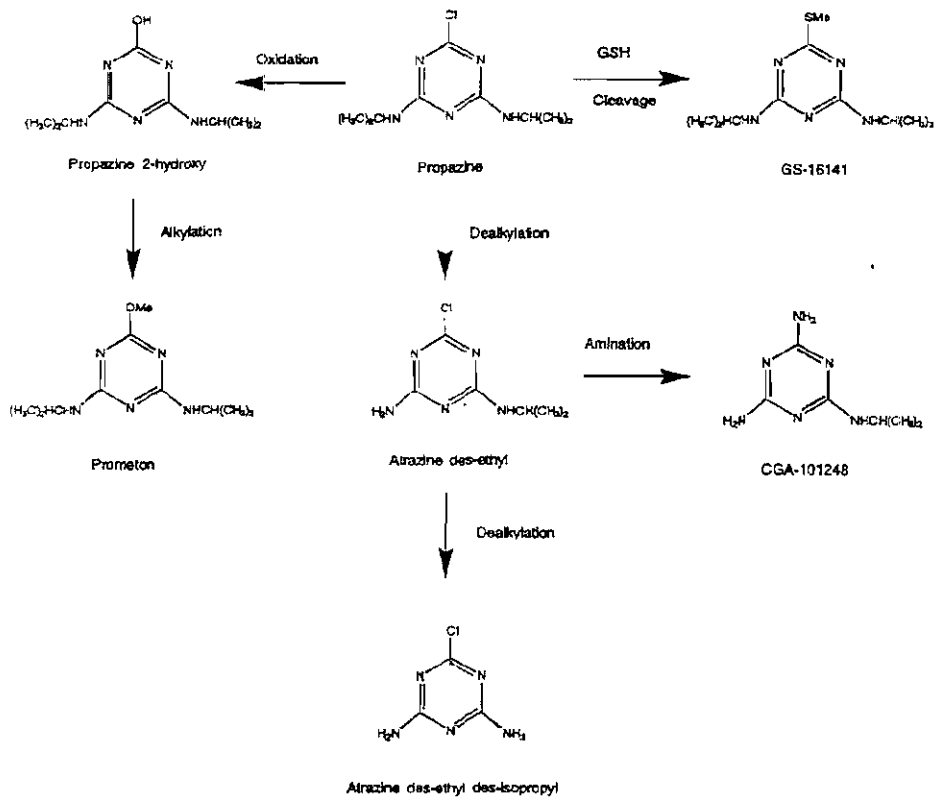
<sup>4</sup> Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) \* 100.



### C.3. Proposed Metabolic Profile

#### FIGURE C.3.1. Proposed Metabolic Profile of Propazine in Rotated Crops.

This figure was copied without alteration from MRID 44184810.







Common name/code Figure C.3.1 ID No	Chemical name	Chemical structure
Propazine	2-chloro-4,6-bis(isopropylamino)-s-triazine	
Atrazine des-ethyl	Not reported	
Propazine 2-hydroxy	Not reported	
Atrazine des-ethyl 2-hydroxy	Not reported	

#### D. CONCLUSION

TRR accumulated at  $\geq 0.01$  ppm in all rotated crops planted 29, 120 or 365 days following a single application of [ $^{14}\text{C}$ ]propazine to bare soil at a total rate of 2.39 lb ai/A; severe phytotoxicity occurred with the 29-day PBI lettuce and turnip and 365-day PBI turnip crops, and samples were not collected. TRR were highest in wheat straw, grain, and forage. Generally TRR decreased in wheat crop matrices with increased plantback intervals (PBIs); however, TRR actually increased from the 120-day to 365-day PBI in wheat forage and lettuce. At the 29-day PBI, residues were 1.298, 1.680, and 5.787 ppm in wheat forage, grain, and straw, respectively; lettuce and turnips were not sampled at this plantback interval. At the 120-day PBI, residues were 0.355, 0.928, and 1.987 ppm in wheat forage, grain, and straw, respectively, and 0.057-0.179 ppm in lettuce, turnip tops, and turnip roots. At the 365-day PBI, residues were 0.450, 0.245, and 1.028 ppm in wheat forage, grain, and straw, respectively, and 0.209 ppm in lettuce; turnips were not sampled at this plantback interval.



Extraction with methanol and methanol/water released the majority of the TRR (65-99% TRR) from rotational lettuce, turnip tops and roots, and wheat forage; the majority of the radioactivity was released with the initial methanol extraction. Extraction with methanol and methanol/water was variable in wheat grain and straw: ~50-79% TRR from 29- and 120-day PBI grain and straw and ~16-18% TRR from 365-day PBI grain and straw. Subsequent acid extraction, mild and strong acid hydrolysis, and/or base hydrolysis released ~7-21% TRR in lettuce, ~11-18% TRR in turnip tops and roots, ~14-26% TRR in wheat forage, ~23-61% TRR in wheat grain, and ~19-55% TRR in wheat straw; the majority of the radioactivity in mature wheat matrices (grain and straw) was tightly bound and released with strong acid and base hydrolysis. Nonextractable residues remaining following extraction/hydrolysis accounted for  $\leq 8\%$  TRR in all rotational crop matrices, except for 365-day PBI wheat straw (13.1% TRR, 0.135 ppm nonextractable).

Total identified residues ranged 27-88% TRR in all rotated crop commodities, except in 365-day PBI grain and straw for which only 4-5% TRR was identified. Propazine was identified ( $<1-43\%$  TRR) in all rotational crop matrices from all plantback intervals, but appears to decrease with the longer plantback intervals. Atrazine des-ethyl, another chloro-residue, was identified at significant levels in 120-day turnip tops, and 29- and 120-day PBI forage, and at minor levels in 120- and 365-day PBI lettuce, 120-day PBI turnip roots, 365-day PBI wheat forage, 29- and 120-day PBI wheat grain and straw; atrazine des-ethyl was not detected in 365-day PBI wheat grain and straw. The hydroxymetabolite, atrazine des-ethyl 2-hydroxy, was also present in all rotational crop matrices from all plantback intervals. Atrazine des-ethyl 2-hydroxy was a significant residue identified in lettuce, turnip tops and roots, and wheat forage (all plantback intervals), and in 29-day PBI wheat grain and 120-day PBI straw. Atrazine des-ethyl 2-hydroxy was identified as a minor residue in 120- and 365-day PBI wheat grain, and 29- and 365-day PBI wheat straw. Another hydroxymetabolite, propazine 2-hydroxy, was identified only in 120-day PBI turnip tops, 29-day PBI wheat forage, 29- and 120-day PBI wheat grain, and 29-day PBI wheat straw at 3-11% TRR.

Based on the results of the confined rotational crop study, the petitioner concluded that the primary metabolic products in rotational crops were similar to those found in a sorghum metabolism study (refer to the DER for MRIDs 44184813, 44184814, and 44287315). Propazine metabolism in plants involves N-dealkylation, hydrolysis, and conjugation with glutathione. The petitioner further states that the study results confirm literature concerning the metabolism of other triazine herbicides, except that propazine and chloro-residues were detected in wheat grain in the subject study and chloro-residues are typically not seen in grain with chloro-s-triazine herbicides.



## E. REFERENCES

44184813 O'Neal, S; Bentley, W. (1996) [<sup>14</sup>C]Propazine: Metabolic Fate and Distribution in Grain Sorghum: Lab Project Number: 817E/514W: 817E: 103S/817E. Unpublished study prepared by PTRL East, Inc. 69 p.

44184814 Jalali, K; Saber, A; O'Neal, S. *et al.* (1996) [<sup>14</sup>C]Propazine: Metabolic Fate and Distribution in Grain Sorghum: Lab Project Number: CHW 6641-104: AM-067: GP96-018. Unpublished study prepared by Corning Hazleton Inc. 317 p.

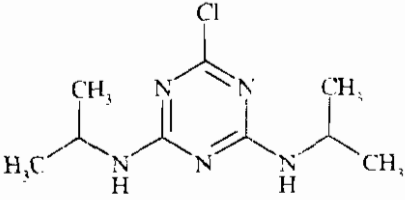
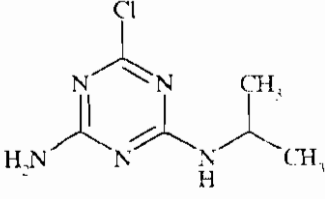
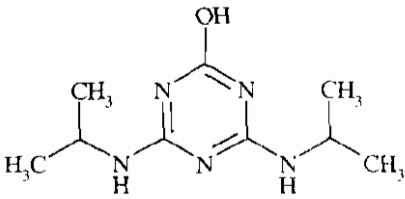
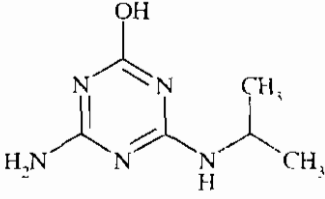
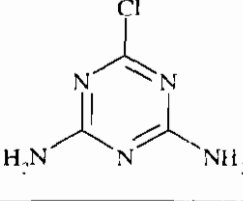
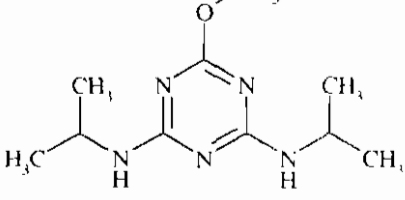
44287315 Jalali, K.; Saber, A.; O'Neal, S.; *et al.* (1997) [<sup>14</sup>C]Propazine: Metabolic Fate and Distribution in Grain Sorghum: Amended (Final) Report: Lab Project Number: 817E/514W: 817E/514W-1: 817E. Unpublished study prepared by PTRL East, Inc. and PTRL West, Inc. 356 p.

## F. DOCUMENT TRACKING

RDI: P.V. Shah (8/25/05), RAB1 Chemists (8/3/05)  
G.F. Kramer:806T:CM#2:(703)305-5079:7509C:RAB1  
Petition Number(s): 7F4837  
DP#: 323273  
PC Code: 080808

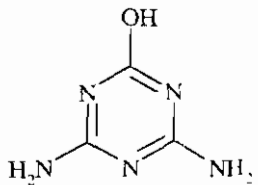
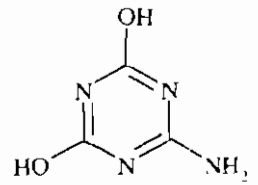
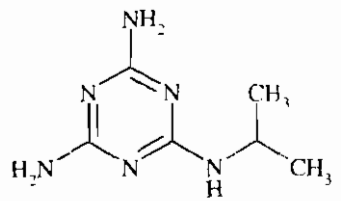
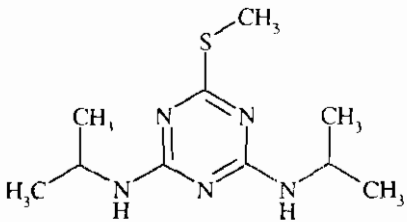
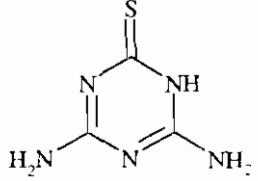
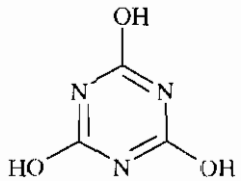
Template Version: September 2003



APPENDIX I. Chemical Names and Structures of Reference Standards Used in Rotational Crop Study.		
Common name, Company code	Chemical name	Chemical structure
Propazine	2-chloro-4,6-bis(isopropylamino)-s-triazine	
Atrazine des-ethyl (G-30033)	2-amino-4-chloro-6-(1-methylethylamino)-s-triazine	
Propazine 2-hydroxy (GS-11526)	2-hydroxy-4,6-bis(1-methylethylamino)-s-triazine	
Atrazine des-ethyl 2-hydroxy (GS-17794)	2-amino-4-hydroxy-6-(1-methylethylamino)-s-triazine	
Atrazine des-ethyl des-isopropyl (G-28273)	2,4-diamino-6-chloro-s-triazine	
Prometon (G-31435)	2-methoxy-4,6-bis(1-methylethylamino)-s-triazine	



**APPENDIX 1. Chemical Names and Structures of Reference Standards Used in Rotational Crop Study.**

Common name, Company code	Chemical name	Chemical structure
Ammeline (GS-17791)	2,4-diamino-6-hydroxy- <i>s</i> -triazine	
Ammelide (G-35713)	2,4-diamino-6-amino- <i>s</i> -triazine	
CGA-101248	N-(1-methyl)-1,3,5-triazine-2,4,6-triamine	
GS-16141	2,4-bis (1-methylethylamino)-6-methylsulfinyl- <i>s</i> -triazine	
CGA-236433	Not reported	
Cyanuric acid	Not reported	



Primary Evaluator: George F. Kramer  
George F. Kramer, Ph.D., Chemist Date: 07-DEC-2005  
Registration Action Branch 1 (RAB1)  
Health Effects Division (HED) (7509C)

Approved by: \_\_\_\_\_  
P.V. Shah, Ph.D., Branch Senior Date: 07-DEC-2005  
Scientist/RAB1/HED (7509C)

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This DER was originally prepared under contract by Dynamac Corporation (20440 Century Boulevard, Suite 100; Germantown, MD 20874; submitted 07/13/2005). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

### **STUDY REPORT:**

44184811 Hughes, D. (1996) Propazine: Field Rotational Crop Study Using Milo-Pro 4L: Final Report: Lab Project Number: 6641-101: CHW 6641-101: AA950605. Unpublished study prepared by American Agricultural Services, Inc. and Corning Hazleton Inc. 287 p.

### **EXECUTIVE SUMMARY:**

Griffin Corporation has submitted a limited field rotational crop study with propazine. Two trials were conducted in Regions 2 (NC) and 8 (TX). At each trial site, a 4 lb/gal flowable concentrate (FIC) formulation of propazine was applied as a preemergence ground spray to grain sorghum, the primary crop, at a nominal rate of 1.2 lb ai/A. The test substance was applied either on the day of planting (NC) or five days after planting (TX).

The primary crop was to be removed (by cutting) from the plots prior to 90 days after the test substance application since the target plantback intervals (PBIs) the petitioner initially intended to investigate were 90, 120, and 180 or 210/240 days. However, due to unusually cold and wet weather, the actual plantback intervals used in the study were 94, 127, and 242/280 days for the NC field site and 97, 120, 195, and 239 days for the TX field site. The following rotational crops were planted at the plantback intervals listed above for each field site: radish or turnip (a root vegetable), lettuce or mustard (a leafy vegetable), and winter or spring wheat (a cereal grain). The rotational crops were allowed to grow according to good agricultural practices. It was reported that extremely cold weather during the winter months impacted the development and yield of some crops at both test sites. Samples of radish (roots and tops), turnip (roots and tops), leaf lettuce (leaves), mustard (leaves), wheat (forage, hay, grain, and straw) were collected at appropriate crop growth stage or at maturity.

A gas chromatography/mass-selective detector (GC/MSD) method (CHW 6641-101, Method 1) was used for the analysis of harvested crop commodities for residues of propazine and its two chlorometabolites: 2-amino-4-chloro-6-isopropylamino-s-triazine (desethyl atrazine or DEA; aka G-30033) and 2,4-diamino-6-chloro-s-triazine (diamino atrazine or DAA; aka G-28273). The limit of quantitation (LOQ) for propazine, DEA, and DAA in all RACs is 0.0500 ppm for each analyte. The efficiency of the method was verified by fortifying aliquots of control matrix



with propazine and its chlorometabolite DAA, each at 0.05, 0.1, and 0.2 ppm and with the chlorometabolite DEA at 0.0575, 0.115, 0.230 ppm. Average method recoveries ranged 86.8-106% for propazine, 83.3-110% for DEA, and 76.7-98.6% for DAA. The method is adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen prior to residue analysis. The maximum storage intervals, from harvest to analysis, were 129 days (4.2 months) for lettuce, 79 days (2.6 months) for mustard leaves, 100 days (3.3 months) for radish tops and roots, 79 days (2.6 months) for turnip tops and roots, 141 days (4.6 months) for wheat forage, 125 days (4.1 months) for wheat hay, and 89 days (2.9 months) for wheat grain and straw. No supporting storage stability data were included in the subject study. In a separate submission for a residue field study on sorghum (MRID 44287316), it was reported that a storage stability study has been initiated and will be submitted in a separate report. It was also reported in a sorghum metabolism study (MRID 44287315) that the metabolic profiles of sorghum extracts did not change 24 months after the initial chromatographic analysis.

The results of the NC trial indicate that residues of propazine, DEA (G-30033), and DAA (G-28273) were each below the LOQ of 0.0500 ppm in/on all samples of rotational crop commodities (mustard leaves, turnip tops/roots, and spring/winter wheat forage, hay, straw, and grain) at all PBIs (94, 127, and 242/280 days).

The results of the TX trial indicate that residues of propazine, DEA (G-30033), and DAA (G-28273) were each below the LOQ of 0.0500 ppm in/on the following rotational crop commodities and plantback intervals: (i) lettuce leaves at a 97-day PBI; (ii) radish root at PBIs of 97 and 239 days; (iii) wheat forage at PBIs of 120 and 195 days; (iv) wheat hay, straw, and grain at PBIs of 97, 120, and 195 days. A few rotational crop commodities showed quantifiable residues including: (i) lettuce leaves at the 239-day PBI which bore residues of propazine (0.0505-0.0510 ppm), DEA (0.137-0.139 ppm), and DAA (0.139 ppm); (ii) radish tops at the 97-day PBI which bore quantifiable residues of propazine (0.051-0.052 ppm) but nondetectable (< LOQ) residues of DEA and DAA; and (iii) wheat forage at the 97-day PBI which bore quantifiable residues of DEA (0.102-0.107 ppm) but nondetectable (< LOQ) residues of propazine and DAA.

The discrepancies of results from the two test locations were attributed by the petitioner to be mainly due the fact that the rotational crops in TX were planted on 10/9/95 which is much later than normal (crops would not typically be planted for commercial production at this time of the year), and the environmental conditions were adverse for plant growth especially for lettuce and radishes.

#### **STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:**

Provided the storage stability of residues in rotational crops is demonstrated, the field rotational crop residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision (TRED) Document for propazine.



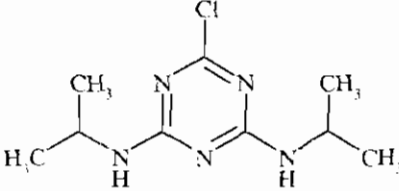
## COMPLIANCE:

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

Propazine (6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine) is a member of the chloro triazine class of herbicides. Other members of this pesticide class include atrazine, cyanazine, and simazine. Propazine is a selective herbicide that can be applied before planting, at planting, and after crop emergence for the preemergence control of annual broadleaf weeds. Currently, the only registered uses are for weed control of ornamental plants grown in containers under greenhouse conditions. There are presently no registered food/feed uses of propazine.

Propazine was previously registered for use on sorghum. The 5/19/87 Propazine Residue Chemistry Chapter along with the 12/88 Propazine Reregistration Standard (Guidance Document) identified several data deficiencies for the reregistration of propazine. Ciba-Geigy, which was then the basic manufacturer of propazine, elected to cancel its registrations of propazine. Another registrant, Griffin Corporation, is now supporting the previously-cancelled uses of propazine on grain sorghum. The structure and nomenclature of propazine are presented in Table A.1. The physicochemical properties of propazine are listed in Table A.2.

TABLE A.1. Propazine Nomenclature	
PC Code 006308	
Chemical structure	
Common name	Propazine
Molecular Formula	C <sub>9</sub> H <sub>16</sub> N <sub>5</sub> Cl
Molecular Weight	229.7
IUPAC name	6-chloro- <i>N,N'</i> -di-isopropyl-1,3,5-triazine-2,4-diamine
CAS name	6-chloro- <i>N,N'</i> -bis(1-methylethyl)-1,3,5-triazine-2,4-diamine
CAS #	139-40-2





Parameter	Value	Reference
Melting point	217.7 °C	RD D219079, 9/26/95, S. Malak
pH	5.66	
Density, bulk density, or specific gravity	0.46 g/mL	
Water solubility	3.8 ppm at 25 °C	
Solvent solubility (at 25 °C)	14,252 ppm in acetone 4,696 ppm in 1-octanol	
Vapor pressure	2.9 x 10 <sup>-8</sup> mm Hg at 20 °C  2.98 x 10 <sup>-5</sup> Torr at 45 °C	Product Chemistry Chapter of the Propazine Reregistration Standard, 5/19/87  RD D219079, 9/26/95, S. Malak
Dissociation constant, pK	Not applicable; practically insoluble in water	RD D219079, 9/26/95, S. Malak
Octanol/water partition coefficient	P = 1234.7 Log P = 3.08	

## B. EXPERIMENTAL DESIGN

### B.1. Study Site Information

Trial Identification (City, State; Year)	Soil characteristics <sup>1</sup>				Meteorological data	
	Type	%OM	pH	CEC (meq/100 g soil)	Overall monthly rainfall range (inches) <sup>2</sup>	Overall monthly temperature range (°C)
Lucama, NC; 1995-1996	0-6 inch depth: Sandy loam	1.5	6.4	6.7	1.64-9.12 (i)	-1.7 to 33.3
	6-12 inch depth: Sandy clay loam	0.4	5.0	6.9		
Groom, TX; 1995-1996	0-6 inch depth Loam	3.2	7.5	30.3	0.00-5.55 (i)	-7.8 to 32.2
	6-12 inch depth Clay loam	2.2	7.6	32.1		

<sup>1</sup> %OM = % Organic Matter, CEC = Cation Exchange Capacity

<sup>2</sup> (i) indicates that supplemental irrigation was received.

Weather conditions were normal during the sorghum growing season. However, unusually cold temperatures altered normal growth, development, and maturity of the rotational crops at both test sites. The TX test site experienced the coldest winter in nine years. The freezing temperatures in January and March killed the radish and lettuce crops in the 120- and 195-day PBIs. The NC test site also experienced cold temperatures during the winter months though not



as severe as the TX test site. The months of November through January and March were 3 to 7 °F colder than normal. The total rainfall for the NC test site was slightly above the 10-year average, and the total rainfall for the TX test site was slightly below the historical rainfall average. Irrigation was used to supplement as needed.

**TABLE B.1.2. Study Use Pattern.**

Location (City, State; Year)	EP <sup>1</sup>	Application					Tank Mix Adjuvants
		Method, Timing	Vol. (GPA <sup>2</sup> )	Rate (lb ai/A)	RTI <sup>3</sup> (days)	Total Rate (lb ai/A)	
Lucama, NC, 1995-1996	4 lb/gal FIC	Preemergence ground application	30.8	1.19	Not applicable (NA)	1.19	None
Groom, TX, 1995-1996	4 lb/gal FIC	Preemergence ground application	21.1	1.21	NA	1.21	None

<sup>1</sup> EP = End-use Product

<sup>2</sup> GPA = Gallons per acre

<sup>3</sup> RTI = Retreatment Interval

## B.2. Sample Handling and Preparation

Duplicate samples of rotational crop commodities were collected from the treated plots, and single samples were collected from the untreated plots. Samples of lettuce, mustard leaves, radish roots and tops, turnip roots and tops, and wheat straw and grain were harvested at crop maturity. The wheat forage samples were collected at the 6-8 inch stage to flag leaf stage. The wheat hay samples were collected at the early flower to soft dough stage. All samples were frozen (-36 to -6 °C) after collection and shipped frozen via ACDs freezer trucks or on dry ice by Federal Express to Corning Hazelton, Inc. (Madison, WI) for analysis. Samples were stored frozen (temperature unspecified) prior to analysis.

## B.3. Analytical Methodology

Rotational crop samples were analyzed for residues of propazine and its chlorometabolites using a GC/MSD method (CHW 6641-101, Method 1) entitled "Determination of Propazine, Desethyl Atrazine (DEA), and Diamino Atrazine (DAA) in Field Rotational Crops using Capillary Gas Chromatography with Mass-Selective Detection," dated 4/10/96. A complete description of the method was included in the submission.

Briefly, a representative sample is soxhlet-extracted with a mixture of methanol and water. The methanol is removed by rotary evaporation, and the resulting water mixture is cleaned up on a Chem-Elut column. Residues are eluted with 15% ethyl acetate/hexane for isolation of propazine and DEA (Fraction A). The DAA (Fraction B) is eluted from the same column with 50% ethyl acetate/hexane. The resulting eluates are evaporated to dryness. Fraction A is redissolved in ethyl acetate, and analyzed for propazine and DEA using GC/MSD. Fraction B is cleaned up on a Florisil Sep-Pak. The resulting solution is evaporated to dryness, redissolved in ethyl acetate, and analyzed for DAA using GC/MSD. The LOQ for propazine, DEA, and DAA in all RACs is 0.0500 ppm.



Method verification was performed prior to sample analysis. The analytical method was validated for propazine, DEA, and DAA in/on lettuce by analyzing two control samples fortified at 0.0500 ppm, 0.100 ppm, and 0.500 ppm. Recoveries of propazine ranged 95.0-101%, recoveries of DEA ranged 92.2-99.1%, and recoveries of DAA ranged 82.5-93.4%.

## C. RESULTS AND DISCUSSION

Concurrent method recovery data are presented in Table C.1. The method is adequate for data collection based on acceptable concurrent method recovery data. Apparent residues of propazine, DEA, and DAA were each below the method LOQ (<0.0500 ppm) in/on all untreated samples of lettuce, mustard, radish (tops and roots), turnip (tops and roots), and wheat (forage, hay, straw, and grain) grown in untreated soil.

Sample storage conditions and intervals are summarized in Table C.2. The maximum storage intervals from harvest to analysis were 129 days (4.2 months) for lettuce, 79 days (2.6 months) for mustard leaves, 100 days (3.3 months) for radish tops and roots, 79 days (2.6 months) for turnip tops and roots, 141 days (4.6 months) for wheat forage, 125 days (4.1 months) for wheat hay, and 89 days (2.9 months) for wheat grain and straw. No storage stability data were included in the subject study. In a separate submission for a residue field study on sorghum (MRID 44287316), it was reported that a storage stability study has been initiated and will be submitted in a separate report. It was also reported in a sorghum metabolism study (MRID 44287315) that the metabolic profiles of sorghum extracts did not change 24 months after the initial chromatographic analysis.

Residue data from the field rotational crop study are presented in Table C.3.; a summary of residue data in rotational crop matrices is presented in Table C.4.

The results of the NC trial indicate that residues of propazine, DEA (G-30033), and DAA (G-28273) were each below the LOQ of 0.0500 ppm in/on all samples of rotational crop commodities (mustard leaves, turnip tops/roots, and spring/winter wheat forage, hay, straw, and grain) at all PBIs (94, 127, and 242/280 days).

The results of the TX trial indicate that residues of propazine, DEA (G-30033), and DAA (G-28273) were each below the LOQ of 0.0500 ppm in/on the following rotational crop commodities and plantback intervals: (i) lettuce leaves at a 97-day PBI; (ii) radish root at PBIs of 97 and 239 days; (iii) wheat forage at PBIs of 120 and 195 days; (iv) wheat hay, straw, and grain at PBIs of 97, 120, and 195 days. A few rotational crop commodities showed quantifiable residues including: (i) lettuce leaves at the 239-day PBI which bore residues of propazine (0.0505-0.0510 ppm), DEA (0.137-0.139 ppm), and DAA (0.139 ppm); (ii) radish tops at the 97-day PBI which bore quantifiable residues of propazine (0.051-0.052 ppm) but nondetectable (< LOQ) residues of DEA and DAA; and (iii) wheat forage at the 97-day PBI which bore quantifiable residues of DEA (0.102-0.107 ppm) but nondetectable (< LOQ) residues of propazine and DAA.



No residues at or above the LOQ were detected in any RAC for any of the intervals from samples harvested from the NC test site. At the TX test site, samples of wheat forage from the 97-day PBI contained measurable residues of the chlorometabolite DEA, samples of lettuce from the 239-day PBI contained measurable residues of propazine and its chlorometabolites DEA and DAA, and samples of radish tops from the 97-day PBI contained measurable residues of propazine. This site was grown under cold dry environmental conditions.

<b>TABLE C.1. Summary of Concurrent Recoveries of Propazine and its Chlorometabolites, DEA and DAA from Rotational Lettuce, Mustard, Radish, Turnip, and Wheat Matrices.</b>				
Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev
<b>Propazine</b>				
Lettuce, leaf	0.100	3	92.5, 112, 114	106 ± 11.9
Mustard, leaf	0.0500	1	86.2	91.9 ± 5.1
	0.100	2	93.5, 96.0	
Radish, root	0.0500	1	106	104
	0.100	1	101	
Radish, top	0.0500	1	105	87.3
	0.100	1	69.5	
Turnip, root	0.0500	1	84.8	94.6 ± 8.6
	0.100	2	98.0, 101	
Turnip, top	0.0500	1	78.6	91.0 ± 13.9
	0.100	2	88.5, 106	
Wheat, forage	0.0500	1	103	96.2 ± 14.1
	0.100	4	83.0, 88.0, 95.5, 121	
	0.200	1	86.5	
Wheat, hay	0.100	5	78.5, 79.0, 82.5, 95.0, 99.0	86.8 ± 9.5
	0.200	1	83.0	
Wheat, straw	0.0500	1	94.8	100 ± 13.1
	0.100	5	83.5, 108, 108, 110, 115	
	0.200	1	83.5	
Wheat, grain	0.0500	1	99.0	106 ± 7.4
	0.100	4	99.5, 104, 111, 116	
<b>DEA</b>				
Lettuce, leaf	0.115	3	92.2, 113, 117	107 ± 13.3
Mustard, leaf	0.0575	1	129	110 ± 16.5
	0.115	2	98.3, 103	
Radish, root	0.0575	1	102	98.9
	0.115	1	95.7	
Radish, top	0.0575	1	106	86.5
	0.115	1	67.0	
Turnip, root	0.0575	1	122	109 ± 11.9
	0.115	2	99.1, 105	



**TABLE C.1. Summary of Concurrent Recoveries of Propazine and its Chlorometabolites, DEA and DAA from Rotational Lettuce, Mustard, Radish, Turnip, and Wheat Matrices.**

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean $\pm$ std dev
Turnip, top	0.0575	1	87.8	96.7 $\pm$ 12.5
	0.115	2	91.3, 111	
Wheat, forage	0.0575	1	88.7	93.2 $\pm$ 14.0
	0.115	4	73.9, 92.2, 96.5, 117	
	0.230	1	90.9	
Wheat, hay	0.115	5	60.0, 86.5, 89.6, 89.6, 93.0	83.3 $\pm$ 12.1
	0.230	1	80.9	
Wheat, straw	0.0575	1	83.0	97.0 $\pm$ 21.8
	0.115	5	75.7, 87.0, 94.8, 116, 137	
	0.230	1	85.2	
Wheat, grain	0.0575	1	104	104 $\pm$ 5.1
	0.115	4	99.1, 100, 103, 112	
<b>DAA</b>				
Lettuce, leaf	0.100	3	76.5, 103, 104	94.5 $\pm$ 15.6
Mustard, leaf	0.0500	1	90.6	85.5 $\pm$ 4.6
	0.100	2	81.5, 84.5	
Radish, root	0.0500	1	66.8	76.7
	0.100	1	86.5	
Radish, top	0.0500	1	108	94.0
	0.100	1	80.0	
Turnip, root	0.0500	2	79.5, 91.2	90.9 $\pm$ 11.3
	0.100	1	102	
Turnip, top	0.0500	2	81.5, 92.2	87.6 $\pm$ 5.5
	0.100	1	89.0	
Wheat, forage	0.0500	1	108	85.8 $\pm$ 16.8
	0.100	4	68.0, 82.0, 86.5, 102	
	0.200	1	68.0	
Wheat, hay	0.100	5	69.5, 78.0, 87.0, 94.5, 119	84.1 $\pm$ 21.7
	0.200	1	56.5	
Wheat, straw	0.0500	1	77.4	98.6 $\pm$ 36.6
	0.100	5	73.5, 77.5, 101, 122, 170	
	0.200	1	69.0	
Wheat, grain	0.0500	1	95.2	88.3 $\pm$ 9.7
	0.100	4	79.0, 79.5, 87.0, 101	



Matrix (RAC or Extract)	Storage Temp. (°C)	Actual Storage Duration <sup>1</sup>	Interval of Demonstrated Storage Stability
Lettuce, leaves	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	110-129 days (3.6-4.2 months)	No storage stability data are available for rotational crops.
Mustard, leaves	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	22-79 days (0.7-2.6 months)	
Radish, tops	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	83-100 days (2.7-3.3 months)	
Radish, roots	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	83-100 days (2.7-3.3 months)	
Turnip, tops	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	18-79 days (0.6-2.6 months)	
Turnip, roots	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	18-79 days (0.6-2.6 months)	
Wheat, forage	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	22-141 days (0.7-4.6 months)	
Wheat, hay	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	56-125 days (1.8-4.1 months)	
Wheat, straw	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	42-89 days (1.4-2.9 months)	
Wheat, grain	field: -36 to -6 °C laboratory: frozen (temperature unspecified)	41-89 days (1.3-2.9 months)	

<sup>1</sup> Actual storage duration from sample collection to analysis. All samples were analyzed within 1-13 days of extraction



Trial ID (City, State, Year)	Region	Crop: Variety	Commod- ity	Total Rate (lb ai/A)	Harvest DAP <sup>1</sup>	PBI <sup>2</sup> (days)	Residues (ppm)					
							Propazine	DEA	DAA	Total		
Lucama, NC, 1995-1996	2	Mustard: Southern Giant Curled	leaves	1.19	171	94	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150		
					152	127	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150		
					59	242	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150		
			Turnip: Purple Top White Globe		tops	1.19	171	94	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150
							152	127	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150
							59	242	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150
		roots		171	94		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150		
				152	127		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150		
				59	242		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150		
		Wheat, winter; Pioneer 2580	forage	1.19	94	171	94	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
						210		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
						259		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
						259		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
		Wheat, winter; Coker 9835	forage	1.19	127	152	127	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
						177		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
						226		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
						226		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
		Wheat, spring; Anderson 2375	forage	1.19	280	53	280	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
						74		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
						116		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150	
						116		NA <sup>4</sup>	NA	NA	NA	



Trial ID (City, State, Year)	Region	Crop: Variety	Commodity	Total Rate (lb ai/A)	Harvest DAP <sup>1</sup>	PBI <sup>2</sup> (days)	Residues (ppm)						
							Propazine	DEA	DAA	Total			
Groom, TX: 1995-1996	8	Lettuce, leaf: Waldmann's Dark Green	leaves	1.21	82	97	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150			
					-- <sup>3</sup>	120	--	--	--	--			
					-- <sup>3</sup>	195	--	--	--	--			
					80	239	0.0510, 0.0505	0.137, 0.139	0.139, 0.139	0.327, 0.329			
					Radish: Scarlet White Tip	tops	1.21	92	97	0.0510, 0.0520	<0.0500, <0.0500	<0.0500, <0.0500	<0.151, <0.152
								-- <sup>3</sup>	120	--	--	--	--
								-- <sup>3</sup>	195	--	--	--	--
								112	239	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150
								Wheat, winter: TAM-101	forage	1.21	92	97	<0.0500, <0.0500
		-- <sup>3</sup>	120	--							--	--	--
		-- <sup>3</sup>	195	--							--	--	--
		112	239	<0.0500, <0.0500							<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150
		Wheat, winter: TAM-101	hay	1.21							183	97	<0.0500, <0.0500
					240		<0.0500, <0.0500				<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150
					267		<0.0500, <0.0500				<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150
					267		<0.0500, <0.0500				<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150
		Wheat, winter: TAM-101	straw	1.21	165	120	<0.0500, <0.0500				<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150
					217		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150			
					244		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150			
					244		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150			
		Wheat, winter: TAM-101	grain	1.21	124	195	<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150			
					142		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150			
					169		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150			
					169		<0.0500, <0.0500	<0.0500, <0.0500	<0.0500, <0.0500	<0.150, <0.150			

<sup>1</sup> DAP = Days After Planting

<sup>2</sup> PBI = Planback Interval.





<sup>1</sup> Lettuce and radish plants were killed by freezing temperatures.  
<sup>2</sup> NA = Not available for analysis.

TABLE C.4. Summary of Residue Data in Rotational Crops Following Primary Treatment with Propazine.										
Commodity	Analyte	Applic. Rate. (lb ai/A)	PBI (days)	Uncorrected Residue Levels (ppm) <sup>1</sup>						
				n	Min.	Max.	HAFT <sup>2</sup>	Median	Mean	Std. Dev.
Lettuce, leaves	Propazine	1.21	97	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.21	239	2	0.0505	0.0510	0.0508	0.0508	0.0508	0.00035
	DEA			2	0.137	0.139	0.138	0.138	0.138	0.00141
	DAA			2	0.139	0.139	0.139	0.139	0.139	0.0
	Total			2	0.327	0.329	0.328	0.328	0.328	0.00141
Mustard, leaves	Propazine	1.19	94	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19	127	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19	242	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
Radish, tops	Propazine	1.21	97	2	0.0510	0.0520	0.0520	0.052	0.052	0.00071
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.151	<0.152	<0.152	<0.152	<0.152	--
	Propazine	1.21	239	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
Radish, roots	Propazine	1.21	97	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.21	239	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--



**TABLE C.4. Summary of Residue Data in Rotational Crops Following Primary Treatment with Propazine.**

Commodity	Analyte	Applic. Rate, (lb ai/A)	PBI (days)	Uncorrected Residue Levels (ppm) <sup>1</sup>						
				n	Min	Max.	HAFT <sup>2</sup>	Median	Mean	Std. Dev.
Turnip, tops	Propazine	1.19	94	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19	127	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19	242	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
Turnip, roots	Propazine	1.19	94	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19	127	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19	242	2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			2	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			2	<0.150	<0.150	<0.150	<0.150	<0.150	--
Wheat, forage	Propazine	1.19-1.21	94/97	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	0.107	0.105	0.076	0.077	0.032
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.207	<0.205	0.176	0.177	0.032
	Propazine	1.19-1.21	120/127	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19-1.21	195/280	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--



**TABLE C.4. Summary of Residue Data in Rotational Crops Following Primary Treatment with Propazine.**

Commodity	Analyte	Applic. Rate. (lb ai/A)	PBI (days)	Uncorrected Residue Levels (ppm)						
				n	Min.	Max.	HAFT <sup>2</sup>	Median	Mean	Std. Dev.
Wheat hay	Propazine	1.19-1.21	94/97	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19-1.21	120/127	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19-1.21	195/280	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--
Wheat straw	Propazine	1.19-1.21	94/97	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19-1.21	120/127	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19-1.21	195/280	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--



**TABLE C.4. Summary of Residue Data in Rotational Crops Following Primary Treatment with Propazine.**

Commodity	Analyte	Applic. Rate. (lb ai/A)	PBI (days)	Uncorrected Residue Levels (ppm) <sup>1</sup>						
				n	Min.	Max.	HAFT <sup>2</sup>	Median	Mean	Std. Dev.
Wheat, grain	Propazine	1.19-1.21	94/97	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19-1.21	120/127	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--
	Propazine	1.19-1.21	195/280	4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DEA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	DAA			4	<0.0500	<0.0500	<0.0500	<0.0500	<0.0500	--
	Total			4	<0.150	<0.150	<0.150	<0.150	<0.150	--

<sup>1</sup> For the determination of minimum, maximum, HAFT, median, mean, and standard deviation values, the LOQ value for each analyte (<0.0500 ppm) was used for residues reported as <0.0500 ppm in Table C.3

<sup>2</sup> HAFT = Highest Average Field Trial.

## D. CONCLUSION

In two limited field rotational crop trials conducted on the representative crops leaf lettuce, radish, mustard, turnip, and wheat, a single preemergence ground spray applications of the 4 lb/gal FIC formulation was made at 1.19 or 1.21 lb ai/A prior to planting grain sorghum (the primary crop). At the NC trial site, grain sorghum was removed from the 94-day PBI subplots 86 and 87 days after treatment (DAT), however, grain sorghum was cut from the 127-day PBI and 242-day PBI subplots 123 DAT. At the TX trial site, grain sorghum was removed from all plots 95 DAT due to wet weather conditions. At PBIs of 94/97, 120/127, 195, or 239/242/280 days, the following rotational crops were planted: radish or turnip (a root vegetable), lettuce or mustard (a leafy vegetable), and winter or spring wheat (a cereal grain). Samples of radish (roots and tops), turnip (roots and tops), leaf lettuce (leaves), mustard (leaves), wheat (forage, hay, grain, and straw) were collected at appropriate crop growth stage or at maturity.

At the 94/97-day PBI, the combined residues of propazine and its chlorometabolites DEA and DAA were below the LOQ (<0.150 ppm) in/on lettuce leaves, mustard leaves, radish roots, turnip tops and roots, and wheat hay, straw, and grain. At the 120/127-day PBI, the combined residues of propazine and its chlorometabolites DEA and DAA were below the LOQ (<0.150 ppm) in/on mustard leaves, turnip tops and roots, and wheat forage, hay, straw, and grain. At the 195/239/242/280-day PBI, the combined residues of propazine and its chlorometabolites DEA and DAA were below the LOQ (<0.150 ppm) in/on mustard leaves, radish tops and roots, turnip tops and roots, and wheat forage, hay, straw, and grain. At the 97-day PBI, quantifiable residues of propazine were observed in radish tops and quantifiable residues of metabolite DEA were



observed in wheat forage. At the 239-day PBI quantifiable residues of propazine and its chlorometabolites DEA and DAA were observed in lettuce leaves.

## E. REFERENCES

44287315 Jalali, K.; Saber, A.; O'Neal, S.; et al. (1997) [<sup>14</sup>C]Propazine: Metabolic Fate and Distribution in Grain Sorghum: Amended (Final) Report: Lab Project Number: 817E/514W: 817E/514W-1: 817E. Unpublished study prepared by PTRL East, Inc. and PTRL West, Inc. 356 p.

44287316 Bookbinder, M. (1997) Magnitude of the Residue of Propazine (2-Chloro-4,6-bis(isopropylamino)-s-triazine) and its Metabolites in/on Grain Sorghum Forage, Grain, and Stover Harvested after Preemergence Ground Application of Milo-Pro 4L Herbicide: Final Report: Lab Project Number: 6641-106: MGB 94001: 94001. Unpublished study prepared by Corning Hazleton, Inc. 362 p.

## F. DOCUMENT TRACKING

RDI: P.V. Shah (8/24/05), RAB1 Chemists (8/24/05)  
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Petition Number(s): 7F4837  
DP#: 323273  
PC Code: 080808

Template Version September 2003



Primary Evaluator: *George F. Kramer* Date: 07-DEC-2005  
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Health Effects Division (HED) (7509C)

Approved by: *P.V. Shah* Date: 07-DEC-2005  
P.V. Shah, Ph.D., Branch Senior  
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This DER was originally prepared under contract by Dynamac Corporation (20440 Century Boulevard, Suite 100; Germantown, MD 20874; submitted 07/13/2005). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

### **STUDY REPORTS:**

44184813 O'Neal, S; Bentley, W. (1996) [<sup>14</sup>C]Propazine: Metabolic Fate and Distribution in Grain Sorghum: Lab Project Number: 817E/514W: 817E: 103S/817E. Unpublished study prepared by PTRL East, Inc. 69 p.

44184814 Jalali, K; Saber, A; O'Neal, S. et. al. (1996) [<sup>14</sup>C]Propazine: Metabolic Fate and Distribution in Grain Sorghum: Lab Project Number: CHW 6641-104: AM-067: GP96-018. Unpublished study prepared by Corning Hazleton Inc. 317 p.

44287315 Jalali, K.; Saber, A.; O'Neal, S.; et al. (1997) [<sup>14</sup>C]Propazine: Metabolic Fate and Distribution in Grain Sorghum: Amended (Final) Report: Lab Project Number: 817E/514W: 817E/514W-1, 817E. Unpublished study prepared by PTRL East, Inc. and PTRL West, Inc. 356 p.

### **EXECUTIVE SUMMARY:**

Griffin Corporation has submitted a sorghum metabolism study with propazine under greenhouse conditions. Four days after sorghum was seeded in test plots, [<sup>14</sup>C]propazine (labeled uniformly in the triazine ring, specific activity of 49.42 mCi/mmole) was applied as one broadcast spray directed to the soil of test plots at target rates of 2.4 and 4.8 lb ai/A; the achieved application rates were verified at 1.96 and 3.91 lb ai/A, respectively. Sorghum forage samples were harvested 45 days after treatment, while grain and stover samples were harvested 124 days posttreatment. The in-life phase was conducted by PTRL East, Inc. (Richmond, KY), and the analytical phase was conducted by PTRL West, Inc. (Richmond, CA).

Total radioactive residues (TRR) were 0.126, 0.133 and 2.344 ppm in/on sorghum forage, grain and fodder (stover), respectively, following one application of [<sup>14</sup>C]propazine at 1.96 lb ai/A. At the treatment rate of 3.91 lb ai/A, the TRR were 0.084, 0.132 and 2.678 ppm in the forage, grain and stover, respectively. Samples which received the treatment rate of 1.96 lb ai/A were selected for residue characterization and identification.



Residues in/on treated sorghum matrices were extracted using a series of solvent systems. Solvent extraction with methanol and methanol/water released 67.6% of TRR in forage and 53.4% of TRR in stover. For grain, extraction with methanol and methanol/water released 39.7% of TRR, and hydrolysis with 6 N HCl further released 34.1% of TRR. Additional radioactivity was released in sorghum matrices by: (i) methanol/0.1 N HCl for grain; (ii) 0.1 N HCl; and (iii) 3 N KOH. Nonextractable residues following extraction/hydrolysis accounted for 4.8%, 6.0% and 12.1% TRR in the forage, grain and stover, respectively. The accountabilities were 101.6%, 103.8% and 97.4% in forage, grain and stover, respectively. Residues were identified and quantitated primarily by C18 and SCX (strong cation-exchange) high-performance liquid chromatography (HPLC) co-chromatography with confirmatory analysis by HPLC and/or thin-layer chromatography (TLC) co-chromatography. These methods successfully identified the predominant residues in sorghum forage, grain and stover.

In **forage**, chromatographic analysis of the combined methanol and methanol/water extracts (subsample B) identified the parent propazine as a trace component at 0.8% TRR (0.001 ppm). The chlorometabolite, atrazine des-ethyl (G-30033), was identified at 8.7% TRR (0.011 ppm) along with the following hydroxymetabolites: propazine 2-hydroxy (GS-11526) at 13.5% TRR (0.017 ppm) and atrazine des-ethyl 2-hydroxy (GS-17794) at 8.7% TRR (0.011 ppm).

In **grain**, chromatographic analysis of the combined methanol and methanol/water extracts (subsample A) also showed trace amounts of the parent propazine at 0.8% TRR (<0.001 ppm). Other residue components include atrazine des-ethyl 2-hydroxy (GS-17794) at 10.3% TRR (0.013 ppm) and propazine 2-hydroxy (GS-11526) at 2.3% TRR (<0.003 ppm).

In **stover (fodder)**, chromatographic analysis of the chloroform layer of the combined methanol and methanol/water extracts (subsample D) resolved propazine at 0.5% TRR (0.011 ppm). All other residue components were identified at <10% TRR. Atrazine des-ethyl (G-30033) and prometon (G-31435) accounted for 1.7% TRR (<0.039 ppm) and 1.6% TRR (0.037 ppm), respectively. Propazine 2-hydroxy (GS-11526), atrazine des-ethyl 2-hydroxy (GS-17794), and GS-16141 accounted for 2.7% TRR (0.064 ppm), 3.3% TRR (0.077 ppm), and 3.4% TRR (0.080 ppm), respectively (quantified in the 6 N HCl extracts and combined methanol and methanol/water extracts of subsample A). Ammeline (GS-17791) and atrazine des-ethyl des-isopropyl (G-28273) both accounted for 2.2% TRR (<0.052 ppm; quantified in the combined methanol and methanol/water extracts of subsample A). The ammeline (GS-17791) and atrazine des-ethyl des-isopropyl (G-28273) peaks, overlapping in all HPLC methods employed in the study, accounted for an additional 3.7% TRR (0.086 ppm). CGA-101248 accounted for 2.7% TRR (0.064 ppm; quantified in the combined methanol and methanol/water extracts of subsample A).

The remaining radioactivity in sorghum matrices was characterized as unassigned or diffuse radioactivity, accounting for 35.7% TRR (0.045 ppm, ~27 peaks) in forage, 27.1% TRR (0.036 ppm, ~10 peaks) in grain, and 46.1% TRR (1.081 ppm, ~49 peaks) in stover. In forage, ~18% TRR was characterized based on acid hydrolysis (0.1 N HCl and 6 N HCl), and 11.2% TRR was characterized following base hydrolysis. In grain, 2.1% TRR was characterized based on acidic



methanol extraction, approximately 42% TRR was characterized based on acid hydrolysis (0.1 N HCl and 6 N HCl), and 13.6% TRR was characterized following base hydrolysis. In stover, 16.1% TRR was characterized based on acid hydrolysis with 0.1 N HCl, and 2.8% TRR was characterized following base hydrolysis. In forage and grain, the dichloromethane partitioning of the hydrolysates of the 6 N HCl and 3 N KOH extractions, which were found to contain ~10% TRR, indicated that the radioactivity compounds were highly polar, water-soluble materials, not organic. These hydrolysates could not be analyzed by HPLC due to their viscosity after concentration.

An additional subsample of sorghum stover (subsample B) was subjected to a different extraction scheme after the initial extraction with methanol and methanol/water in order to maximize the release of radiocarbon by using increasingly harsh extractions to break down the plant constituents into various classes of organic materials. Solvent extraction with methanol and methanol/water released the majority of the TRR (66.5%). Additional radioactivity was released in sorghum stover by: (i) phosphate buffer (6.5% TRR, 0.152 ppm); (ii)  $\alpha$ -amylase (4.0% TRR, 0.095 ppm); (iii) pronase (2.7% TRR, 0.062 ppm); (iv) pectin (3.1% TRR, 0.072 ppm); (v) lignin (1.8% TRR, 0.043 ppm); (vi) hemicellulose (5.0% TRR, 0.116 ppm); and (vii) cellulose (4.2% TRR, 0.099 ppm). Nonextractable residues following extraction/hydrolysis accounted for 1.4% TRR. No metabolites were identified in the HPLC analyses of the exhaustive/enzymatic extractions.

Sorghum forage samples were stored frozen for ~8 months prior to extraction, while the grain and stover samples were stored frozen for 5 months prior to extraction. The time intervals between extractions and analyses of the test sorghum matrices were not provided. Methanol and methanol/water extraction conducted 24 months after the original extraction date indicated no loss of radioactivity. Subsequent chloroform partitioning of the combined methanol extracts, performed two months after extraction, also yielded a metabolic profile similar to that of the initial chloroform partitioning. No additional storage stability data are required to support the study.

Based on the results of the sorghum metabolism study, propazine is rapidly and extensively metabolized in sorghum via: (i) N-dealkylation; (ii) replacement of chlorine by hydroxy; and (iii) glutathione conjugation. The petitioner stated that the results of the study were similar to other published results of triazine herbicides.

#### **STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:**

Under the conditions and parameters used in the study, the sorghum metabolism data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision (TRED) Document for propazine.





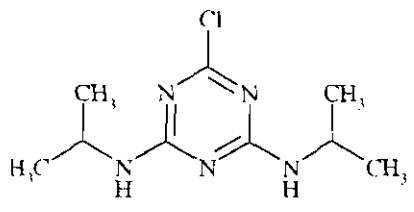
## COMPLIANCE:

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

Propazine (6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine) is a member of the chloro triazine class of herbicides. Other members of this pesticide class include atrazine, cyanazine, and simazine. Propazine is a selective herbicide that can be applied before planting, at planting, and after crop emergence for the preemergence control of annual broadleaf weeds. Currently, the only registered uses are for weed control of ornamental plants grown in containers under greenhouse conditions. There are presently no registered food/feed uses of propazine.

Propazine was previously registered for use on sorghum. The 5/19/87 Propazine Residue Chemistry Chapter along with the 12/88 Propazine Reregistration Standard (Guidance Document) identified several data deficiencies for the reregistration of propazine. Ciba-Geigy, which was then the basic manufacturer of propazine, elected to cancel its registrations of propazine. Another registrant, Griffin Corporation, is now supporting the previously-cancelled uses of propazine on grain sorghum. The structure and nomenclature of propazine are presented in Table A.1. The physicochemical properties of propazine are listed in Table A.2.

TABLE A.1. Propazine Nomenclature	
PC Code 006308	
Chemical structure	
Common name	Propazine
Molecular Formula	C <sub>9</sub> H <sub>16</sub> N <sub>4</sub> Cl
Molecular Weight	229.7
IUPAC name	6-chloro- <i>N,N'</i> -di-isopropyl-1,3,5-triazine-2,4-diamine
CAS name	6-chloro- <i>N,N'</i> -bis(1-methylethyl)-1,3,5-triazine-2,4-diamine
CAS #	139-40-2



Parameter	Value	Reference
Melting point	217.7 °C	RD D219079, 9/26/95. S. Malak
pH	5.66	
Density, bulk density, or specific gravity	0.46 g/mL	
Water solubility	3.8 ppm at 25 °C	
Solvent solubility (at 25 °C)	14,252 ppm in acetone 4,696 ppm in 1-octanol	
Vapor pressure	2.9 x 10 <sup>-8</sup> mm Hg at 20 °C  2.98 x 10 <sup>-5</sup> Torr at 45 °C	Product Chemistry Chapter of the Propazine Reregistration Standard, 5/19/87  RD D219079, 9/26/95. S. Malak
Dissociation constant, pK	Not applicable; practically insoluble in water.	RD D219079, 9/26/95. S. Malak
Octanol/water partition coefficient	P = 1234.7 Log P = 3.08	

## B. EXPERIMENTAL DESIGN

### B.1. Test Site and Crop Information

Testing Environment	Soil characteristics <sup>1</sup>			
	Type	%OM	pH	CEC
Plants were grown in four planting boxes measuring 2.5 ft x 3.0 ft x 2.25 ft (w x l x d) in a greenhouse (Richmond, Kentucky)	sandy loam (Madison County, Kentucky)	2.83	6.99	5.8 meq/100 g

<sup>1</sup> %OM = % Organic Matter. CEC = Cation Exchange Capacity.

Daily climatic parameters such as rainfall, wind direction, minimum and maximum air temperature and relative humidity, were monitored inside and outside of the greenhouse. From planting of sorghum to mature harvest of sorghum samples, maximum air temperatures ranged 41.4 °C to 22.7 °C inside the greenhouse, while minimum air temperatures ranged 22.2 °C to 5.9 °C inside the greenhouse. Average relative humidity was approximately 80% to 16% inside the greenhouse from planting of sorghum to mature harvest of sorghum samples. Natural sunlight, which was supplemented with artificial light as necessary, was employed during the study at the maximum hours of light per day for the crop species (hours of day and night were not specified). Sorghum plants were manually irrigated with a pre-measured volume of water. Soil was fertilized prior to planting, and plants received light weeding and maintenance pesticides as needed. The petitioner reported that the test substance treatment produced no adverse effect on

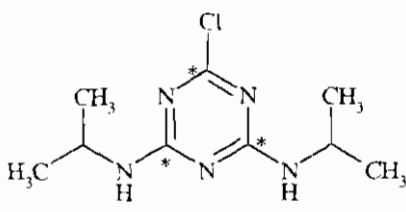


the growth or development of the sorghum plants under testing conditions, i.e., plant growth was normal.

**TABLE B.1.2. Crop Information.**

Crop: crop group	Variety	Growth stage at application	Growth stage at harvest	Harvested RAC	Harvesting procedure
Sorghum: Cereal grains and Foliage and fodder of cereal grains	Hybrid sorghum (Designation ATx2752*RTx430)	Four days after planting (or seeding)	49 and 128 days after planting	Forage, grain and stover	At 49 days after planting, the forage was cut with a razor blade 0.25 inches above the soil line. At 128 days after planting, the crop was harvested, and the mature heads (grain) were separated from the mature fodder (stover).

**B.2. Test Materials****TABLE B.2.1. Test Material Characteristics**

Chemical structure:	
Radiolabel position	[ring-U- <sup>14</sup> C]propazine
Lot No.	812B-4-1
Purity	99.5-99.6% radiochemical purity
Specific activity	49.42 mCi/mmol

**B.3. Study Use Pattern****TABLE B.3.1. Use Pattern Information**

Chemical name	<sup>14</sup> C-propazine
Application method	A stock treatment suspension was prepared by adding radiolabeled propazine to a formulation suspension of non-radiolabeled propazine. The treatment solution was prepared by combining the stock treatment suspension with HPLC-grade water, then broadcast applied using 65-mL glass bottles with a plastic manual trigger sprayer. The soil surface was sprayed in a crosswise application pattern
Application rate	1.96 lb ai/A (measured); 2.4 lb ai/A (nominal)
Number of applications	1
Timing of applications	The application was made 4 days after planting.
PHI	45 days for forage; 124 days for grain and stover

The petitioner also conducted an experiment at 3.91 lb ai/A (measured; 4.8 lb ai/A, nominal). All planting and test material application procedures were the same as those for the lower



application rate, except that only one planting box was used. Metabolite identification work was not conducted on the higher application rate samples.

## **B.4. Identification/Characterization of Residues**

### **B.4.1. Sample Handling and Preparation**

All samples were placed in Ziploc™ bags and stored in a cooler with dry ice. The immature harvest was shipped from PTRL East, Inc. on dry ice to the initial facility (PTRL South, Inc.) on the day of harvest; the mature harvest was shipped on dry ice to PTRL South four days after harvest. At PTRL South, the samples were stored frozen (<0 °C). After the forage, stover and grain were separately processed with dry ice and homogenized, the samples were sent to the analytical testing facility (PTRL West, Inc.). The shipment of the samples to PTRL West occurred 73 days (grain and stover) or 156 days (forage) after shipment to PTRL South.

Forage and grain: A subsample (designated subsample A) of forage or grain was extracted (three times for forage and two times for grain) with methanol via mixing and sonication. The supernatant was removed via centrifugation, and the extraction was repeated until <5% TRR was found in the extract. All extracts were combined. Nonextractable residues following the methanol extraction were extracted (two times for forage and three times for grain) with methanol:water (1:1, v:v). The extract was separated, and the extraction was repeated as necessary. All extracts were combined and added to the combined extract of the methanol extraction prior to HPLC analysis. For grain only, the nonextractable residues from the methanol:water extraction were extracted once with methanol:0.1% HCl (1:1, v:v). The extract was removed. Nonextractable residues following methanol:water extraction (for forage) or methanol:0.1% HCl extraction (for grain) were extracted with 0.1 N aqueous HCl. The extract was separated, and the extraction was repeated again for grain only. Nonextractable residues following 0.1 N HCl extraction were subjected to acid hydrolysis twice with 6 N HCl at 80 °C for 4-6 hours. The hydrolysate was removed via centrifugation, then analyzed by HPLC. Nonextractable residues following 6 N HCl extraction were subjected to base hydrolysis once with 3 N KOH at reflux for 4-6 hours. The hydrolysate was removed via centrifugation. The remaining nonextractable residue was dried prior to combustion/LSC. The hydrolysates of the 6 N HCl and 3 N KOH extraction which were found to contain a significant amount of radioactivity (> 10% TRR) were partitioned with dichloromethane in order to determine the nature of the radioactivity.

The combined methanol extract (from the methanol and methanol:water extractions) of a second subsample (designated subsample B) of forage was concentrated via rotary evaporation to remove methanol, then partitioned with chloroform to selectively remove chloro-metabolites. The aqueous layer and chloroform layer were separated and analyzed by HPLC. Concentration of extracts via rotary evaporation prior to HPLC analyses was performed as necessary.

Stover: A subsample (designated subsample A) of stover was extracted four times with methanol via mixing and sonication. The supernatant was removed via centrifugation, and the extraction



was repeated until <5% TRR was found in the extract. All extracts were combined. Nonextractable residues following the methanol extraction were extracted twice with methanol:water (1:1, v:v). The extract was isolated and combined with the combined extract of the methanol extraction prior to HPLC analysis. Following SCX solid-phase extraction (SPE), the combined extracts were analyzed again by HPLC. Nonextractable residues following methanol:water extraction were extracted three times with 0.1 N aqueous HCl. The extract was removed and analyzed by HPLC, then subjected to C-18 SPE prior to additional HPLC analysis. Nonextractable residues following 0.1 N HCl extraction were subjected to acid hydrolysis twice with 6 N HCl at 80 °C for 4-6 hours. The hydrolysate was removed via centrifugation, then analyzed by HPLC. Following SCX SPE, the hydrolysate was analyzed again by HPLC. Nonextractable residues following 6 N HCl extraction were subjected to base hydrolysis once with 3 N KOH at reflux for 4-6 hours. The hydrolysate was removed via centrifugation, then analyzed by HPLC. The remaining nonextractable residue was dried prior to combustion/LSC.

A subsample (designated subsample B) of stover was extracted with methanol via mixing and sonication. The supernatant was removed via centrifugation, and the extraction was repeated until <5% TRR was found in the extract. All extracts were combined. Nonextractable residues following the methanol extraction were extracted with methanol:water (1:1, v:v). The extract was isolated and combined with the combined extract of the methanol extraction prior to HPLC analysis. Nonextractable residues following methanol:water extraction were subjected to buffer extraction with phosphate buffer (pH 7) extraction via shaking for 10 minutes. The residue was removed via vacuum filtration. The filtrate was isolated and analyzed via HPLC analysis. The residue from the buffer extraction was suspended in the pH 7 phosphate buffer and subjected to starch digestion by incubation with  $\alpha$ -amylase in a shaking water bath at 30 °C for 20 hours. The enzymatic activity of the  $\alpha$ -amylase was verified through control experiments. The residue was removed via vacuum filtration. The filtrate was isolated and analyzed via HPLC analysis. The residue from the starch digestion was mixed with Tris buffer and subjected to protein digestion by incubation with pronase E in a shaking water bath at 25 °C for ~20 hours. The residue was removed via vacuum filtration. The filtrate was isolated and analyzed via HPLC analysis. The residue from the protein digestion was subjected to pectin extraction by mixing with 0.05 M sodium acetate:0.05 M EDTA (1:1, v:v), then incubating in a shaking water bath at 70 °C for ~22 hours. The residue was removed via vacuum filtration. The filtrate was isolated and analyzed via HPLC analysis. The residue from the pectin extraction was mixed with de-ionized water and subjected to lignin extraction by the addition of glacial acetic acid and sodium chlorite four times. After each addition of glacial acetic acid and sodium chlorite, the mixture was incubated in a shaking water bath at 70 °C for 1 hour (4 hours of incubation total). The residue was removed via vacuum filtration. The filtrate was isolated and analyzed via HPLC analysis. The residue from the lignin extraction was subjected to hemicellulose extraction by mixing with aqueous KOH (24%, w:w) and incubating in a shaking water bath at 25 °C for ~40 hours. After mixing with aqueous 6 N HCl for 10 minutes, the residue was removed via vacuum filtration. The filtrate was isolated and analyzed via HPLC analysis. The residue from the hemicellulose extraction was subjected to cellulose extraction by sonication with sulfuric acid (70%) at room temperature for 4 hours. The pH of the hydrolysate was adjusted to 7.0 with aqueous KOH (24%, w:v), then mixed with deionized water to dissolve the potassium sulfate precipitate. The



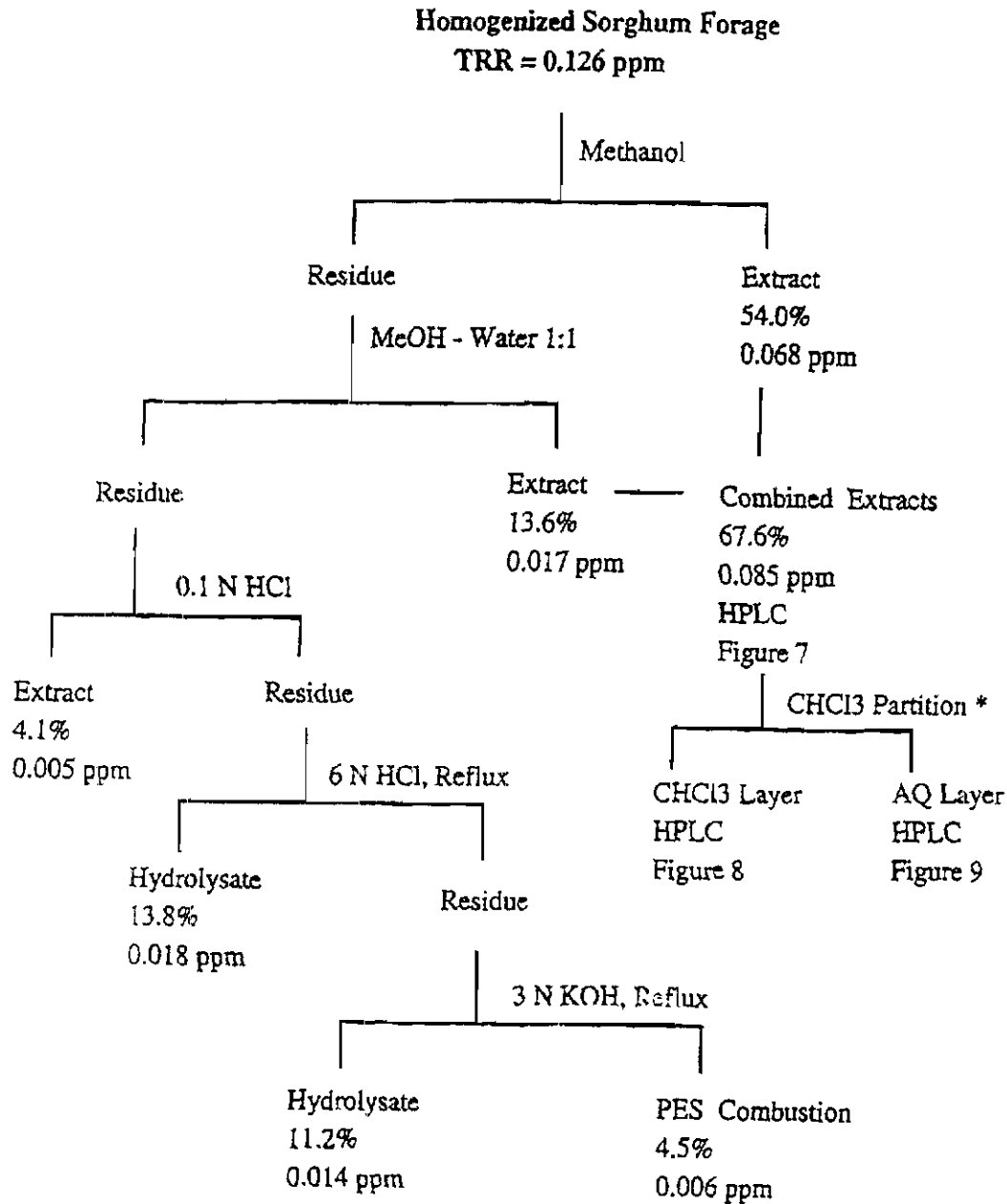
residue was removed via vacuum filtration. The filtrate was isolated and analyzed via HPLC analysis. The remaining nonextractable residue was dried prior to combustion/LSC.

The combined methanol extract (from the methanol and methanol:water extractions which were repeated as described above) of a second subsample (designated subsample D) of stover was concentrated via rotary evaporation to remove methanol after HPLC analysis, then partitioned with chloroform to selectively remove chloro-metabolites. The aqueous layer and chloroform layer were separated, then the chloroform layer was analyzed by HPLC and TLC. Concentration of extracts via rotary evaporation prior to HPLC analyses was performed as necessary.

The extraction procedures for the sorghum matrices are summarized in the flow charts below, which were copied without alteration from MRIDs 44184814 and 44287315.



### Extraction Procedure for Forage (Subsamples A and B)

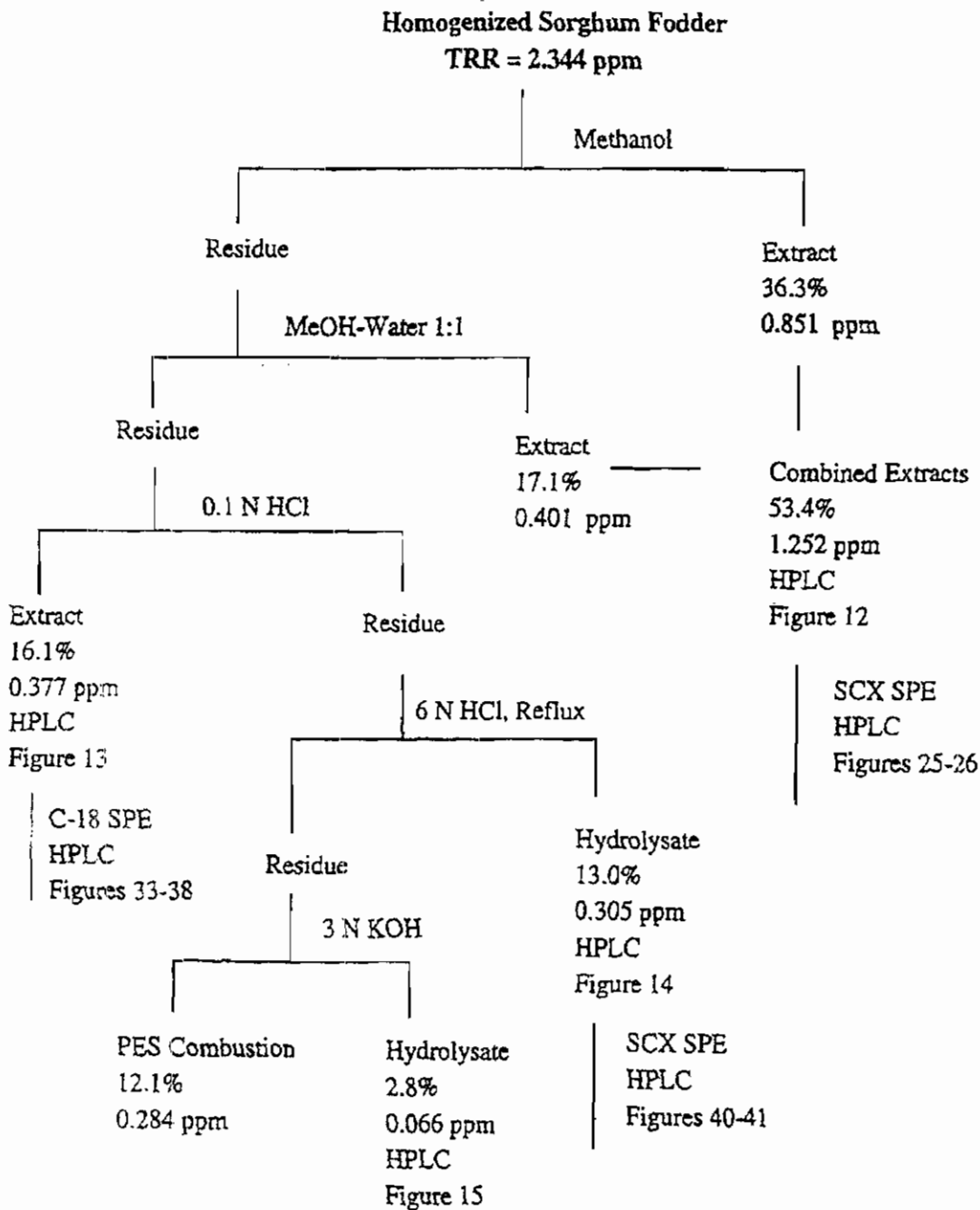


\* This procedure was actually carried out on a second sub-sample (B) of forage.

Total Extracted = 96.8%  
Total Recovered = 101.3%



**Extraction Procedure for Stover (Subsample A)**

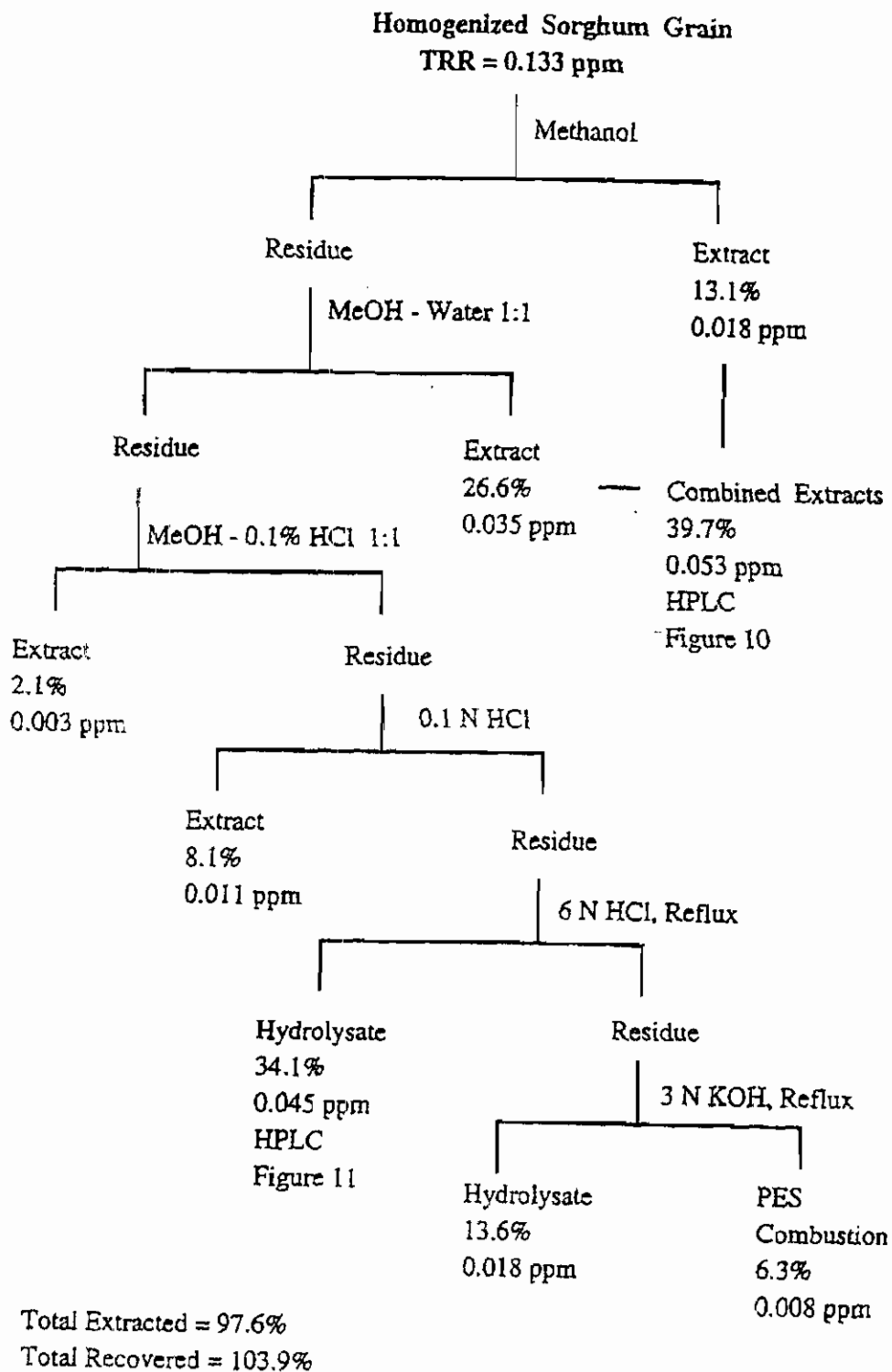


Percent Extracted = 85.3%  
 Total Recovered = 97.4%



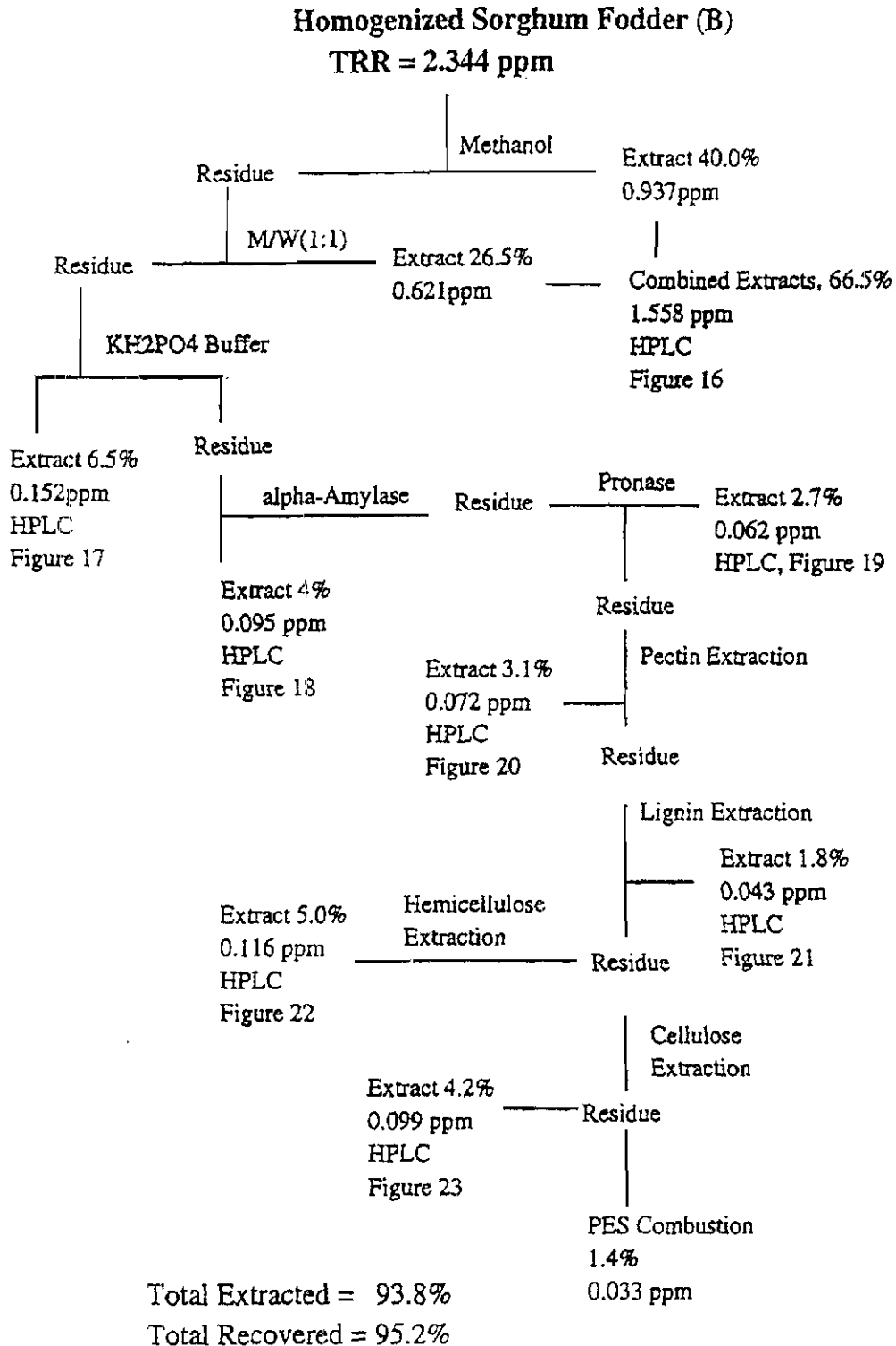


### Extraction Procedure for Grain (Subsample A)



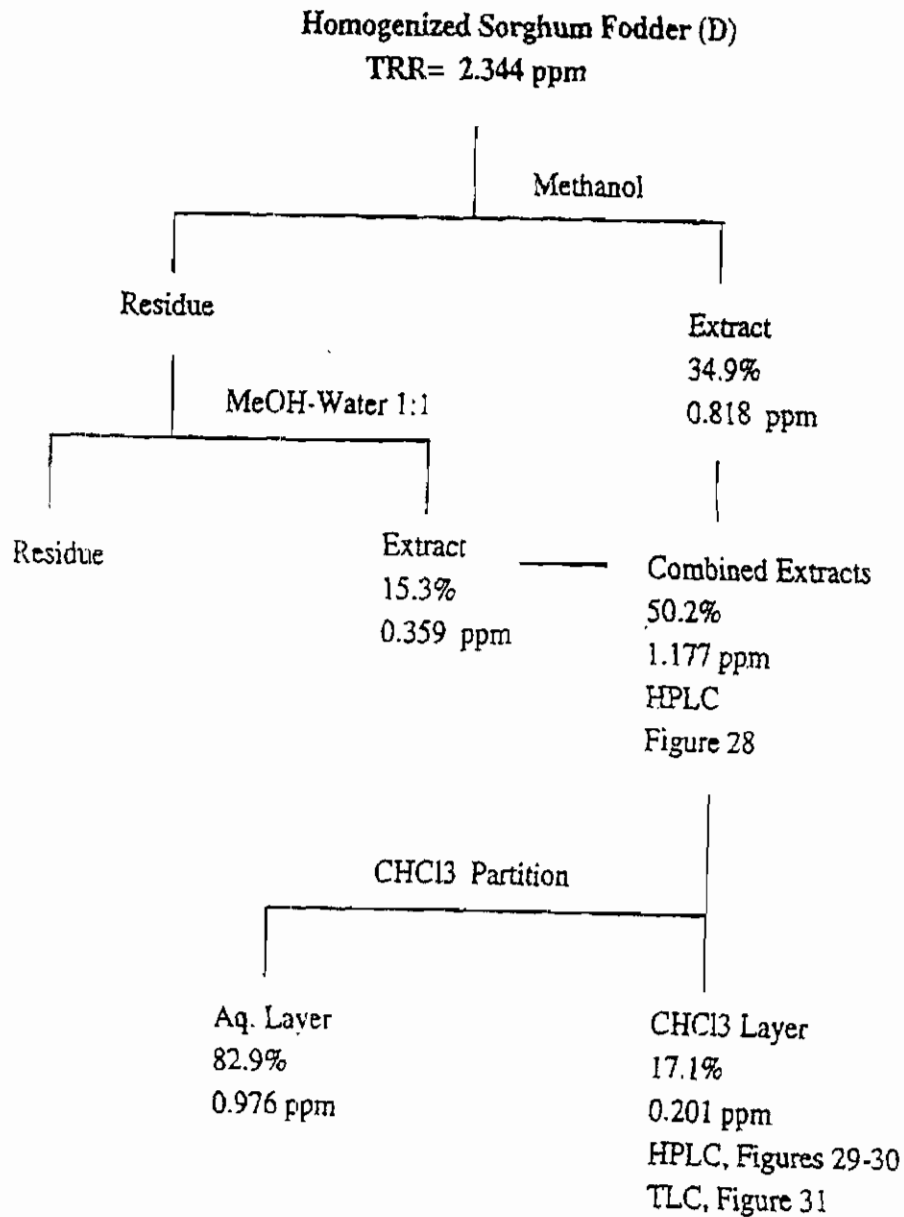


**Extraction Procedure for Stover (Subsample B)**





### Extraction Procedure for Stover (Subsample D)





#### **B.4.2. Analytical Methodology**

TRR in sorghum matrices were determined by combustion/LSC of the processed sorghum samples prior to extraction procedures. The combustion efficiency was 0.994 and 0.980 for the low dose and high dose samples, respectively. The limit of detection (LOD) was reported as 2x background (0.008 ppm for the typical sample size of approximately 0.25 g).

Extracts and hydrolysates of sorghum matrices were subjected to reverse-phase and cation-exchange HPLC analyses for identification and quantification of the test material and its metabolites. HPLC analyses were conducted on systems equipped with a ultraviolet (UV) detector. Radiolabeled compounds were detected by radioassaying fractions (~0.5 mL) which were collected every 30 seconds; HPLC radiochromatograms were reconstructed using a radiochromatograph program. The following column/mobile phase combinations were used: (Methods I and II) analytical C18 column (Microsorb LC18) with a gradient mobile phase of 0.1% phosphoric acid and acetonitrile (ACN) with 0.1% phosphoric acid; (Method III) semi-prep C18 column (Supelco LC18) with a gradient mobile phase of 0.1% phosphoric acid and ACN with 0.1% phosphoric acid; and (Method IV) cation-exchange column (Supelcosil LC-SCX) with a gradient mobile phase of 0.1N phosphoric acid:0.05M NaCl (1:1, v:v; pH 3.5) and 0.15M NaCl:ACN (2:1, v:v). Method I was used for initial profiling; Methods II and IV were mainly used for co-chromatographic comparison with reference standards; and Method III was used for isolation of metabolites in extracts. The LOD for the reconstructed HPLC radiochromatograms was based on the LOD for the LSC data, i.e., 2x background.

Confirmation of the identification of the test material and its metabolites was performed using TLC analyses. TLC analyses were conducted using silica gel F254 plates and two solvent systems: chloroform:methanol:formic acid:water (75:10:1:1, v:v:v:v) and butanol acetic acid:water (6:1:1, v:v:v). For 1D TLC analyses, one of the solvent systems was used; for 2D TLC analyses, both solvent systems were used.

Metabolites were identified by co-chromatography and/or retention time comparisons with reference standards. Chemical names and structures for the reference standards are presented in Appendix I.

### **C. RESULTS AND DISCUSSION**

Total radioactive residues in sorghum matrices are reported in Table C.2.1. TRR were determined by combustion/LSC of the processed forage, grain and stover prior to extraction. In sorghum samples harvested following one application of [<sup>14</sup>C]propazine at 1.96 lb ai/A, TRR were 0.126, 0.133 and 2.344 ppm in the forage, grain and stover, respectively.

The distribution of radioactivity in sorghum matrices is presented in Tables C.2.2.1 (forage), C.2.2.2 (grain) and C.2.2.3 (stover). Solvent extraction with methanol and methanol/water released the majority of the TRR in forage (67.6%) and stover (53.4%). For grain, the extraction



with methanol and methanol/water released a similar amount of TRR (39.7%) as the extraction with 6 N HCl (34.1%). Additional radioactivity was released in sorghum matrices by: (i) methanol/0.1 N HCl for grain; (ii) 0.1 N HCl; and (iii) 3 N KOH. Nonextractable residues following extraction/hydrolysis accounted for 4.8%, 6.0% and 12.1% TRR in the forage, grain and stover, respectively. The accountabilities were 101.6%, 103.8% and 97.4% in forage, grain, and stover, respectively. Residues were identified and quantitated primarily by C18 and SCX HPLC co-chromatography with confirmatory analysis by HPLC and/or TLC co-chromatography. These methods successfully identified the predominant residues in sorghum forage, grain and stover; however, it is noted that the HPLC differentiation between ammeline and atrazine des-ethyl des-isopropyl would be difficult due to their similar retention times in all HPLC Methods which were used in the study.

The characterization and identification of residues in sorghum matrices are summarized in Table C.2.3. Approximately 32%, 13% and 24% TRR were identified in sorghum forage, grain and stover, respectively. Propazine was identified at 0.8% TRR (0.001 ppm) in **forage**. Metabolite propazine 2-hydroxy was identified as the major metabolite in forage, accounting for 13.5% TRR (0.017 ppm). All remaining metabolites were identified at <10% TRR. Atrazine des-ethyl and atrazine des-ethyl 2-hydroxy both accounted for 8.7% TRR (0.011 ppm). Compounds were only identified in the methanol and methanol/water extracts. Quantification of these extracts was based on the data from the chloroform partitioning of the combined methanol and methanol/water extracts (subsample B).

Propazine was identified at 0.8% TRR (<0.001 ppm) in **grain**. Metabolite atrazine des-ethyl 2-hydroxy was identified as the major metabolite in grain, accounting for 10.3% TRR (0.013 ppm). All remaining metabolites were identified at <10% TRR. Propazine 2-hydroxy was the only other metabolite identified, accounting for 2.3% TRR (<0.003 ppm). Compounds were only identified in the methanol and methanol/water extracts. Quantification was based on the data from the combined methanol and methanol/water extracts (subsample A).

Propazine was identified at 0.5% TRR (0.011 ppm) in **stover** (quantified in the chloroform layer of the combined methanol and methanol/water extracts of subsample D). All metabolites were identified at <10% TRR in stover. Atrazine des-ethyl and prometon accounted for 1.7% TRR (<0.039 ppm) and 1.6% TRR (0.037 ppm), respectively (quantified in the chloroform layer of the combined methanol and methanol/water extracts of subsample D). Propazine 2-hydroxy, atrazine des-ethyl 2-hydroxy and GS-16141 accounted for 2.7% TRR (0.064 ppm), 3.3% TRR (0.077 ppm) and 3.4% TRR (0.080 ppm), respectively (quantified in the 6 N HCl extracts and combined methanol and methanol/water extracts of subsample A). Ammeline and atrazine des-ethyl des-isopropyl both accounted for 2.2% TRR (<0.052 ppm; quantified in the combined methanol and methanol/water extracts of subsample A). The peaks for ammeline and atrazine des-ethyl des-isopropyl overlapped in all HPLC methods employed in the study. The combined ammeline and atrazine des-ethyl des-isopropyl peak accounted for 3.7% TRR (0.086 ppm). CGA-101248 accounted for 2.7% TRR (0.064 ppm; quantified in the combined methanol and methanol/water extracts of subsample A).



The remaining radioactivity in sorghum matrices was characterized as unassigned or diffuse radioactivity, accounting for 35.7% TRR (0.045 ppm, ~27 peaks) in forage, 27.1% TRR (0.036 ppm, ~10 peaks) in grain and 46.1% TRR (1.081 ppm, ~49 peaks) in stover. In forage, approximately 18% TRR was characterized based on acid hydrolysis (4.1% with 0.1 N HCl and 13.8% with 6 N HCl), and 11.2% TRR was characterized based on base hydrolysis. In grain, 2.1% TRR was characterized based on acidic methanol extraction, approximately 42% TRR was characterized based on acid hydrolysis (8.1% with 0.1 N HCl and 34.1% with 6 N HCl), and 13.6% TRR was characterized based on base hydrolysis. In stover, 16.1% TRR was characterized based on acid hydrolysis with 0.1 N HCl, and 2.8% TRR was characterized based on base hydrolysis. In forage and grain, the dichloromethane partitioning of the hydrolysates of the 6 N HCl and 3 N KOH extractions, which were found to contain a significant amount of radioactivity (~10% TRR), indicated that the radioactivity compounds were highly polar, water-soluble materials, not organic. These hydrolysates could not be analyzed by HPLC due to their viscosity after concentration.

Identification of propazine in sorghum forage and stover was confirmed by HPLC co-chromatography. In grain, propazine was identified by comparison of HPLC retention times. Identification of metabolites atrazine des-ethyl, propazine 2-hydroxy and atrazine des-ethyl 2-hydroxy were confirmed by HPLC co-chromatography in forage and stover and by comparison of HPLC retention times in grain. Identification of metabolites prometon, GS-16141 and CGA-101248 were confirmed by HPLC co-chromatography in stover. Ammeline and atrazine des-ethyl des-isopropyl were identified in stover by comparison of HPLC retention times.

An additional subsample of sorghum stover (subsample B) was subjected to a different extraction scheme after the initial extraction with methanol and methanol/water in order to maximize the release of radiocarbon by using increasingly harsh extractions to break down the plant constituents into various classes of organic materials. Solvent extraction with methanol and methanol/water released the majority of the TRR (66.5%). Additional radioactivity was released in sorghum stover by: (i) phosphate buffer, 6.5% TRR (0.152 ppm); (ii)  $\alpha$ -amylase, 4.0% TRR (0.095 ppm); (iii) pronase, 2.7% TRR (0.062 ppm); (iv) pectin, 3.1% TRR (0.072 ppm); (v) lignin, 1.8% TRR (0.043 ppm); (vi) hemicellulose, 5.0% TRR (0.116 ppm); and (vii) cellulose, 4.2% TRR (0.099 ppm). Nonextractable residues following extraction/hydrolysis accounted for 1.4% TRR. No metabolites were identified in the HPLC analyses of the exhaustive/enzymatic extractions.

### C.1. Storage Stability

The storage intervals for sorghum samples are presented in Table C.1. Sorghum forage samples were stored frozen for ~8 months prior to extraction, while the grain and stover samples were stored frozen for 5 months prior to extraction. This storage interval includes the shipment of the samples to the processing facility prior to shipment to the analytical facility. The samples were stored frozen at the processing facility for 73 days (grain and stover) or 156 days (forage). The temperature during storage was not specified in terms of °C or °F. The time interval between extractions and analyses of the test sorghum matrices were not provided. Methanol and



methanol:water extraction conducted 24 months after the original extraction date indicated no loss of radiocarbon. Subsequent chloroform partitioning of the combined methanol extracts, performed two months after extraction, yielded a metabolic profile similar to that of the initial chloroform partitioning. The available data indicate that the residues of propazine and its major metabolites were generally stable for the duration of the study. No additional storage stability data are required. The petitioner should note that for future metabolism study submissions, the specific storage temperature for all samples should be provided, as well as dates of analyses.

**TABLE C.1. Summary of Storage Conditions.**

Matrix	Storage Temp (°C)	Actual Storage Duration	Interval of Demonstrated Storage Stability
Forage	frozen*	247 days (- 8 months)	24 months
Grain	frozen*	150 days (5 months)	24 months
Stover	frozen*	150 days (5 months)	24 months

\* Temperature not specified.

## C.2. Identification, Characterization, and Distribution of Residues

**TABLE C.2.1. Total Radioactive Residues (TRR) in Sorghum Matrices.**

Matrix	Timing and Applic. No.	PHI (days)	<sup>14</sup> C-propazine, ppm	
			1.96 lb ai/A	3.91 lb ai/A
Forage	one directed soil application four days after seeding	45	0.126	0.084
Grain		124	0.133	0.132
Stover		124	2.344	2.678

**TABLE C.2.2.1 Distribution of the Parent and the Metabolites in Sorghum Forage Following Application of [<sup>14</sup>C]Propazine at 1.96 lb ai/A.**

Metabolite Fraction	Forage TRR = 0.126 ppm	
	%TRR <sup>1</sup>	ppm
Methanol and Methanol/water	67.5	0.085
Chloroform	12.7	0.016
Propazine	0.8	0.001
Atrazine des-ethyl	8.7	0.011
Unassigned <sup>2</sup>	3.2	0.004
Aqueous	54.8	0.069
Propazine 2-hydroxy	13.5	0.017
Atrazine des-ethyl 2-hydroxy <sup>3</sup>	8.7	0.011
Unassigned <sup>2</sup>	32.5	0.041
Nonextractable <sup>4</sup>	34.1	0.043
0.1 N HCl	4.0	0.005
6 N HCl	14.3	0.018
3 N KOH	11.1	0.014



**TABLE C.2.2.1 Distribution of the Parent and the Metabolites in Sorghum Forage Following Application of [<sup>14</sup>C]Propazine at 1.96 lb ai/A.**

Metabolite Fraction	Forage TRR = 0.126 ppm	
	%TRR <sup>1</sup>	ppm
Nonextractable	4.8	0.006

<sup>1</sup> The petitioner did not provide the %TRR values for identified compounds. All %TRR values of identified compounds were reviewer-calculated from the ppm values provided by the petitioner using the following equation: (ppm of compound)/(total TRR ppm) x 100. For example, (0.016 ppm)/(0.126 ppm) x 100 = 12.7%.

<sup>2</sup> Unassigned radioactivity was reviewer-calculated by determining the ppm of unassigned peaks in the HPLC raw data, then using the equation for conversion to %TRR mentioned above.

<sup>3</sup> Assigned based on chromatographic comparison with reference standards by only one method.

<sup>4</sup> The petitioner did not provide the %TRR and ppm values for the nonextractable residues after methanol and methanol/water extractions; therefore, the reviewer calculated these values by summing the ppm of 0.1 N HCl, 6 N HCl and 3 N KOH extractions with the remaining nonextractables, then calculating the %TRR using the equation for conversion to %TRR mentioned above.

**TABLE C.2.2.2 Distribution of the Parent and the Metabolites in Sorghum Grain Following Application of [<sup>14</sup>C]Propazine at 1.96 lb ai/A.**

Metabolite Fraction	Grain TRR = 0.133 ppm	
	%TRR <sup>1</sup>	ppm
Methanol and Methanol/water	39.8	0.053
Propazine	0.8	<0.001
Propazine 2-hydroxy	2.3	<0.003
Atrazine des-ethyl 2-hydroxy <sup>2</sup>	9.8	0.013
Unassigned <sup>3</sup>	27.1	0.036
Nonextractable <sup>4</sup>	63.9	0.085
Methanol/0.1 N HCl	2.3	0.003
0.1 N HCl	8.3	0.011
6 N HCl	33.8	0.045
3 N KOH	13.5	0.018
Nonextractable	6.0	0.008

<sup>1</sup> The petitioner did not provide the %TRR values for identified compounds. All %TRR values of identified compounds were reviewer-calculated from the ppm values provided by the petitioner using the following equation: (ppm of compound)/(total TRR ppm) x 100. For example, (0.001 ppm)/(0.133 ppm) x 100 = 0.8%.

<sup>2</sup> Assigned based on chromatographic comparison with reference standards by only one method.

<sup>3</sup> Unassigned radioactivity was reviewer-calculated by determining the ppm of unassigned peaks in the HPLC raw data, then using the equation for conversion to %TRR mentioned above.

<sup>4</sup> The petitioner did not provide the %TRR and ppm values for the nonextractable residues after methanol and methanol/water extractions; therefore, the reviewer calculated these values by summing the ppm of Methanol/0.1 N HCl (grain only), 0.1 N HCl, 6 N HCl and 3 N KOH extractions with the remaining nonextractables, then calculating the %TRR using the equation for conversion to %TRR mentioned above.





Propazine/PC Code 080808/Griffin Corp.

DACO 6.3/OPPTS 860.1300/OECD II 6.2.2, 6.2.3 & IIIA 8.2, 8.4.1, 8.4.2

Nature of the Residues in Plants - Sorghum

**TABLE C.2.2.3 Distribution of the Parent and the Metabolites in Sorghum Stover Following Application of [<sup>14</sup>C]Propazine at 1.96 lb ai/A.**

Metabolite Fraction	Stover					
	Subsample A		Subsample B		Subsample D	
	TRR = 2.344 ppm		TRR = 2.344 ppm		TRR = 2.344 ppm	
	%TRR <sup>1</sup>	ppm	%TRR	ppm	%TRR <sup>1</sup>	ppm
Methanol and Methanol/water	55.4	1.252	66.5	1.558	50.2	1.177
Propazine 2'-hydroxy	0.9	0.022				
Atrazine des-ethyl 2'-hydroxy	2.0	0.047				
Atrazine des-ethyl des-isopropyl <sup>2</sup>	2.2	<0.052				
Ammeline	2.2	<0.052				
Atrazine des-ethyl des-isopropyl/Ammeline*	3.7	0.086				
CGA-101248	2.7	0.064				
GS-16141	2.4	0.057				
Unassigned <sup>3</sup>	37.2	0.871				



**TABLE C.2.2.3 Distribution of the Parent and the Metabolites in Sorghum Stover Following Application of [<sup>14</sup>C]Propazine at 1.96 lb ai/A.**

Metabolite Fraction	Stover					
	Subsample A		Subsample B		Subsample D	
	TRR = 2.344 ppm		TRR = 2.344 ppm		TRR = 2.344 ppm	
	%TRR <sup>1</sup>	ppm	%TRR	ppm	%TRR <sup>1</sup>	ppm
Chloroform <sup>4</sup>					8.6	0.201
Propazine					0.5	0.011
Atrazine des-ethyl					1.7	<0.039
Prometon					1.6	0.037
Unassigned <sup>3</sup>					4.9	0.114
Aqueous <sup>4</sup>					41.6	0.976
Nonextractable	44.1	1.034	28.7	0.672	49.8	1.167
0.1 N HCl	16.1	0.377				
6 N HCl	13.0	0.305				
Propazine 2-hydroxy	1.8	0.042				
Atrazine des-ethyl 2-hydroxy	1.3	0.030				
GS-16141	1.0	0.023				
Unassigned <sup>3</sup>	9.0	0.210				
3 N KOH	2.8	0.066				
Phosphate buffer			6.5	0.152		
α-Amylase			4.0	0.095		
Pronase			2.7	0.062		
Pectin			3.1	0.072		
Lignin			1.8	0.043		
Hemicellulose			5.0	0.116		
Cellulose			4.2	0.099		
Nonextractable	12.1	0.284	1.4	0.033		

Note: Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question

<sup>1</sup> The petitioner did not provide the %TRR values for identified compounds. All %TRR values of identified compounds were reviewer-calculated from the ppm values provided by the petitioner using the following equation: (ppm of compound)/(total TRR ppm) x 100. For example, (0.011 ppm)/(2.344 ppm) x 100 = 0.5%.

<sup>2</sup> Assigned based on chromatographic comparison with reference standards by only one method.

<sup>3</sup> Since the quantification of the identified compounds was based on different (C18 and SCX) HPLC radiochromatograms, the reviewer calculated the ppm of the unassigned radioactivity as the difference between the total ppm of the extract and the sum of the ppm of the identified compounds of that extract. Then, the %TRR was calculated using the equation for conversion to %TRR mentioned above.

<sup>4</sup> The petitioner did not provide the %TRR values for the chloroform and aqueous layers, only the percent of the combined extracts of the methanol and methanol/water extractions; therefore, the reviewer calculated these values by using the equation for conversion of ppm to %TRR mentioned above.

<sup>5</sup> The petitioner did not provide the %TRR and ppm values for the nonextractable residues after methanol and methanol/water extractions; therefore, the reviewer calculated these values by summing the ppm of further extractions and the remaining nonextractables, then calculating the %TRR using the equation for conversion to %TRR mentioned above. In the case of subsample D where no further extractions were performed, the reviewer calculated the ppm of the nonextractable residues as



the difference between the total residues and the residues extracted after methanol and methanol/water extractions, then calculating the % TRR using the equation for conversion to % TRR mentioned above.

Compound	Forage <sup>1</sup>		Grain <sup>1</sup>		Stover <sup>1</sup>	
	TRR = 0.126 ppm		TRR = 0.133 ppm		TRR = 2.344 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
<b>Identified</b>						
Propazine <sup>2</sup>	0.8	0.001	0.8	<0.001	0.5	0.011
Atrazine des-ethyl <sup>3</sup>	8.7	0.011	--	--	1.7	<0.039
Propazine 2-hydroxy	13.5	0.017	2.3	<0.003	2.7	0.064
Atrazine des-ethyl 2-hydroxy	8.7	0.011	10.3	0.013	3.3	0.077
Atrazine des-ethyl des-isopropyl	--	--	--	--	2.2	<0.052
Ammeline	--	--	--	--	2.2	<0.052
Atrazine des-ethyl des-isopropyl/Ammeline	--	--	--	--	3.7	0.086
CGA-101248	--	--	--	--	2.7	0.064
Prometon <sup>2</sup>	--	--	--	--	1.6	0.037
GS-16141	--	--	--	--	3.4	0.080
<b>Characterized</b>						
Methanol/0.1 N HCl	--	--	2.3	0.003	--	--
0.1 N HCl	4.0	0.005	8.3	0.011	16.1	0.377
6 N HCl	14.3	0.018	33.8	0.045	--	--
3 N KOH	11.1	0.014	13.5	0.018	2.8	0.066
Unassigned	35.7	0.045	27.1	0.036	46.1	1.081
Total identified	31.7	0.040	13.4	<0.017	24.0	<0.562
Total characterized	65.1	0.082	85.0	0.113	65.0	1.524
Total extractable	96.8	0.122	97.7	0.130	89.0	2.086
Unextractable (PFS) <sup>4</sup>	4.8	0.006	6.0	0.008	12.1	0.284
Accountability <sup>4</sup>	101.6		103.8		97.4	

<sup>1</sup> The reported values for each metabolite/fraction reflect the total amount found in all extracts and hydrolysates. Refer to Tables C.2.2.1, C.2.2.2, and C.2.2.3 for details.

<sup>2</sup> The data for the quantification was based on the HPLC of the chloroform layer of the chloroform partitioning of the combined extracts of methanol and methanol/water extractions of subsample D.

<sup>3</sup> Residues remaining after exhaustive extractions.

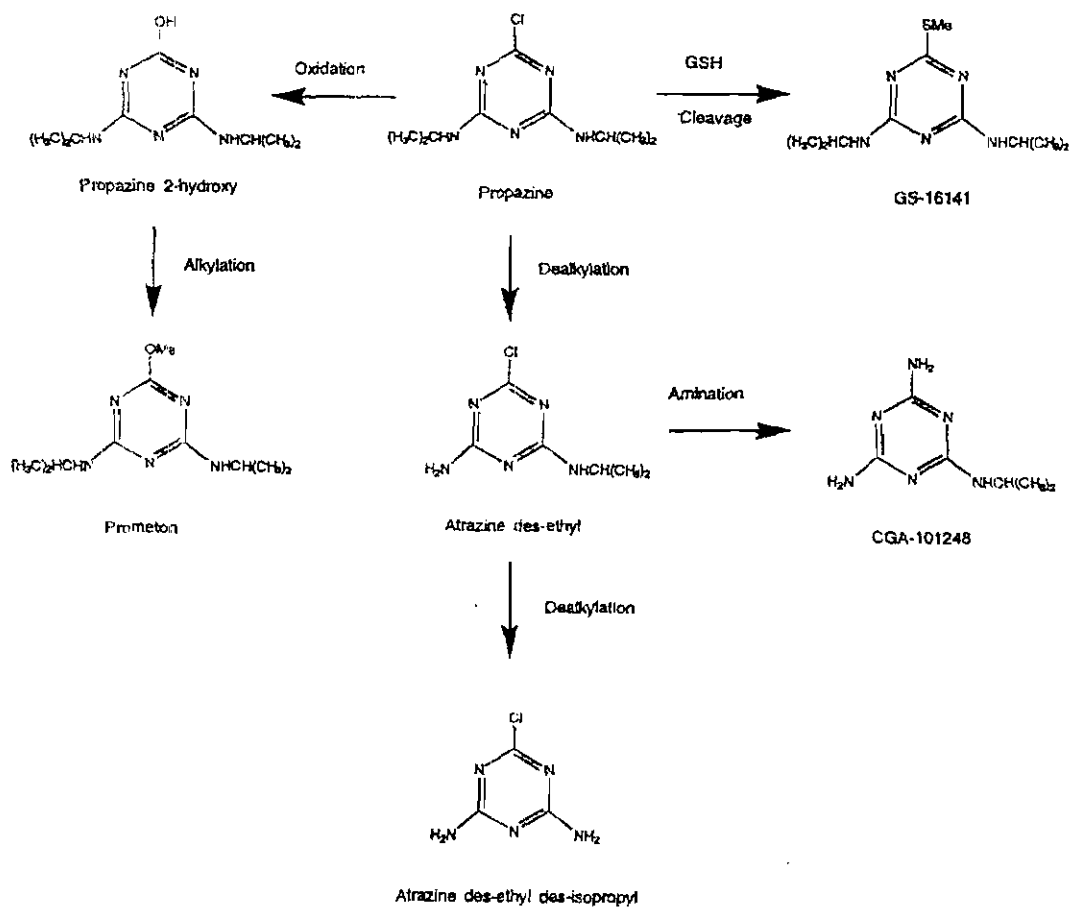
<sup>4</sup> Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis: see TABLE C.2.1) \* 100.



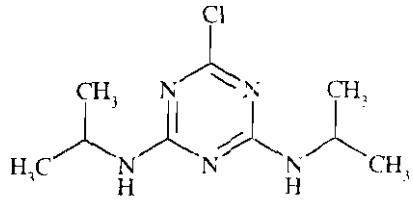
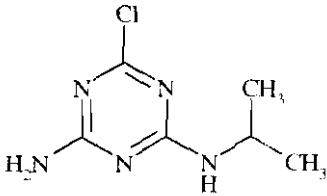
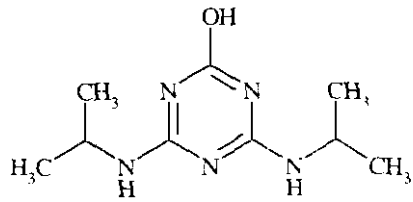
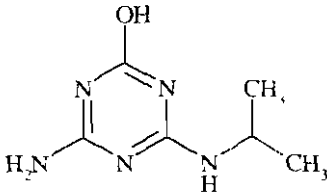
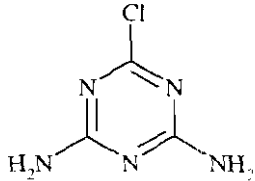
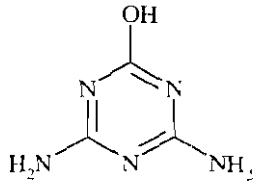
### C.3. Proposed Metabolic Profile

#### FIGURE C.3.1. Proposed Metabolic Profile of Propazine in Sorghum

This figure was copied without alteration from MRIDs 44184814 and 44287315.



**TABLE C.3.1. Identification of Compounds from Metabolism Study.**

Common name/code Figure C.3.1 ID No	Chemical name	Chemical structure
Propazine	2-chloro-4,6-bis(isopropylamino)-s-triazine	
Atrazine des-ethyl	2-amino-4-chloro-6-(1-methylethylamino)-s-triazine	
Propazine 2-hydroxy	2-hydroxy-4,6-bis(1-methylethylamino)-s-triazine	
Atrazine des-ethyl 2-hydroxy	2-amino-4-hydroxy-6-(1-methylethylamino)-s-triazine	
Atrazine des-ethyl des-isopropyl	2,4-diamino-6-chloro-s-triazine	
Ammeline	2,4-diamino-6-hydroxy-s-triazine	



Common name/code Figure C.3.1 ID No	Chemical name	Chemical structure
CGA-101248	N-(1-methyl)-1,3,5-triazine-2,4,6-triamine	
Prometon	2-methoxy-4,6-bis(1-methylethylamino)-s-triazine	
GS-16141	2,4-bis(1-methylethylamino)-6-methylsulfinyl-s-triazine	

## D. CONCLUSION

Total radioactive residues in sorghum matrices harvested following one application of  $^{14}\text{C}$ [propazine] at 1.96 lb ai/A were 0.126, 0.133 and 2.344 ppm in the forage, grain and stover, respectively. Solvent extraction with methanol and methanol/water released the majority of the TRR in forage (67.6%) and stover (53.4%). For grain, the extraction with methanol and methanol/water released a similar amount of TRR (39.7%) as the extraction with 6 N HCl (34.1%). Additional radioactivity was released in sorghum matrices by: (i) methanol/0.1 N HCl for grain; (ii) 0.1 N HCl; and (iii) 3 N KOH. Nonextractable residues following extraction/hydrolysis accounted for 4.8%, 6.0% and 12.1% TRR in the forage, grain and stover, respectively. The accountabilities were 101.6%, 103.8% and 97.4% in forage, grain, and stover, respectively.

Propazine was identified at 0.8% TRR (0.001 ppm) in **forage**. Metabolite propazine 2-hydroxy was identified as the major metabolite in forage, accounting for 13.5% TRR (0.017 ppm). All remaining metabolites were identified at <10% TRR, including atrazine des-ethyl and atrazine des-ethyl 2 hydroxy. Propazine was identified at 0.8% TRR (<0.001 ppm) in **grain**. Metabolite atrazine des-ethyl 2 hydroxy was identified as the major metabolite in grain, accounting for 10.3% TRR (0.013 ppm). Propazine 2-hydroxy was the only other metabolite identified,



accounting for <10% TRR. Propazine was identified at 0.5% TRR (0.011 ppm) in stover. All metabolites were identified at <10% TRR in stover, including atrazine des-ethyl, prometon, propazine 2-hydroxy, atrazine des-ethyl 2 hydroxy, GS-16141, ammeline and atrazine des-ethyl des-isopropyl (overlapping peaks in all HPLC methods employed in the study), and CGA-101248. Remaining radioactivity (27.1-46.1% TRR) in sorghum matrices was characterized as unassigned or diffuse radioactivity.

An additional subsample of sorghum stover was subjected to a different extraction scheme after the initial extraction with methanol and methanol/water in order to maximize the release of radiocarbon by using increasingly harsh extractions to break down the plant constituents into various classes of organic materials. Solvent extraction with methanol and methanol/water released the majority of the TRR (66.5%). Nonextractable residues following extraction/hydrolysis accounted for 1.4% TRR. No metabolites were identified in the HPLC analyses of the exhaustive/enzymatic extractions.

Based on the results of the sorghum metabolism study, the petitioner concluded that propazine is rapidly and extensively metabolized in sorghum via: (i) N-dealkylation; (ii) replacement of chlorine by hydroxy; and (iii) glutathione conjugation. The petitioner stated that the results of the study were similar to other published results of triazine herbicides.

## **E. REFERENCES**

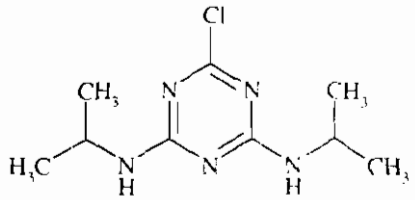
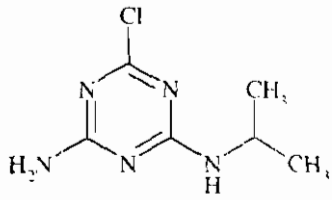
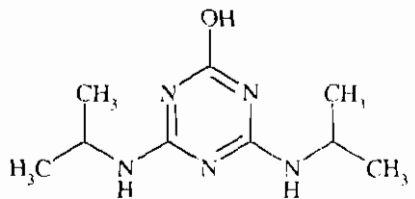
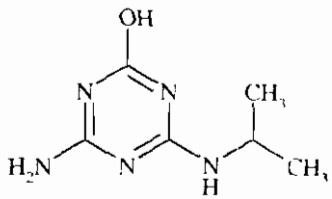
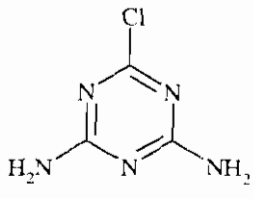
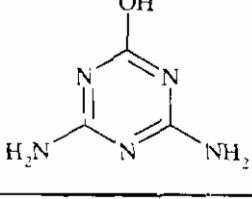
None.

## **F. DOCUMENT TRACKING**

RDI: P.V. Shah (8/25/05), RAB1 Chemists (8/3/05)  
G.F. Kramer:806T:CM#2:(703)305-5079:7509C:RAB1  
Petition Number(s): 7F4837  
DP#: 323273  
PC Code: 080808

Template Version September 2003

**APPENDIX I. Chemical Names and Structures of Reference Standards Used in Sorghum Metabolism Study.**

Common name. Company code	Chemical name	Chemical structure
Propazine	2-chloro-4,6-bis(isopropylamino)-s-triazine	
Atrazine des-ethyl (G-30033)	2-amino-4-chloro-6-(1-methylethylamino)-s-triazine	
Propazine 2-hydroxy (GS-11526)	2-hydroxy-4,6-bis(1-methylethylamino)-s-triazine	
Atrazine des-ethyl 2-hydroxy (GS-17794)	2-amino-4-hydroxy-6-(1-methylethylamino)-s-triazine	
Atrazine des-ethyl des-isopropyl (G-28273)	2,4-diamino-6-chloro-s-triazine	
Ammeline (GS-17791)	2,4-diamino-6-hydroxy-s-triazine	



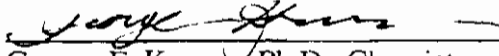



APPENDIX I. Chemical Names and Structures of Reference Standards Used in Sorghum Metabolism Study.		
Common name, Company code	Chemical name	Chemical structure
Ammelide (G-35713)	2,4-diamino-6-amino-s-triazine	 <chem>Nc1nc(O)c(O)n1</chem>
CGA-101248	N-(1-methyl) 1,3,5-triazine-2,4,6-triamine	 <chem>CC(C)Nc1nc(N)c(N)n1</chem>
Prometon (G-31435)	2-methoxy-4,6-bis(1-methylethylamino)-s-triazine	 <chem>CC(C)Nc1nc(OC)c(NC(C)C)n1</chem>
GS-16141	2,4-bis(1-methylethylamino)-6-methylsulfinyl-s-triazine	 <chem>CC(C)Nc1nc(SC)c(NC(C)C)n1</chem>
CGA-236433	Not reported	 <chem>Nc1nc(=S)c(N)n1</chem>



<b>APPENDIX I. Chemical Names and Structures of Reference Standards Used in Sorghum Metabolism Study.</b>		
Common name, Company code	Chemical name	Chemical structure
Cyanuric acid	Not reported	 <chem>Oc1nc(O)n(O)c1</chem>



Primary Evaluator:   
George F. Kramer, Ph.D., Chemist Date: 07-DEC-2005  
Registration Action Branch I (RAB1)  
Health Effects Division (HED) (7509C)

Approved by:   
P.V. Shah, Ph.D., Branch Senior Date: 07-DEC-2005  
Scientist/RAB1/HED (7509C)

In the absence of signatures, this document is considered to be a draft with deliberative material for internal use only.

---

This DER was originally prepared under contract by Dynamac Corporation (20440 Century Boulevard, Suite 100; Germantown, MD 20874; submitted 07/13/2005). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

### **STUDY REPORT:**

44184815 Krautter, G.; Downs, J.; Marsh, J. (1996) [<sup>14</sup>C]Propazine: Metabolism in a Lactating Goat Following Oral Administration for Seven Consecutive Days: Lab Project Number: 822: 1614: 101. Unpublished study prepared by PTRL East, Inc. 232 p.

### **EXECUTIVE SUMMARY:**

Griffin Corporation has submitted a goat metabolism study with propazine. The test substance, [<sup>14</sup>C]propazine (labeled uniformly in the triazine ring, specific activity of 49.42 mCi/mmmole), was administered orally to a single lactating goat at 9.9 ppm in the diet. The goat was dosed once per day for seven consecutive days. Milk was collected twice daily throughout the study, and tissues (muscle, fat, liver, and kidney) were collected at sacrifice. The in-life and analytical phases of the study were conducted by PTRL East, Inc. (Richmond, KY).

Total radioactive residues (TRR) were 0.080-0.238 ppm in milk, 1.123 ppm in liver, 1.041 ppm in kidney, 0.209 ppm in muscle, and 0.160 ppm in fat. Radioactivity was highest in liver and kidney, and lowest in fat. Residues in milk were generally highest in samples collected 8 hours after dosing and appeared to have reached a plateau after two days of dosing. The study reported that a large portion of the administered dose was excreted, with urine and feces (including cage washes and solids) accounting for a total of ~74% of the administered dose.

Radioactive residues in goat milk and tissues were adequately extracted using water and a combination of organic solvents. Enzyme hydrolysis was also used to release bound residues in muscle and fat tissues only. In milk, ~91% of TRR was retained in the aqueous fraction with acidified hexane extraction. In tissues, ~86-98% of TRR was extractable with water, and additional minor amounts (<3% TRR) were subsequently extracted with acetonitrile (ACN)/water, ACN, and hexane. Nonextractable residues after solvent extraction and enzyme hydrolysis were 18.9% TRR (0.042 ppm) for milk, 10.8% TRR (0.113 ppm) for kidney, 6.1% TRR (0.068 ppm) for liver, 5.9% TRR (0.012 ppm) for muscle, and 7.2% TRR (0.012 ppm) for



fat. These data suggest that further attempts should have been made to release the nonextractable/bound residues in kidney and liver.

Residues in extracts and hydrolysates were subjected to high-performance liquid chromatography (HPLC) analysis. Metabolites were identified by comparison of retention times or co-chromatography with 17 reference standards including standards of known chloro- and hydroxy-metabolites of triazine herbicides. The identities of metabolites were confirmed by thin-layer chromatography (TLC) co-chromatography.

Approximately 73% of TRR was identified in goat milk, 50% TRR in fat, 26% TRR in muscle, and <3% TRR in kidney and liver. The parent propazine was not detected in goat milk or tissues. Atrazine-desethyl-desisopropyl (G-28273) was the principal residue component identified in milk (63.4% TRR, 0.141 ppm), fat (50.4% TRR, 0.080 ppm), muscle (26.1% TRR, 0.054 ppm), and liver (2.7% TRR, 0.031 ppm). The metabolite atrazine-desethyl (G-30033) was only identified in milk (9.4% TRR, 0.021 ppm).

The remaining radioactivity in goat milk and tissues was characterized to be comprised of up to six unknown metabolites. Although each unknown accounted for <7% TRR in milk, several unknowns were present at significant levels in goat tissues. None of these unknown residues co-chromatographed with propazine, propazine-2-hydroxy, ammelide or any other reference standards used in the study. Region G was the major unknown component in kidney (59.5% TRR, 0.619 ppm) and liver (76.1% TRR, 0.855 ppm) but was present at lower levels in muscle (5.8% TRR, 0.012 ppm) and fat (15.6% TRR, 0.025 ppm). Region G was characterized by the petitioner as stable to glucuronidase, sulfatase, and 3 N HCl hydrolysis. Based on the metabolism of other triazine herbicides, the petitioner proposed that the unknown may be an acid-stable glutathione conjugate of propazine or one of its biotransformation products.

Another unknown, Region A, was quantitated at >10% TRR in muscle (19.9% TRR, 0.042 ppm), fat (10.3% TRR, 0.016 ppm), and kidney (10.2% TRR, 0.106 ppm). Region E was detected in kidney as a significant residue at 21.2% TRR (0.221 ppm). The petitioner stated that acid and enzyme hydrolysis was conducted on the pronase hydrolysate of the aqueous extract of kidney to further characterize unknown residues. However, no discussion of the results and no chromatograms for the acid and enzyme hydrolysates were presented.

Milk samples were stored frozen for <6 months and tissues for ~7 months. Adequate storage stability data were submitted demonstrating the stability of the metabolic profile in goat kidney and liver for up to ~23 months.

Based on the results of the study, the petitioner concluded that propazine is metabolized in goats via sequential dealkylation of the isopropyl alkyl groups with excretion in the urine, primarily as the di-dealkylated metabolite (atrazine-desethyl-desisopropyl or G-28273). A water-soluble, hydrolytically-stable conjugate of propazine or one of its metabolites may also be formed, which is the major metabolite in goat tissues.



## **STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:**

When the study is evaluated according to OPPTS GLN 860.1300, the goat metabolism data are classified as scientifically unacceptable because of insufficient characterization of radioactive residues in goat matrices particularly in kidney, liver, and muscle. In a Memorandum of Understanding between HED and Griffin for Propazine (1/11/96, M. Metzger), HED has indicated that if the available goat metabolism studies adequately and separately determine residues of each chlorometabolite, each hydroxymetabolite, and TRR for each commodity for which data are required, further identification work for the metabolism study in which parent propazine was fed should not be required. Other regulatory conclusions resulting from this study will be addressed in the forthcoming Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision (TRED) Document for propazine.

## **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.

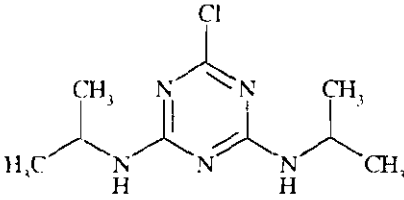
### **A. BACKGROUND INFORMATION**

Propazine (6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine) is a member of the chloro triazine class of herbicides. Other members of this pesticide class include atrazine, cyanazine, and simazine. Propazine is a selective herbicide that can be applied before planting, at planting, and after crop emergence for the preemergence control of annual broadleaf weeds. Currently, the only registered uses are for weed control of ornamental plants grown in containers under greenhouse conditions. There are presently no registered food/feed uses of propazine.

Propazine was previously registered for use on sorghum. The 5/19/87 Propazine Residue Chemistry Chapter along with the 12/88 Propazine Reregistration Standard (Guidance Document) identified several data deficiencies for the reregistration of propazine. Ciba-Geigy, which was then the basic manufacturer of propazine, elected to cancel its registrations of propazine. Another registrant, Griffin Corporation, is now supporting the previously-cancelled uses of propazine on grain sorghum. The structure and nomenclature of propazine are presented in Table A.1. The physicochemical properties of propazine are listed in Table A.2.



**TABLE A.1. Propazine Nomenclature**

PC Code 006308	
Chemical structure	
Common name	Propazine
Molecular Formula	C <sub>9</sub> H <sub>16</sub> N <sub>5</sub> Cl
Molecular Weight	229.7
IUPAC name	6-chloro- <i>N,N'</i> -di-isopropyl-1,3,5-triazine-2,4-diamine
CAS name	6-chloro- <i>N,N'</i> -bis(1-methylethyl)-1,3,5-triazine-2,4-diamine
CAS #	139-40-2

**TABLE A.2. Physicochemical Properties of Propazine**

Parameter	Value	Reference
Melting point	217.7 °C	RD D219079, 9/26/95, S. Malak
pH	5.66	
Density, bulk density, or specific gravity	0.46 g/mL	
Water solubility	3.8 ppm at 25 °C	
Solvent solubility (at 25 °C)	14,252 ppm in acetone 4,696 ppm in 1-octanol	
Vapor pressure	2.9 x 10 <sup>-8</sup> mm Hg at 20 °C  2.98 x 10 <sup>-5</sup> Torr at 45 °C	Product Chemistry Chapter of the Propazine Reregistration Standard, 5/19/87  RD D219079, 9/26/95, S. Malak
Dissociation constant, pK	Not applicable; practically insoluble in water.	RD D219079, 9/26/95, S. Malak
Octanol/water partition coefficient	P = 1234.7 Log P = 3.08	



## B. EXPERIMENTAL DESIGN

### B.1. Livestock

Species	Breed	Age	Weight at study initiation (kg)	Health Status	Description of housing/holding area
Lactating goat	Cross-bred	3 years (treated goat); 6 years (control goat)	45-50	No observable toxicological signs.	Individual stainless steel metabolism cages (4' x 5.5'), located in the animal facility maintained under ambient conditions (15-29 °C with 35-80% relative humidity) with ~16 hours of illumination.

Composition of Diet	Feed consumption (kg/day)	Water	Acclimation period	Predosing
Dairy goat feed and hay <sup>1</sup>	1.560-1.880 (treated goat); 2.072-2.235 (control goat)	Potable water, <i>ad libitum</i>	14 days	None

<sup>1</sup> Feed was provided *ad libitum* during the first week of acclimation, and then reduced to ~4% of body weight to maintain a typical dietary intake.

Treatment Type	Feeding Level (ppm test material in food)	Vehicle	Timing/Duration
Oral	9.9	Gelatin capsule via a balling gun; each dose was split into two capsules.	Once per day after morning milking for seven consecutive days.

### B.2. Test Materials

Chemical structure	
Radiolabel position	[ <sup>14</sup> C-ring-UL]propazine
Lot No.	812B-4-1
Purity	99.6% (radiochemical purity)
Specific activity	49.42 mCi/mmol; 45.54 l dpm/μg (isotopically diluted test substance)



### B.3. Sampling Information

Milk collected	Urine, feces and cage wash collected	Interval from last dose to sacrifice	Tissues harvested and analyzed
Milk was collected twice daily, immediately prior to dosing and approximately 8-10 hours later. The final sample was collected directly before sacrifice. Daily milk production during dosing (2.217-3.163 g/day) was similar to daily milk production during acclimation (2.452-4.330 g/day).	Urine and feces were collected daily; cage wash and solids were collected at sacrifice.	- 24 hours	Liver, kidneys, composite muscle, and composite fat; actual types of muscle and fat were not identified.

### B.4. Identification/Characterization of Residues

#### B.4.1. Sample Handling and Preparation

Milk was collected twice daily. An aliquot of each sample was radioassayed, and additional subsamples from the 24-36, 96-108, and 144-156 hour sampling were composited for metabolite identification. The composite and remaining milk samples were stored frozen ( $\leq -5$  °C). Tissue samples were rinsed with tap water following collection, and liver, kidney, and muscle samples were chopped into small cubes. Tissue samples were then stored frozen until further processing. Prior to processing, fat was also cubed, and all tissues were homogenized in a frozen state with dry ice.

Milk: The composite milk sample was adjusted to pH 3 with 3 N HCl and extracted (2x) with n-hexane. The aqueous phase was concentrated by lyophilization for HPLC analysis.

Tissues: Triplicate subsamples of kidney, liver, muscle, and fat were extracted sequentially with water, acetonitrile (ACN):water (4:1, v:v), ACN, and hexane. Each extract was collected following centrifugation. The water extract was concentrated by lyophilization and subjected to protease hydrolysis (Pronase E<sup>®</sup> enzyme in 0.01 M KH<sub>2</sub>PO<sub>4</sub> pH 7.4 buffer at 37 °C for 18 hours). Nonextractable residues in muscle and fat were also subjected to protease hydrolysis, as described for the water extract. The protease hydrolysate of the water extract and nonextractable residues were each concentrated for HPLC analysis.

The protease hydrolysate of the kidney water extract was further hydrolyzed with 3 N HCl (at 100 °C for 3 hours). The resulting acid hydrolysate, containing acid-released aglycons, was neutralized and concentrated for HPLC analysis.

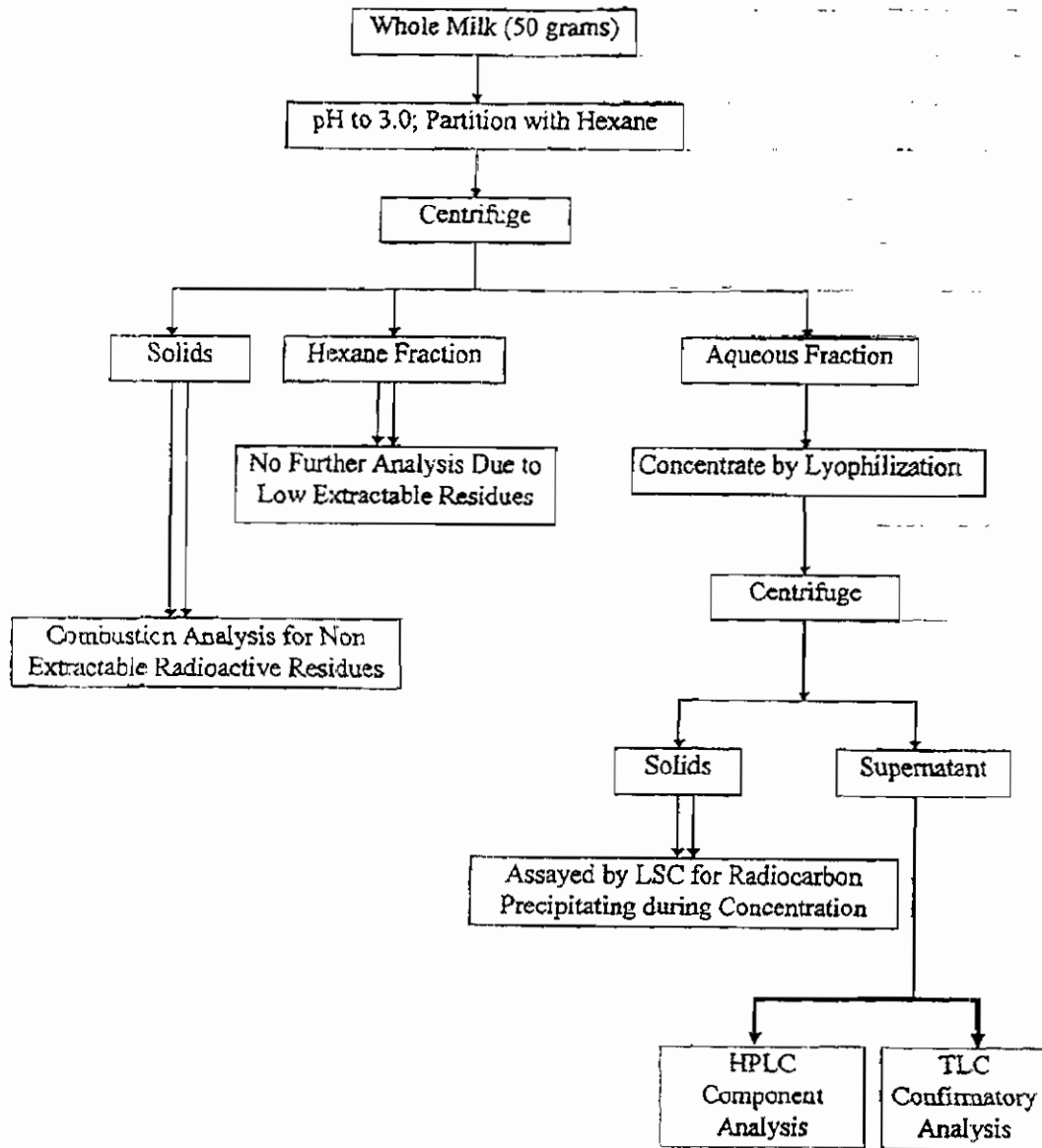
A subsample of the protease hydrolysate of the kidney water extract was also subjected to enzyme hydrolysis. Separate aliquots were incubated with beta-glucuronidase or sulfatase (at 37 °C for 3 hours). The enzyme hydrolysates were isolated with centrifugation and concentrated by nitrogen evaporation for HPLC analysis.

The extraction procedures for the milk and tissue samples are summarized in the flow charts below, which were copied without alteration from MRID 44184815.



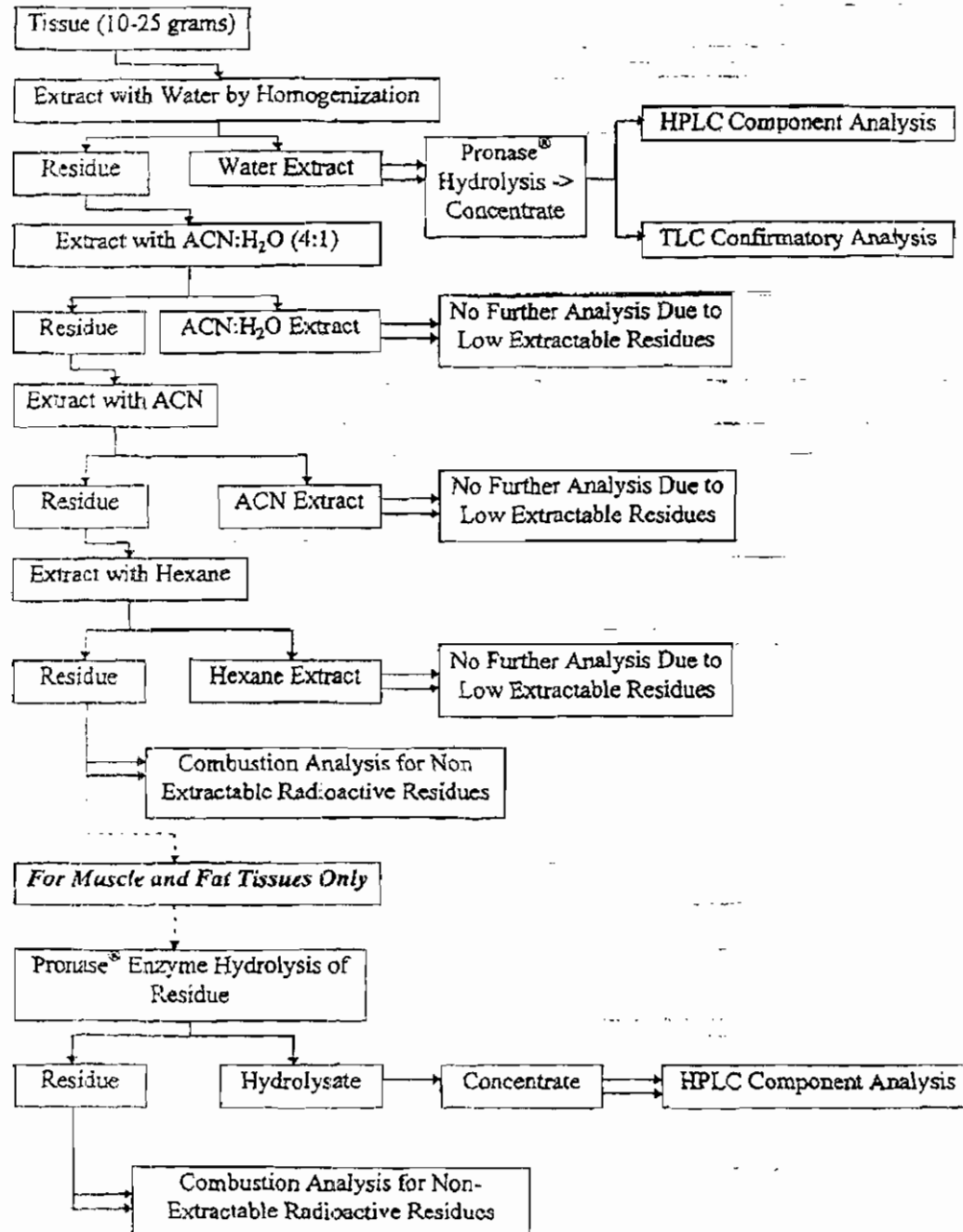


### Extraction procedures for milk:





### Extraction procedures for tissues:





#### B.4.2. Analytical Methodology

Total radioactive residues were measured in milk samples by direct liquid-scintillation counting (LSC) in triplicate. Tissue samples were radioassayed by combustion/LSC (in triplicate). Radioactivity in the extracts and hydrolysates was determined by LSC, and radioactivity in the nonextractable/solids was determined by combustion/LSC. The limits of quantitation (LOQs) for TRR determination were 0.001 ppm for milk, 0.002 ppm for liver, kidney, and muscle, and 0.010 ppm for fat.

Aqueous extracts and hydrolysates were analyzed by HPLC using a system equipped with a C18 column, ultraviolet (UV) detector (240 nm, 230 nm, or 215 nm), a radiodetector, and a gradient mobile phase of: (i) water and ACN, each containing 1% acetic acid; (ii) water and ACN, each with 0.5% acetic acid and 0.1% triethylamine; or (iii) water and ACN, each with 0.1% phosphoric acid. Metabolites were identified by comparison of retention times or co-chromatography with reference standards; the chemical names and structures of the reference standards used in this study are presented in Appendix I.

TLC was used for confirmation of the identification of the mono- and di-dealkylated metabolites of propazine. 1D-TLC analyses were conducted using silica gel 60 F254 plates and a solvent system of chloroform:methanol:formic acid:water (75:20:4:2, v:v:v:v); metabolites were co-chromatographed with reference standards. Radioactive compounds were quantified using a radioanalytic imaging system.

### C. RESULTS AND DISCUSSION

The storage intervals and conditions of samples taken from the goat metabolism study are presented in Table C.1.

TRR in goat milk and tissues are reported in Table C.2.1. TRR were 0.080-0.238 ppm in milk, 0.209 ppm in muscle, 0.160 ppm in fat, 1.041 ppm in kidney, and 1.123 ppm in liver from a goat dosed orally with [U-<sup>14</sup>C]propazine at 9.9 ppm in the diet for seven consecutive days. Radioactivity was highest in liver and kidney, and lowest in fat. Residues in milk were generally highest in samples collected 8 hours after dosing and appear to have reached a plateau after two days of dosing; a graph of the residue levels in milk over the course of the study is presented in Figure C.2.1. A large portion of the administered dose was excreted, with urine and feces (including cage washes and solids) accounting for a total of ~74% of the administered dose.

The distribution of radioactivity in goat matrices is presented in Table C.2.2. The majority of the radioactivity (~91% TRR) in the milk was retained in the aqueous fraction with hexane extraction, and nonextractable residues were <0.05 ppm (18.9% TRR, 0.042 ppm). For tissues, the majority (~60-98% TRR) of radioactivity was extracted with water, and additional minor amounts (<3% TRR) were sequentially extracted with ACN/water, ACN, and hexane. Pronase hydrolysis released additional radioactivity (10% and 35% TRR) from the nonextractable residues of muscle and fat. Following extraction, nonextractable residues were 10.8% and 6.1%



TRR (0.113 and 0.068 ppm) in kidney and liver, respectively. Nonextractable residues after solvent extraction and enzyme hydrolysis, were 5.9% and 7.2% TRR (0.012 ppm) in muscle and fat. Accountabilities were ~93-113%.

The characterization and identification of residues in goat matrices is summarized in Table C.2.3. Approximately 73% TRR was identified in goat milk, 50% TRR in fat, 26% TRR in muscle, and <3% TRR in kidney and liver. The parent, propazine, was not detected in goat milk or tissues. Atrazine-desethyl-desisopropyl (G-28273) was the major residue identified accounting for 63.4% TRR (0.141 ppm) in milk, 50.4% TRR (0.080 ppm) in fat, and 26.1% TRR (0.054 ppm) in muscle; the di-dealkylated metabolite of propazine was also identified in liver as a minor residue (2.7% TRR, 0.031 ppm). The mono-alkylated metabolite of propazine, atrazine-desethyl (G-30033), was only identified in milk at 9.4% TRR (0.021 ppm).

The remaining radioactivity was characterized as up to six additional metabolites in milk and tissues. Each unknown accounted for <7% TRR in milk; however, several of these unknowns were present at significant levels in goat tissues. None of these unknown residues co-chromatographed with propazine, propazine-2-hydroxy, ammelide or any other reference standards used in the study. Region G was the major residue detected in kidney at 59.5% TRR (0.619 ppm) and liver at 76.1% TRR (0.855 ppm); Region G was also detected in muscle and fat at 5.8% TRR (0.012 ppm) and 15.6% TRR (0.025 ppm), respectively. Region G was characterized as stable to glucuronidase, sulfatase, and 3 N HCl hydrolysis. Based on the metabolism of other triazine herbicides the petitioner proposed that the unknown may be an acid-stable glutathione conjugate of propazine or one of its biotransformation products. Region A was present in kidney and muscle as a significant residue at 10.2-19.9% TRR (0.042-0.106 ppm); Region B was present in liver and muscle as a significant residue at 10.6-29.0% TRR (0.119-0.060 ppm); and Region E was present in kidney as a significant residue at 21.2% TRR (0.221 ppm).

The petitioner stated that acid and enzyme hydrolysis was conducted on the pronase hydrolysate of the aqueous extract of kidney to further characterize unknown residues. However, no discussion of the results and no chromatograms for the acid and enzyme hydrolysates were presented. Attempts to further characterize or isolate Regions A, B, and E should have been conducted. In addition, because Region G was the major residue present in kidney and liver, further attempts should also have been made to further isolate the unknown for confirmation of the proposed compound type.

### **C.1. Storage Stability**

Samples of goat matrices were stored frozen after collection. The petitioner provided information pertaining to relevant dates including extraction, hydrolysis, and analysis for milk and tissues. The maximum storage intervals were ~5 months for milk and ~7 months for tissues. To provide storage stability data, samples of liver and kidney were extracted and analyzed by HPLC after approximately 23 months of frozen storage. The extraction efficiencies and metabolic profiles of the stored samples were qualitatively and quantitatively similar to the initial analyses, suggesting that the metabolite profile was reasonably stable in kidney and liver for up



to ~2 years. In addition, samples of milk, liver, and muscle from an untreated goat were fortified with [<sup>14</sup>C]propazine to demonstrate stability of the parent compound; less than 5% degradation occurred following 4 months of frozen storage.

Matrix	Storage Temp. (°C)	Actual Storage Duration	Interval of Demonstrated Storage Stability
Milk	-5	134-148 days (4.4-4.9 months)	None required, stored <6 months
Tissues		169-213 days (5.6-7.0 months)	Metabolic profile is relatively stable in kidney and liver for up to ~23 months.
-kidney (with enzyme and acid hydrolysis)		220 days (7.2 months)	

## C.2. Identification, Characterization, and Distribution of Residues

Matrix	Collection Timing (hours after first dose)	[ <sup>14</sup> C]propazine	
		ppm	% of Administered Dose
Urine	0-24	--	5
	24-48	--	5.7
	48-72	--	7.4
	72-96	--	5.1
	96-120	--	1.5
	120-144	--	7.1
	144-sacrifice	--	4.8
	Total	--	62.0
Feces	0-24	--	0.6
	24-48	--	1.8
	48-72	--	2.1
	72-96	--	2.2
	96-120	--	1.6
	120-144	--	2.4
	144-sacrifice	--	1.3
	Total	--	12.0
Cage wash	At sacrifice	--	1.8
Cage solids	At sacrifice	--	23.6

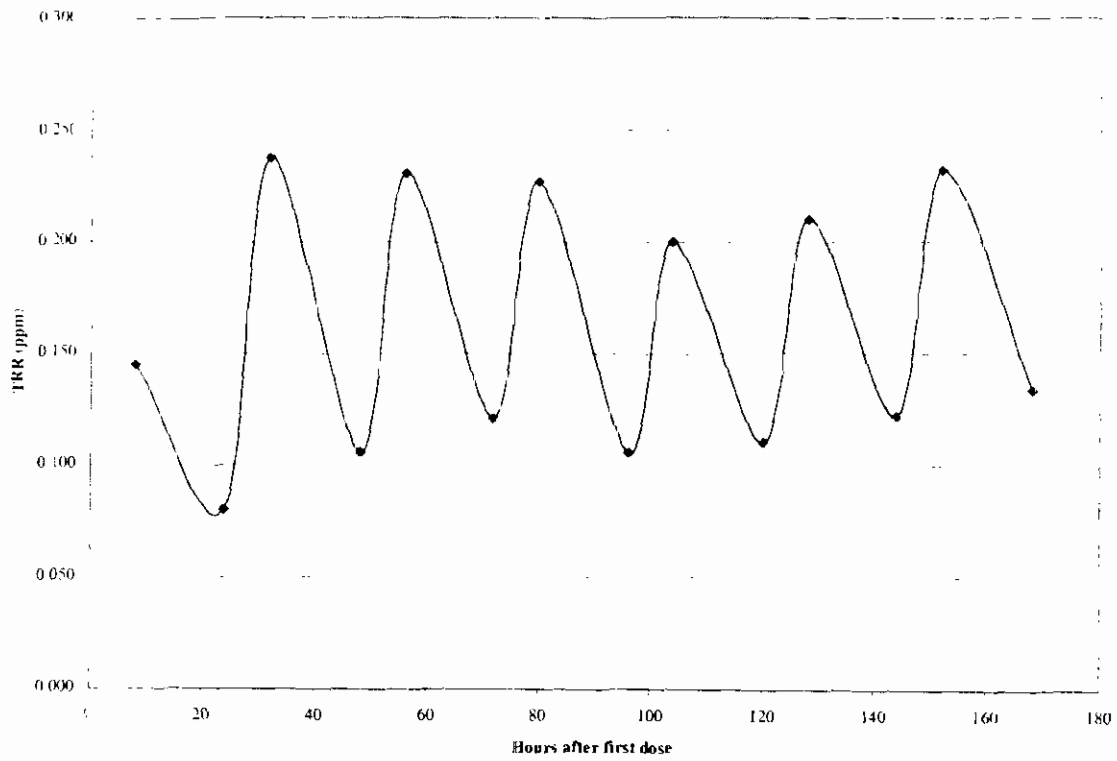


**TABLE C.2.1. Total Radioactive Residues in Goat Milk and Tissues Following Oral Dosing with [<sup>14</sup>C]Propazine at 9.9 ppm in the Diet.**

Matrix	Collection Timing (hours after first dose)	<sup>14</sup> C]propazine	
		ppm	% of Administered Dose
Milk	0-8	0.145	0.2
	8-24	0.080	0.1
	24-32	0.238	0.2
	32-48	0.106	0.2
	48-56	0.231	0.1
	56-72	0.121	0.2
	72-80	0.227	0.2
	80-96	0.106	0.2
	96-104	0.200	0.2
	104-120	0.110	0.1
	120-128	0.210	0.2
	128-144	0.122	0.2
	144-152	0.232	0.2
	152-sacrifice	0.134	0.2
Milk composite sample	24-36, 96-108 and 144-156	0.223	--
Liver	At sacrifice	1.123	0.9
Kidney	At sacrifice	1.041	0.1
Fat	At sacrifice	0.160	0.6
Muscle	At sacrifice	0.209	3.8
Total % of Administered Dose	--	--	82.3



**FIGURE C.2.1. TRR of Propazine in Milk of Lactating Goat.**





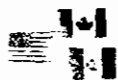
**TABLE C.2.2. Distribution of the Parent and the Metabolites in Goat Matrices Following Dosing with [<sup>14</sup>C]Propazine at 9.9 ppm in the Diet.**

Metabolite Fraction	Milk		Kidney		Liver		Muscle		Fat	
	TRR=0.223 ppm		TRR=1.041 ppm		TRR=1.123 ppm		TRR=0.209 ppm		TRR=0.160 ppm	
	% TRR	ppm	%TRR	ppm	%TRR	ppm	% TRR	ppm	% TRR	ppm
Aqueous extract	90.5	0.202								
Atrazine-desethyl-desisopropyl (G-28273)	63.4	0.141								
Atrazine-desethyl (G-30035)	9.4	0.021								
Region A (5.0-6.0 mins)	6.4	0.014								
Region D (13.5-16.5 mins)	6.2	0.014								
Region E (18.0-21.5 mins)	2.4	0.005								
Region H (44.5 mins)	2.7	0.006								
Organic (hexane) extract	4.2	0.009								
Water extract			94.0	0.979	98.0	1.101	59.8	0.125	73.0	0.117
-Pronase hydrolysate			93.6	0.974	98.2	1.103	62.8	0.131	73.4	0.117
Atrazine-desethyl-desisopropyl (G-28273)			--	--	2.7	0.031	26.1	0.054	50.4	0.080
Region A (5.0-6.0 mins)			10.2	0.106	6.9	0.077	--	--	--	--
Region B (6.5-7.0 mins)			2.5	0.026	10.6	0.119	14.4	0.030	--	--
Region D (13.5-16.5 mins)			--	--	1.9	0.021	--	--	--	--
Region E (18.0-21.5 mins)			21.2	0.221	--	--	16.5	0.034	7.5	0.012
Region G (34.5-37.0 mins) <sup>2</sup>			59.5	0.619	76.1	0.855	5.8	0.012	15.6	0.025
ACN/water extract			0.8	0.009	0.6	0.007	1.6	0.003	2.3	0.004
ACN extract			ND	ND	ND	ND	ND	ND	ND	ND
Hexane extract			ND	ND	0.1	0.001	ND	ND	ND	ND
Nonextractable	18.9	0.042	10.8	0.113	6.1	0.068	37.2	0.078	27.4	0.044
-Pronase hydrolysate							34.5	0.072	10.3	0.016
Region A (5.0-6.0 mins)							19.9	0.042	10.3	0.016
Region B (6.5-7.0 mins)							14.6	0.030	--	--
-Nonextractable							5.9	0.012	7.2	0.012

<sup>1</sup> Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.  
 ND = None detected.

<sup>2</sup> Not released with acid or enzyme hydrolysis of liver extract, and characterized as a glutathione conjugate of propazine or a dealkylated metabolite based on "known 2-chloro-s-triazine herbicide metabolism."





**TABLE C.2.3. Summary of Characterization and Identification of Radioactive Residues in Goat Matrices Following Dosing with [<sup>14</sup>C]Propazine at 9.9 ppm in the Diet.**

Compound	Milk		Kidney		Liver		Muscle		Fat	
	TRR=0.223 ppm		TRR=1.041 ppm		TRR=1.123 ppm		TRR=0.209 ppm		TRR=0.160 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
<b>Identified residues</b>										
Atrazine-des-ethyl-desisopropyl (G-28273)	63.4	0.141	--	--	2.7	0.031	26.1	0.054	50.4	0.080
Atrazine-desethyl (G-30033)	9.4	0.021	--	--	--	--	--	--	--	--
<b>Characterized residues</b>										
Region A	6.4	0.014	10.2	0.106	6.9	0.077	19.9	0.042	10.3	0.016
Region B	--	--	2.5	0.026	10.6	0.119	29.0	0.060	--	--
Region D	6.2	0.014	--	--	1.9	0.021	--	--	--	--
Region E	2.4	0.005	21.2	0.221	--	--	16.5	0.034	7.5	0.012
Region G <sup>1</sup>	--	--	59.5	0.619	76.1	0.855	5.8	0.012	15.6	0.025
Region H	2.7	0.006	--	--	--	--	--	--	--	--
ACN/water extract	--	--	0.8	0.009	0.6	0.007	1.6	0.003	2.3	0.004
ACN extract	--	--	--	--	--	--	--	--	--	--
Hexane extract	4.2	0.009	--	--	0.1	0.001	--	--	--	--
Total identified	72.8	0.162	0.0	0.000	2.7	0.031	26.1	0.054	50.4	0.080
Total characterized	21.9	0.048	94.2	0.981	96.2	1.080	72.8	0.151	35.7	0.057
Total extractable	94.7	0.211	94.8	0.988	98.7	1.109	95.9	0.200	85.6	0.137
Unextractable (PES) <sup>2</sup>	18.9	0.042	10.8	0.113	6.1	0.068	5.9	0.012	7.2	0.012
Accountability <sup>3</sup>	113		106		105		101		93.1	

<sup>1</sup> Not released with acid or enzyme hydrolysis of liver extract, and characterized as a glutathione conjugate of propazine or a dealkylated metabolite based on "known 2-chloro-s-triazine herbicide metabolism."

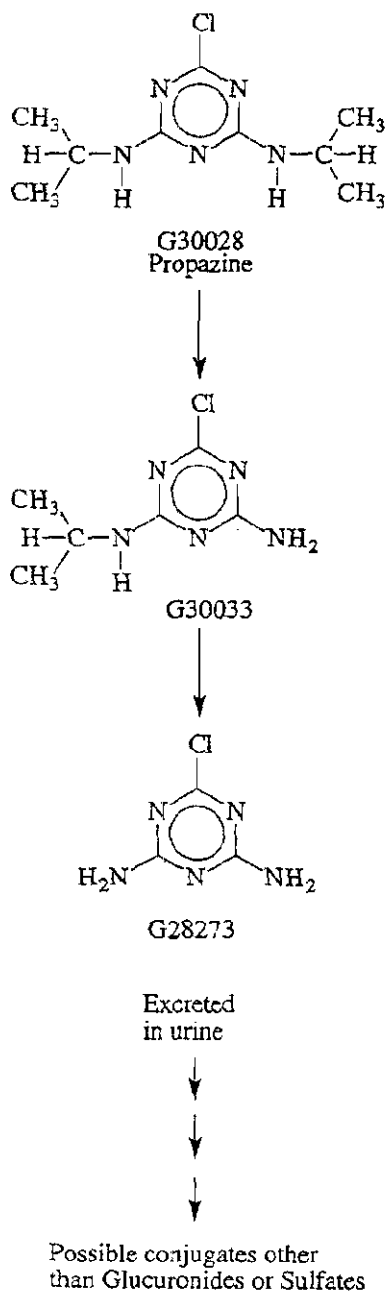
<sup>2</sup> Residues remaining after exhaustive extractions.

<sup>3</sup> Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) \* 100.

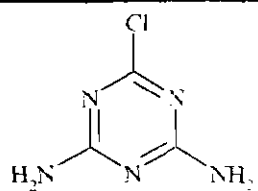
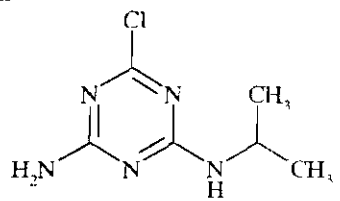


### C.3. Proposed Metabolic Profile

FIGURE C.3.1. Proposed Metabolic Profile of Propazine in Lactating Goat





Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Atrazine-desethyl- desisopropyl/G-28273	2,4-diamino-6-chloro- <i>s</i> -triazine	
Atrazine-desethyl/G-30033	2-amino-4-chloro-6-(1-methylethyl- amino)- <i>s</i> -triazine	

#### D. CONCLUSION

TRR in goat milk and tissues were 0.080-0.238 ppm in milk, 0.209 ppm in muscle, 0.160 ppm in fat, 1.041 ppm in kidney and 1.123 ppm in liver from a goat dosed orally with [U-<sup>14</sup>C]propazine at 9.9 ppm in the diet for seven consecutive days. Residues in milk appear to have reached a plateau after two days of dosing. A large portion (~74%) of the administered dose was excreted.

The majority of the radioactivity (~91% TRR) in the milk was retained in the aqueous fraction with hexane extraction, and nonextractable residues were <0.05 ppm. For tissues, the majority (~60-98% TRR) of radioactivity was extracted with water, and additional minor amounts (<3% TRR) were sequentially extracted with ACN/water, ACN, and hexane. Pronase hydrolysis released additional radioactivity (10% and 35% TRR) from the nonextractable residues of muscle and fat. Following extraction and/or pronase hydrolysis, nonextractable residues were 10.8% TRR (0.113 ppm) in kidney and <8% TRR in liver, muscle, and fat. Accountabilities were ~93-113%.

Approximately 73% TRR was identified in goat milk, 50% TRR in fat, 26% TRR in muscle, and <3% TRR in kidney and liver. The parent, propazine, was not detected in goat milk or tissues. Atrazine-desethyl-desisopropyl (G-28273) was the principal residue identified accounting for 2.7-63.4% TRR; the di-dealkylated metabolite of propazine was also identified in liver as a minor residue (<3% TRR). The mono-alkylated metabolite of propazine, atrazine-desethyl (G-30033), was only identified in milk at 9.4% TRR. The remaining radioactivity was characterized as up to six additional metabolites in milk and tissues. Each unknown accounted for <7% TRR in milk; however, several of these unknowns were present at significant levels in goat tissues. None of these unknown residues co-chromatographed with propazine, propazine-2-hydroxy, ammelide or any other reference standards used in the study. Region G was the major residue detected in kidney and liver at 59.5-76.1% TRR. Region G was characterized as stable to glucuronidase, sulfatase, and 3 N HCl hydrolysis. Based on the metabolism of other triazine



herbicides the petitioner proposed that the unknown may be an acid-stable glutathione conjugate of propazine or one of its biotransformation products. Three other unknowns (Regions A, B, and E) were present in kidney, liver, and/or muscle as a significant residue at 10.2-29.0% TRR. No information concerning attempts to further characterize these unknowns was presented.

Based on the results of the study, the petitioner concluded that propazine is metabolized in goats via sequential dealkylation of the isopropyl alkyl groups with excretion in the urine, primarily as the di-dealkylated metabolite (atrazine-desethyl-desisopropyl). A water-soluble, hydrolytically-stable conjugate of propazine or one of its metabolites may also be formed, which is the major metabolite in goat tissues.

## **E. REFERENCES**

None.

## **F. DOCUMENT TRACKING**

RDI: P.V. Shah (8/24/05), RAB1 Chemists (8/24/05)  
G.F. Kramer:806T:CM#2:(703)305-5079:7509C:RAB1  
Petition Number(s): 7F4837  
DP#: 323273  
PC Code: 080808

Template Version: September 2003

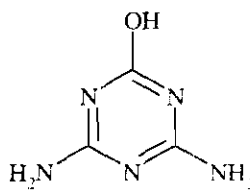
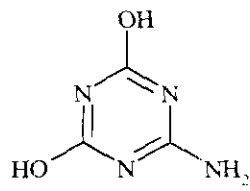
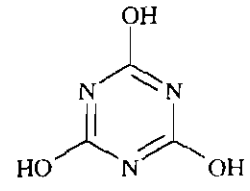
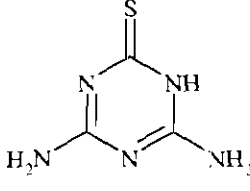
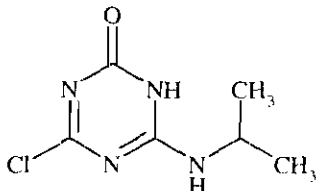


APPENDIX I. Chemical Names and Structures of Reference Standards Used in Goat Metabolism Study.		
Common name Company code	Chemical name	Chemical structure
Propazine, G-30028	2-chloro-4,6-bis(1-methylethylamino)-s-triazine	
Atrazine-desethyl, G-30033	2-amino-4-chloro-6-(1-methylethylamino)-s-triazine	
Atrazine-desethyl-desisopropyl, G-28273	2,4-diamino-6-chloro-s-triazine	
Propazine-2-hydroxy, G-S11526	2-hydroxy-4,6-bis(1-methylethylamino)-s-triazine	
Propazine-hydroxymethyl	2-chloro-4-(1-hydroxymethylethylamino)-6-(1-methylethylamino)-s-triazine	
Propazine-carboxymethyl	2-chloro-4-(1-carboxymethylethylamino)-6-(1-methylethylamino)-s-triazine	




APPENDIX I. Chemical Names and Structures of Reference Standards Used in Goat Metabolism Study.		
Common name Company code:	Chemical name	Chemical structure
Propazine-2,4-dihydroxy. G-S11957	2,4-dihydroxy-6-(1-methylethyl- amino)-s-triazine	
Propazine-2-methylsulfinyl. GS-16141	2,4-bis (1-methylethylamino)-6- methylsulfinyl-s-triazine	
Prometon; G-31435	2-methoxy-4,6-bis (1-methylethyl- amino)-s-triazine	
Triazine-methyl-triamine; CGA 101248	N-(1-methyl)-1,3,5-triazine-2,4,6- triamine	
Propazine-mercapturic acid	2-S-acetylcysteinyl-4,6-bis (1-methyl- ethylamino)-s-triazine	
Atrazine-desethyl-2-hydroxy. GS-17794	2-amino-4-hydroxy-6-(1-methyl- ethylamino)-s-triazine	



<b>APPENDIX I. Chemical Names and Structures of Reference Standards Used in Goat Metabolism Study.</b>		
Common name, Company code	Chemical name	Chemical structure
Ammeline; GS-17791	2,4-diamino-6-hydroxy- <i>s</i> -triazine	
Ammelide; G-35713	2,4-dihydroxy-6-amino- <i>s</i> -triazine	
Triazine-trihydroxy; G-28521	2,4,6-trihydroxy- <i>s</i> -triazine	
Triazine-diamino-thione; CGA-236433	4,6-diamino-1,3,5-triazine-2(1H)- thione	
Triazine-chloro-one	4-chloro-6-(1-methylethylamino)- 1,3,5-triazine-2(1H)-one	

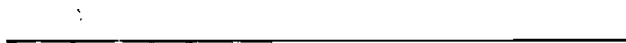


Primary Evaluator:

  
George F. Kramer, Ph.D., Chemist  
Registration Action Branch 1 (RAB1)  
Health Effects Division (HED) (7509C)

Date: 07-DEC-2005

Approved by:

  
P.V. Shah, Ph.D., Branch Senior  
Scientist/RAB1/HED (7509C)

Date: 07-DEC-2005

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This DER was originally prepared under contract by Dynamac Corporation (20440 Century Boulevard, Suite 100; Germantown, MD 20874; submitted 07/13/2005). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

### **STUDY REPORT:**

44184816 Krautter, G.; Downs, J.; Marsh, J. (1996) The Metabolism of <sup>14</sup>C-Propazine in Laying Hens Following Oral Administration: Lab Project Number: 823: 1829: 102. Unpublished study prepared by PTRL East, Inc. 148 p.

### **EXECUTIVE SUMMARY:**

Griffin Corporation has submitted a study investigating the metabolism of [<sup>14</sup>C]propazine (labeled uniformly in the triazine ring; specific activity of 49.42 mCi/mole) in laying hens. The test substance was orally administered to five hens at 20.3 ppm in the diet. The hens were dosed once per day for 14 consecutive days. Eggs were collected twice daily, and tissues (liver, fat, and muscle) were collected at sacrifice. The in-life and analytical phases of the study were conducted by PTRL East, Inc.

Total radioactive residues (TRR) were 0.019-0.448 ppm in whole egg, 0.010-0.669 ppm in egg yolk, 0.024-0.327 ppm in egg white, 1.196 ppm in liver, 0.961 ppm in composite muscle, and 0.172 ppm in composite fat. Residues in eggs appeared to plateau after 9 days of dosing. A large portion of the administered dose was excreted, ~77% in the collected excreta and ~5% in the cage wash.

Approximately 72-104% of TRR in poultry liver, egg yolk, and egg white were readily extracted using water. For muscle and fat, water extraction only released ~42-45% of TRR. Subsequent extraction with acetonitrile (ACN)/water released <5% of the radioactivity from all matrices; additional extractions with organic solvents released <2% of the radioactivity. Nonextractable residues remaining after these solvent extractions measured 15.9% TRR (0.191 ppm) in liver, 50.6% TRR (0.587 ppm) in muscle, 103.6% TRR (0.178 ppm) in fat, 22.6% TRR (0.151 ppm) in egg yolk, and 0.3% TRR (0.001 ppm) in egg white. The nonextractable residues of all of these matrices, except egg white, were subjected to protease hydrolysis. The nonextractable residues remaining after protease hydrolysis measured 0.5% TRR (0.006 ppm) in liver, 3.9% TRR (0.045 ppm) in muscle, 34.2% TRR (0.059 ppm) in fat and 0.5% TRR (0.003 ppm) in egg yolk. The accountabilities ranged ~92-105% for all hen matrices, except fat (~132%).





Residues in extracts and hydrolysates were characterized primarily by high-performance liquid chromatography (HPLC) analysis. Residue components were identified by co-chromatography and/or retention time comparison with 17 reference standards which included several putative chloro- and hydroxy-metabolites of triazine herbicides; see Appendix 1. Thin-layer chromatography (TLC) analysis was performed as a confirmatory technique.

Characterization of the radioactive residues in hen tissues and egg samples by HPLC indicated the presence of at least eight metabolites. The parent propazine was not detected in any extracts and/or hydrolysates. The only residue component identified was atrazine-desethyl-desisopropyl (G-28273) which was quantitated in poultry matrices as follows: liver (4.3% TRR, 0.171 ppm), muscle (18.3% TRR, 0.212 ppm), fat (48.1% TRR, 0.083 ppm), egg yolk (35.3% TRR, 0.236 ppm), and egg white (51.9% TRR, 0.170 ppm). Seven unknown compounds were found in the matrices: A (RT 4.0-5.5 min.), B (RT 6.0-7.0 min.), C (RT 9.0-9.5 min.), E (RT 14.0 min.), F (RT 15.0-16.5 min.), G (RT 17.0-18.0 min.) and H (RT 25.0-26.0 min.). Compounds A, B, C, G and H were observed at >10% TRR in various matrices. HED would have preferred that additional attempts, such as liquid chromatography/mass spectroscopy (LC/MS) analysis, were made to identify these compounds. However, the petitioner characterized these unknown metabolites to be relatively more polar than propazine based on the chromatographic profiles.

Samples were stored frozen for up to 4 months prior to residue characterization. To demonstrate the stability of frozen samples while in storage, the extracts of liver tissue and egg white were reanalyzed by HPLC after approximately 19 months of sample collection. The results of these analyses indicate that metabolite profiles were stable in liver extracts during frozen storage. In the case of the egg white extracts, reanalysis indicated that a conjugated form of atrazine-desethyl-desisopropyl degraded to atrazine-desethyl-desisopropyl during frozen storage.

Based on the study results, the petitioner concluded that all of the metabolites which were observed in the study were more polar than propazine, indicating that propazine is readily metabolized in the laying hen to more-polar metabolites. Propazine was metabolized via dealkylation of the two isopropyl alkyl group, generating atrazine-desethyl-desisopropyl as a major metabolite. Further degradation to the multiple polar metabolites was suggested to occur via oxidation and/or conjugation.

#### **STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:**

When the study is evaluated according to OPPTS GLN 860.1300, the hen metabolism data are classified as scientifically unacceptable because of insufficient characterization of radioactive residues in all poultry matrices. In a Memorandum of Understanding between HED and Griffin for Propazine (1/11/96, M. Metzger), HED has indicated that if the TRR in poultry matrices, when normalized to 1x, are 0.001-0.006 ppm in all edible tissues, further metabolite identification and characterization is not required. Other regulatory conclusions resulting from this study will be addressed in the forthcoming Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision (TRED) Document for propazine.



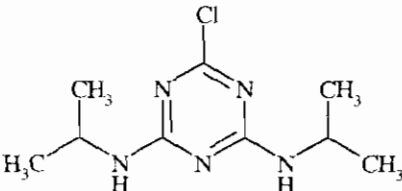
## COMPLIANCE:

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

Propazine (6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine) is a member of the chloro triazine class of herbicides. Other members of this pesticide class include atrazine, cyanazine, and simazine. Propazine is a selective herbicide that can be applied before planting, at planting, and after crop emergence for the preemergence control of annual broadleaf weeds. Currently, the only registered uses are for weed control of ornamental plants grown in containers under greenhouse conditions. There are presently no registered food/feed uses of propazine.

Propazine was previously registered for use on sorghum. The 5/19/87 Propazine Residue Chemistry Chapter along with the 12/88 Propazine Reregistration Standard (Guidance Document) identified several data deficiencies for the reregistration of propazine. Ciba-Geigy, which was then the basic manufacturer of propazine, elected to cancel its registrations of propazine. Another registrant, Griffin Corporation, is now supporting the previously-cancelled uses of propazine on grain sorghum. The structure and nomenclature of propazine are presented in Table A.1. The physicochemical properties of propazine are listed in Table A.2.

<b>TABLE A.1. Propazine Nomenclature</b>	
PC Code 006308	
Chemical structure	
Common name	Propazine
Molecular Formula	C <sub>9</sub> H <sub>16</sub> N <sub>5</sub> Cl
Molecular Weight	229.7
IUPAC name	6-chloro- <i>N,N'</i> -di-isopropyl-1,3,5-triazine-2,4-diamine
CAS name	6-chloro- <i>N,N'</i> -bis(1-methylethyl)-1,3,5-triazine-2,4-diamine
CAS #	139-40-2



Parameter	Value	Reference
Melting point	217.7 °C	RD D219079, 9/26/95, S. Malak
pH	5.66	
Density, bulk density, or specific gravity	0.46 g/mL	
Water solubility	3.8 ppm at 25 °C	
Solvent solubility (at 25 °C)	14,252 ppm in acetone 4,696 ppm in 1-octanol	
Vapor pressure	2.9 x 10 <sup>-8</sup> mm Hg at 20 °C  2.98 x 10 <sup>-5</sup> Torr at 45 °C	Product Chemistry Chapter of the Propazine Reregistration Standard, 5/19/87  RD D219079, 9/26/95, S. Malak
Dissociation constant, pK	Not applicable; practically insoluble in water.	RD D219079, 9/26/95, S. Malak
Octanol/water partition coefficient	P = 1234.7 Log P = 3.08	

## B. EXPERIMENTAL DESIGN

### B.1. Livestock

Species	Breed	Age	Weight at study initiation (kg)	Health Status	Description of housing/holding area
Laying hens	White Leghorn (White Hy-Liner W77)	~ 54 weeks	1.2-1.7	Hens appeared healthy before dosing. After dosing, there were no observable toxicological signs.	Individual metabolism cages equipped with a wire mesh floor, feed container, and excrement collection pan in ambient environmental conditions (13-28°C, relative humidity 27-85%) with 16 hours of illumination.

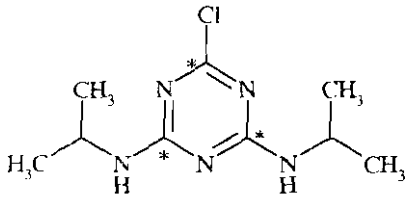
A total of five hens were dosed. In addition, a control group of five hens were not dosed.

Composition of Diet	Feed consumption (kg/day)	Water	Acclimation period	Predosing
Hi-Tech XL-A Laying Mash	Control group: 0.1263 (mean) Treated group: 0.1259 (mean)	Water (unspecified), <i>ad libitum</i>	at least 7 days prior to treatment	None



Treatment Type	Feeding Level (ppm test material in food)	Vehicle	Timing/Duration
Oral	20.3 (verified dose level); 20.0 (nominal)	Gelatin capsule (No. 1 size) inserted directly into the manually restrained hens' throat to ensure swallowing.	Once per day, after morning egg collection, for 14 consecutive days.

## B.2. Test Materials

Chemical structure:	
Radiolabel position	[ring- <sup>14</sup> C]propazine
Lot No.	822-1A [a mixture of 812B-4-1 and 812B-26-2 (both radiolabeled) and 821-6 (non-radiolabeled)]
Purity	<b>Before radiodilution:</b> 812B-4-1, 99.6% (radio-chemical purity) and 812B-26-2, 99.53% (radio-chemical purity) <b>After radiodilution:</b> 822-1A, 96.9-97.3% (radio-chemical purity)
Specific activity	<b>Before radiodilution:</b> 812B-4-1, 49.42 mCi/mnole and 812B-26-2, 130.7 μCi/mg <b>After radiodilution:</b> 822-1A, 39705 dpm/μg

## B.3. Sampling Information

Eggs collected	Excreta and cage wash collected	Interval from last dose to sacrifice	Tissues harvested and analyzed
Eggs were collected twice daily. The total egg production per hen was reported over the total course of the acclimation period and dosing period. For the treated hens, the average daily egg production was the same during acclimation and dosing (0.84 eggs). For the control hens, the average daily egg production was more during acclimation (0.82 eggs) than during dosing (0.67 eggs)	Excreta was collected once daily. After sacrifice, excreta collection pans were rinsed with water, and the rinses were collected as a collective cage wash sample.	22-24 hours	Liver, kidneys, muscle (breast and thigh), and composite fat.



## B.4. Identification/Characterization of Residues

### B.4.1. Sample Handling and Preparation

Eggs were collected twice daily and refrigerated prior to processing. The egg shells were washed with soap and water by scrubbing with a nylon brush, then the white and yolk components of each sample was separated, combined by component type into a daily sample, homogenized and stored frozen (unreported temperature) until extraction and analysis.

The collected tissues were rinsed with tap water; all tissue samples were stored frozen prior to processing. Tissues samples were partially thawed and cubed. The frozen cubed liver, muscle (breast and thigh), and composite fat were homogenized with dry ice and then stored frozen ( $-20^{\circ}\text{C}$ ) until extraction and analysis.

Extraction procedure for all tissues and egg: Subsamples of hen tissues and eggs were successively extracted three times with HPLC-grade water, once with acetonitrile:water (4:1 v:v), once with acetonitrile, and once with hexane. All extractions were performed in the same manner. The sample and extraction solvent were mixed with a homogenizer for 3 minutes, then allowed to settle for approximately 10 minutes before centrifuging for 30 minutes at 10000-39000 g. The water extracts were combined, and each organic phase was analyzed by liquid-scintillation counting (LSC). A portion of the remaining post-extraction solids (PES) was analyzed by combustion/LSC.

Protease hydrolysis: The PES present in liver, muscle, fat and egg yolk, and all combined water extracts were subjected to protease hydrolysis (the combined water extracts were concentrated by lyophilization prior to the protease hydrolysis procedure). For the protease hydrolysis, samples were homogenized with 0.01 M  $\text{KH}_2\text{PO}_4$  buffer (pH 7.4), then incubated at  $37^{\circ}\text{C}$  in a shaking water bath. Protease was added to the homogenate at 0 and 2 hours post-incubation. After approximately 18 hours of incubation, the sample was centrifuged for 10 minutes at 3000 rpm. The protease extract was separated, then concentrated by lyophilization prior to HPLC analysis (System 2). The concentrated protease extract of the water extracts was also analyzed by TLC (System 2). The post-hydrolyzed solids (PHS) of the PES samples were analyzed by combustion/LSC.

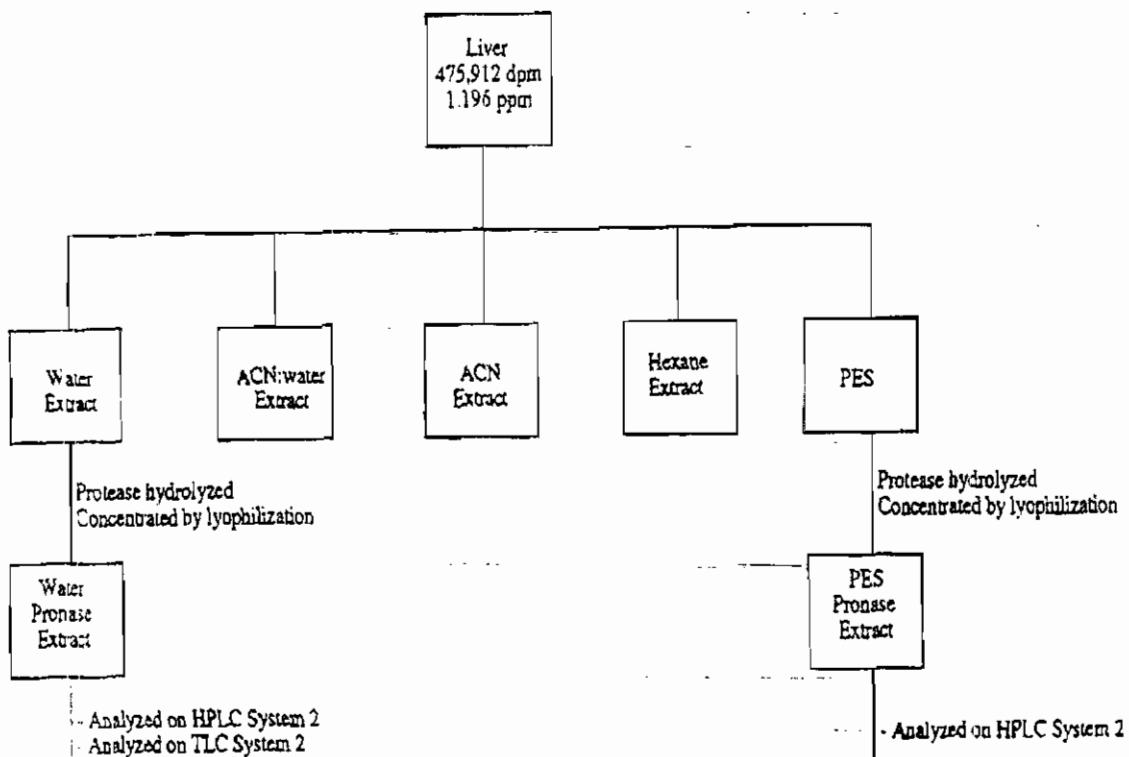
The extraction procedures for the egg and tissue samples are summarized in the flow charts below, which were copied without alteration from MRID 44184816.



### Extraction procedures for liver:

Amount Extracted: 10.023 g

Date Extracted: 1-5-95

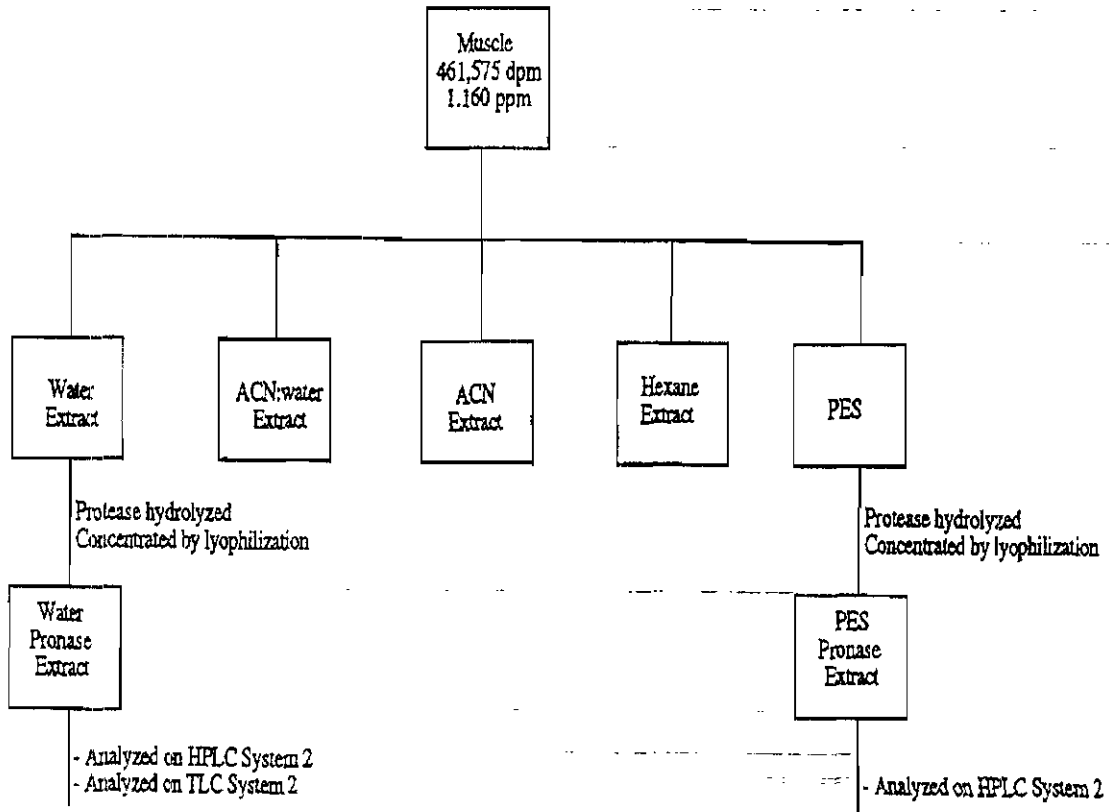




**Extraction procedures for muscle:**

Amount Extracted: 10.024 g

Date Extracted: 1-19-95

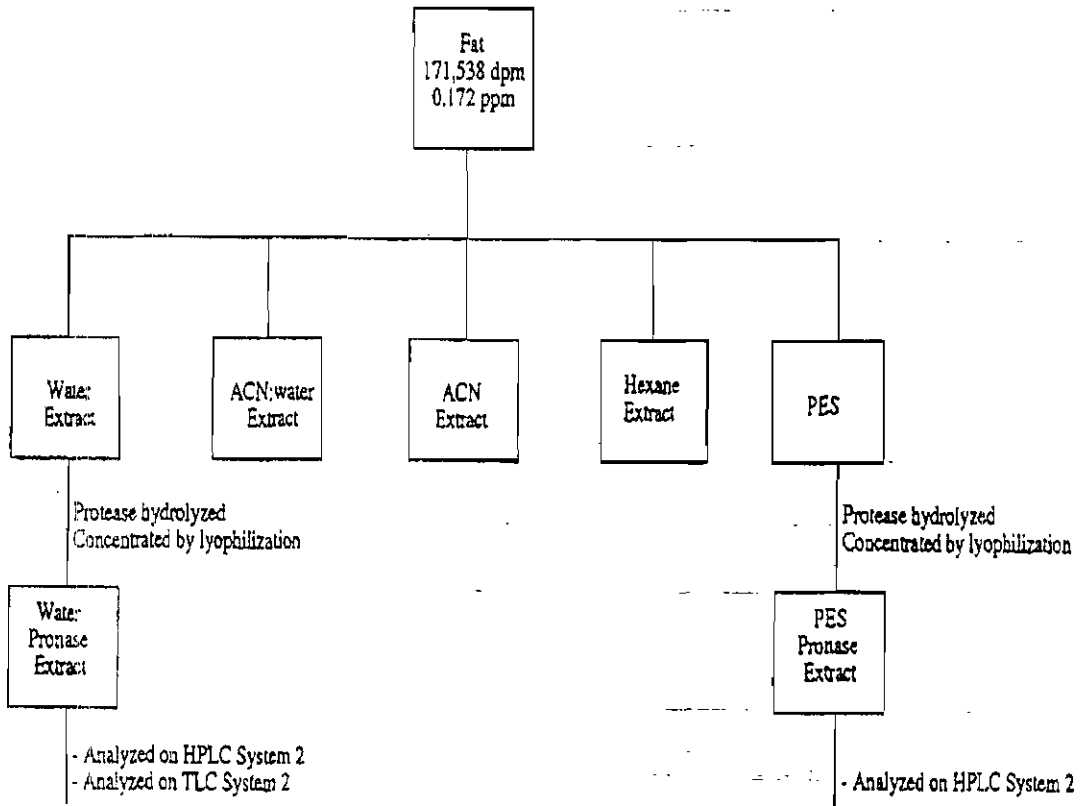




### Extraction procedures for fat:

Amount Extracted: 25.108 g

Date Extracted: 1-5-95



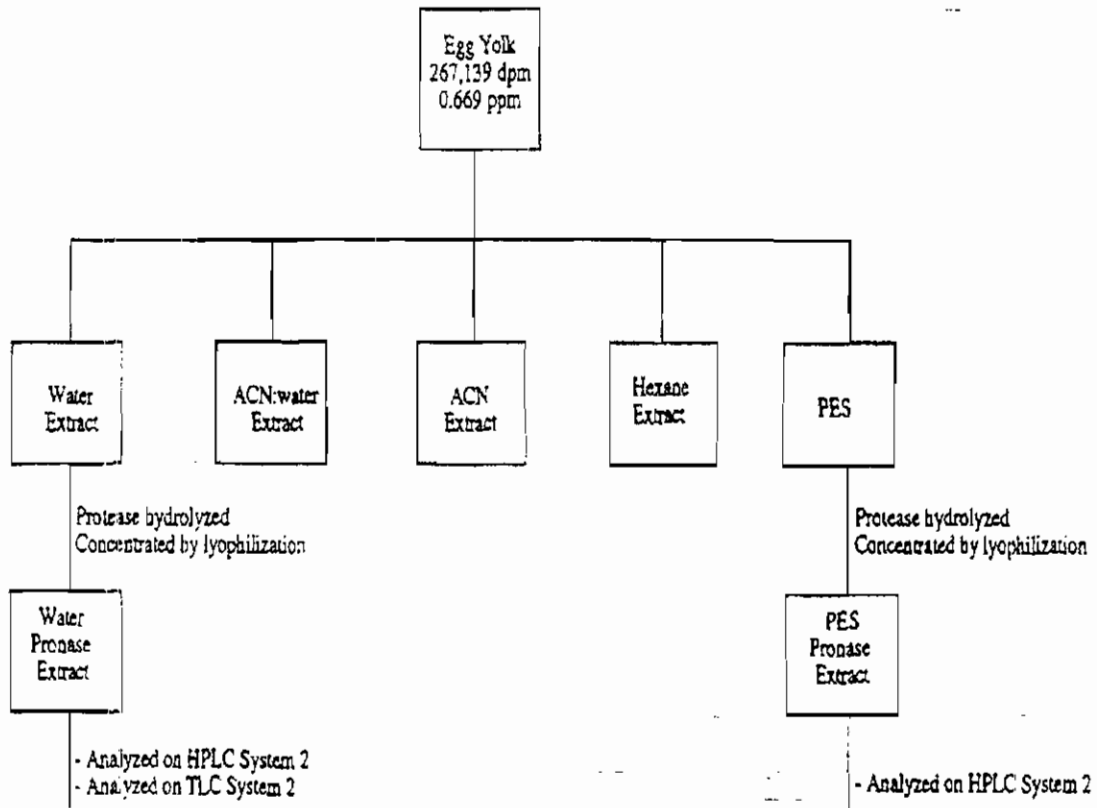




### Extraction procedures for egg yolk:

Amount Extracted: 10.050 g

Date Extracted: 1-5-95

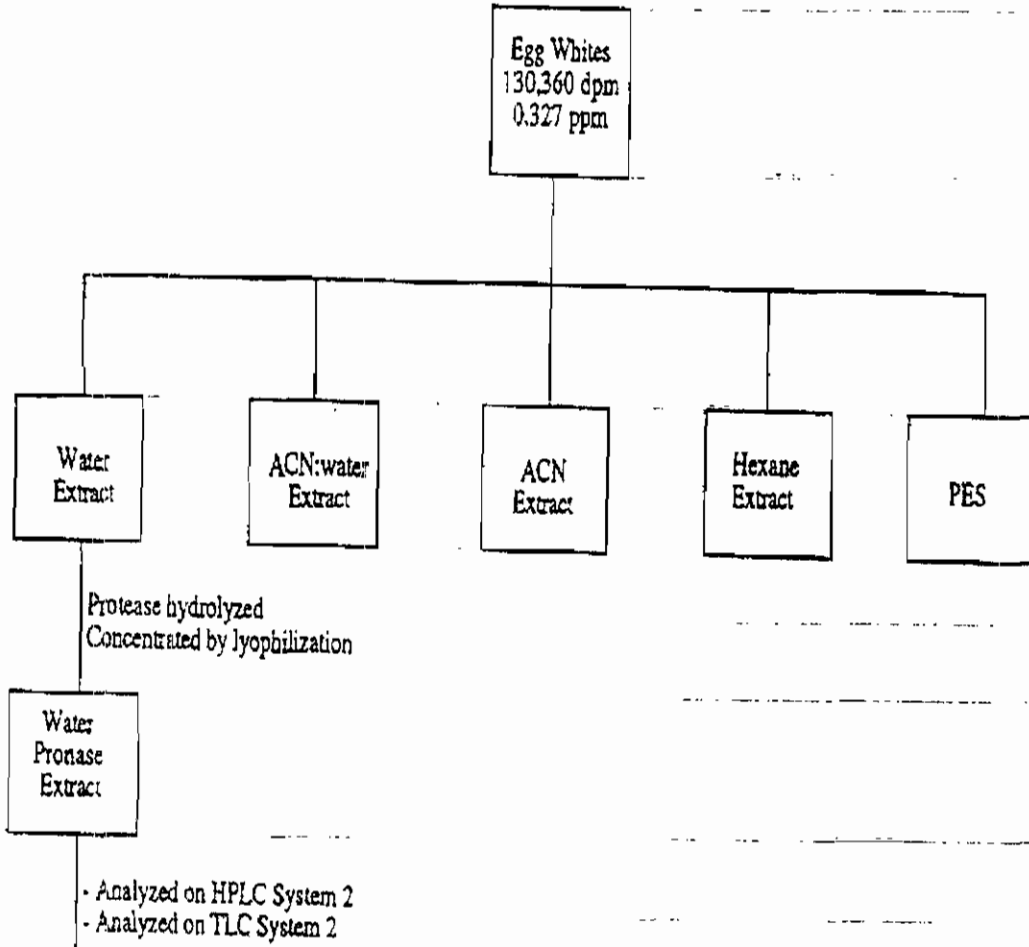




**Extraction procedures for egg white:**

Amount Extracted: 10.030 g

Date Extracted: 1-5-95





### B.4.2. Analytical Methodology

TRR were measured in the tissue and egg samples by combustion/LSC (in triplicate). Aliquots of egg yolk and egg white were weighed onto absorbent pads in combustion cones prior to analysis. Aliquots of liver and muscle were analyzed directly in combustion cones. The limit of quantitation (LOQ) for TRR determinations were <0.01 ppm (liver 0.003 ppm, muscle 0.004 ppm, fat 0.006 ppm, egg yolk 0.004 ppm, egg white 0.003 ppm); the limit of detection (LOD) was 2xs the background. Samples from the control set of hens were used to determine the background radioactivity level.

Extracts and hydrolysates of liver, composite muscle, composite fat, egg yolk, and egg white were analyzed by HPLC using a system equipped with a C18 RP column (Zorbax 5  $\mu$ m LC-18 RP), a ultraviolet (UV) detector (230 or 215 nm), a radiodetector and one of the following UV detection/mobile phases: (System 2) UV (230 nm) and gradient mobile phase of water and acetonitrile, each containing 0.5% acetic acid and 0.1% triethylamine; and (System 3) UV (215 nm) and gradient mobile phase of water and acetonitrile, each containing 0.1% phosphoric acid. System 2 was used for propazine and metabolite identification and quantification. The LOQ for HPLC System 2 of all tissues and egg components was  $\leq$ 0.03 ppm; the LOD was not reported. System 3 was reportedly used for analysis of selected sample extracts; however, no data or chromatograms were provided which show that this system was actually employed in the study.

Confirmation of the identification of propazine was performed using 2D-TLC analysis; 1D-TLC analysis was used for confirmation of the identities of the metabolites. TLC analyses were conducted using silica gel 60 F254 plates and two solvent systems: ethyl acetate and chloroform:methanol:formic acid:water (75:20:4:2, v:v:v:v). For 1D-TLC analyses, the second solvent system was used; for 2D-TLC analyses, both solvent systems were used. Compounds were quantified by scraping the TLC spots from the plates and analyzing by LSC.

Propazine and its metabolites were identified by co-chromatography and/or retention time comparisons with reference standards. Chemical names and structures for the reference standards are presented in Appendix I.

## C. RESULTS AND DISCUSSION

TRR in hen egg and tissues are reported in Table C.2.1. TRR were 0.019-0.448 ppm in whole egg, 0.010-0.669 ppm in egg yolk, 0.024-0.327 ppm in egg white, 1.196 ppm in liver, 0.961 ppm in composite muscle, and 0.172 ppm in composite fat that were obtained from hens dosed orally with [ $^{14}$ C]propazine at 20.3 ppm in the diet for 14 consecutive days. Residues in eggs appeared to plateau after 9 days of dosing. A large portion of the administered dose, 76.9% (cumulative) in the excreta and 4.9% in the cage wash, was excreted.

The distribution of the radioactivity in the hen matrices is presented in Table C.2.2. The characterized egg yolk sample was collected at day 14 (TD14); the characterized egg white sample was collected at day 11 (TD11). The majority of the radioactivity in the liver, egg yolk and egg white (> 72-104% TRR) was extracted using HPLC-grade water. For the muscle and fat,



the water extraction only released half of the radioactivity (~42-45% TRR). Subsequent extraction with ACN/water released <5% of the radioactivity from all matrices; additional extractions with organic solvents released <2% of the radioactivity. Nonextractable residues remaining after these solvent extractions measured 15.9% TRR (0.191 ppm) in liver, 50.6% TRR (0.587 ppm) in muscle, 103.6% TRR (0.178 ppm) in fat, 22.6% TRR (0.151 ppm) in egg yolk, and 0.3% TRR (0.001 ppm) in egg white. The nonextractable residues of all of these matrices, except egg white, were subjected to protease hydrolysis. Nonextractable residues remaining after protease hydrolysis measured 0.5% TRR (0.006 ppm) in liver, 3.9% TRR (0.045 ppm) in muscle, 34.2% TRR (0.059 ppm) in fat and 0.5% TRR (0.003 ppm) in egg yolk. The accountabilities ranged ~92-105% for all hen matrices, except fat (~132%). Residues were characterized primarily by HPLC analysis, using TLC analyses for confirmation.

The characterization and identification of residues in hen matrices is summarized in Table C.2.3. No propazine was identified. Atrazine-desethyl-desisopropyl was the only characterized metabolite in the matrices, accounting for a significant portion of the radioactivity. Atrazine-desethyl-desisopropyl was found to be a major metabolite, at 14.3% TRR (0.171 ppm) in liver, 18.3% TRR (0.212 ppm) in muscle, 48.1% TRR (0.083 ppm) in fat, 35.3% TRR (0.236 ppm) in egg yolk, and 51.9% TRR (0.170 ppm) in egg white. Seven identified unknown compounds were found in the matrices: A (RT 4.0-5.5 min.), B (RT 6.0-7.0 min.), C (RT 9.0-9.5 min.), E (RT 14.0 min.), F (RT 15.0-16.5 min.), G (RT 17.0-18.0 min.) and H (RT 25.0-26.0 min.). Compounds A, B, C, G and H were observed at >10% in various matrices.

The major metabolite atrazine-desethyl-desisopropyl was identified in fat, egg yolk, egg white, liver and muscle by HPLC co-chromatography with an unlabeled reference standard. Its presence and identity in the hen matrices was confirmed by one-dimensional TLC co-chromatography. No residues of propazine or other reference standards were detected in the egg or tissue samples.

### C.1. Storage Stability

Samples of hen matrices were stored frozen prior to analysis. The temperature of frozen storage was specified for the tissues as ~-20 °C. In the case of the eggs, the whole eggs were stored refrigerated until the separation of the egg yolk and white. The temperature and time interval of the refrigerated storage was not reported. After separation, the egg yolk and white were stored frozen, but the specific temperature was not reported. The petitioner provided ranges of dates for processing, radioanalysis, extraction and HPLC analysis for each of the types of matrices. For the tissues, processing and radioanalysis occurred within 0-29 days of collection (<1 month). The extraction and HPLC analysis of tissues were completed 63-85 days (~2-3 months) and 77-106 days (~2.5-3.5 months) after collection, respectively. For the egg yolk and white, processing and radioanalysis occurred within 5-43 days of collection (<1.5 month). The extraction and HPLC analysis of egg yolk and white were completed 77-99 days (~2.5-3.5 months) and 91-120 days (~3-4 months) after collection, respectively.

To demonstrate frozen storage stability, the extracts of liver tissue and egg white were reanalyzed by HPLC after approximately 19 months after sample collection (approximately 16 months after



initial extraction). Chromatograms from the initial and final analyses were included. The results of these analyses indicate that metabolite profiles were stable in liver extracts during frozen storage for approximately 16 months. In the case of the egg white extracts, reanalysis indicated that a conjugated form of atrazine-desethyl-desisopropyl degrades to atrazine-desethyl-desisopropyl during frozen storage for approximately 16 months.

Matrix	Storage Temp (°C)	Actual Storage Duration	Interval of Demonstrated Storage Stability
Liver	frozen (-20 °C)	For processing and LSC: 0-29 days (<1 month)	- 19 months after collection
Muscle		For extraction: 63-85 days ( 2-3 months)	
Fat		For HPLC: 77-106 days ( 2.5-3.5 months)	
Egg yolk	frozen <sup>1,2</sup>	For processing and LSC: 5-43 days (<1.5 months)	None demonstrated
Egg white		For extraction: 77-99 days ( 2.5-3.5 months) For HPLC: 91-120 days ( 3-4 months)	- 19 months after collection

<sup>1</sup> Temperature not specified

<sup>2</sup> The whole egg was refrigerated (temperature not specified) after collection before separation: time interval <14 days.

## C.2. Identification, Characterization, and Distribution of Residues

Matrix	Collection Timing Treatment Day (TD)	ppm TRR, expressed as <sup>14</sup> C-propazine equivalents		
		Whole egg	Egg yolk	Egg white
Egg	TD1	0.019	0.010	0.024
	TD2	0.265	0.229	0.286
	TD3	0.278	0.278	0.278
	TD4	0.341	0.385	0.316
	TD5	0.367	0.447	0.318
	TD6	0.388	0.520	0.312
	TD7	0.388	0.536	0.306
	TD8	0.379	0.549	0.282
	TD9	0.419	0.604	0.322
	TD10	0.414	0.589	0.319
	TD11	0.439	0.623	0.327
	TD12	0.439	0.654	0.304
	TD13	0.412	0.648	0.279
	TD14	0.448	0.669	0.291
Liver	At sacrifice	1.196		
Muscle, composite (breast and thigh)	At sacrifice	0.961		
Fat, composite	At sacrifice	0.172		



**TABLE C.2.2. Distribution of the Parent and the Metabolites in Hen Matrices Following Dosing with [<sup>14</sup>C]Propazine at 20.3 ppm in the Diet.**

Metabolite Fraction	Liver		Muscle, composite		Fat, composite		Egg yolk (TD14)		Egg white (TD11)	
	TRR = 1.196 ppm		TRR = 1.160 ppm		TRR = 0.172 ppm		TRR = 0.669 ppm		TRR = 0.327 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Water	87.0	1.041	45.3	0.526	42.0	0.072	72.3	0.483	104.3	0.341
Pronase	87.2	1.043	42.0	0.487	31.5	0.054	69.0	0.462	97.0	0.317
Atrazine-desethyl-desisopropyl	14.3	0.171	12.1	0.140	42.0	0.072	32.5	0.217	51.9	0.170
Others <sup>1</sup> - collectively	72.8	0.871	33.2	0.386	0.0	0.000	39.8	0.266	52.4	0.172
ACN:water	0.0	0.000	1.0	0.012	1.9	0.003	4.6	0.031	0.0	0.000
ACN	0.0	0.000	0.2	0.002	2.6	0.005	1.2	0.008	0.0	0.000
Hexane	0.0	0.000	0.2	0.002	1.0	0.002	1.6	0.010	0.0	0.000
Nonextractable	15.9	0.191	50.6	0.587	103.6	0.178	22.6	0.151	0.3	0.001
Pronase	5.9	0.070	41.2	0.478	50.4	0.087	15.8	0.106	NA	NA
Atrazine-desethyl-desisopropyl	0.0	0.000	6.2	0.072	6.1	0.011	2.8	0.019	--	--
Others <sup>2</sup> - collectively	5.9	0.070	34.9	0.406	44.2	0.077	13.0	0.087	--	--
Post-Pronase Solids	0.5	0.006	3.9	0.045	34.2	0.059	0.5	0.003	NA	NA

<sup>1</sup> Composed of 7 compounds designated A (RT 4.0-5.5 min.: 20.9-31.4%), B (RT 6.0-7.0 min.: 9.9-39.8%), C (RT 9.0-9.5 min.: 5.2-7.8%), E (RT 14.0 min.: 3.6%), F (RT 15.0-16.5 min.: 1.4-3.5%), G (RT 17.0-18.0 min.: 12.0%) and H (RT 25.0-26.0 min.: 4.4-17.7%).

<sup>2</sup> Composed of 4 of 5 of the compounds listed above: B (RT 6.0-7.0 min.: 4.7-29.9%), C (RT 9.0-9.5 min.: 2.9-7.0%), F (RT 15.0-16.5 min.: 4.4-4.6%), G (RT 17.0-18.0 min.: 0.6-3.3%) and H (RT 25.0-26.0 min.: 0.6-1.3%).

**TABLE C.2.3. Summary of Characterization and Identification of Radioactive Residues in Hen Matrices Following Dosing with Radiolabeled Propazine at 20.3 ppm in the Diet.**

Compound	Liver		Muscle, composite		Fat, composite		Egg yolk (TD14)		Egg White (TD11)	
	TRR = 1.196 ppm		TRR = 1.160 ppm		TRR = 0.172 ppm		TRR = 0.669 ppm		TRR = 0.327 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Propazine	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000
Atrazine-desethyl-desisopropyl	14.3	0.171	18.3	0.212	48.1	0.083	35.3	0.236	51.9	0.170
Others <sup>1</sup> - collectively	78.7	0.941	68.1	0.792	44.2	0.077	52.8	0.353	52.4	0.172
Total identified	93.0	1.112	86.4	1.004	92.3	0.160	88.1	0.589	104.3	0.342
Total characterized	14.3	0.171	18.3	0.212	48.1	0.083	35.3	0.236	51.9	0.170
Total extractable	92.9	1.111	87.9	1.020	98.0	0.169	95.5	0.639	104.3	0.341
Unextractable (PES) <sup>1</sup>	0.5	0.006	3.9	0.045	34.2	0.059	0.5	0.003	0.3	0.001
Accountability <sup>1</sup>	93.4		91.8		132.2		96.0		104.6	

<sup>1</sup> Composed of 7 compounds designated A (RT 4.0-5.5 min.: 20.9-31.4%), B (RT 6.0-7.0 min.: 14.6-49.9%), C (RT 9.0-9.5 min.: 2.9-14.8%), E (RT 14.0 min.: 3.6%), F (RT 15.0-16.5 min.: 3.5-5.8%), G (RT 17.0-18.0 min.: 3.3-12.6%) and H (RT 25.0-26.0 min.: 5.7-18.3%).

<sup>1</sup> Residues remaining after exhaustive extractions.

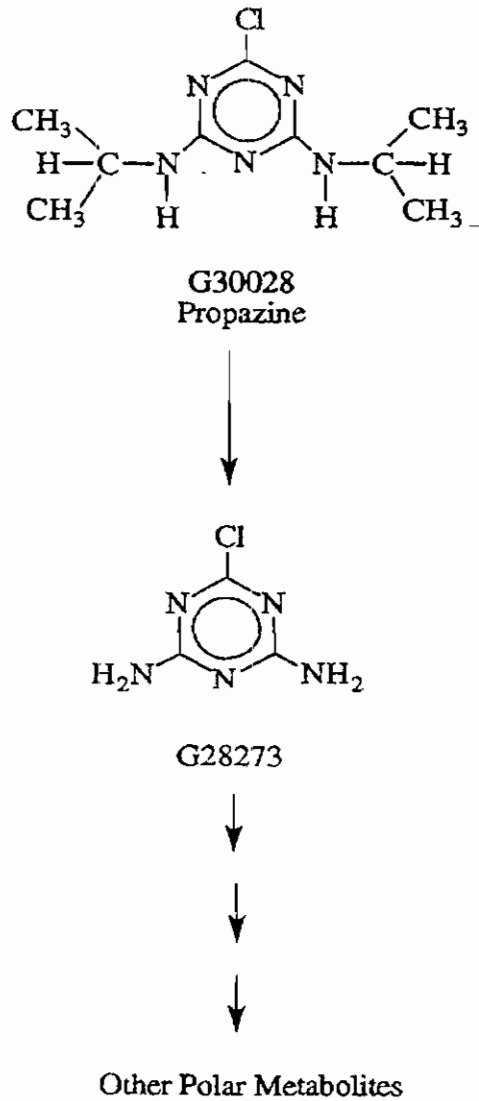
<sup>1</sup> Accountability = (Total extractable + Total unextractable) / (TRR from combustion analysis; see TABLE C.2.1) + 100



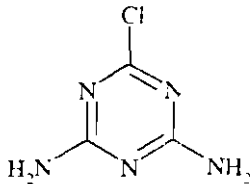
### C.3. Proposed Metabolic Profile

**FIGURE C.3.1. Proposed Metabolic Profile of Propazine in Laying Hen**

The figure below was copied without alteration from MRID 44184816.



**TABLE C.3.1. Identification of Compounds from Metabolism Study**

Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Atrazine-desethyl- desisopropyl (G-28273)	2,4-diamino-6-chloro-s-triazine	

## D. CONCLUSION

TRR in hen egg and tissues were 0.019-0.448 ppm in whole egg, 0.010-0.669 ppm in egg yolk, 0.024-0.327 ppm in egg white, 1.196 ppm in liver, 0.961 ppm in composite muscle, and 0.172 ppm in composite fat from hens dosed orally with [<sup>14</sup>C]propazine at 20.3 ppm in the diet for 14 consecutive days. A large portion of the administered dose, ~77% (cumulative) in the excreta and ~5% in the cage wash, was excreted.

The majority of the radioactivity (~72-104% TRR) in the liver, egg yolk (TD14) and egg white (TD11) was extracted using HPLC-grade water. For the muscle and fat, the water extraction only released half of the radioactivity (~42-45% TRR). Subsequent extraction with ACN/water released <5% of the radioactivity from all matrices; additional extractions with organic solvents released <2% of the radioactivity. Nonextractable residues remaining after these solvent extractions measured 15.9% TRR (0.191 ppm) in liver, 50.6% TRR (0.587 ppm) in muscle, 103.6% TRR (0.178 ppm) in fat, 22.6% TRR (0.151 ppm) in egg yolk and 0.3% TRR (0.001 ppm) in egg white. The nonextractable residues of all of these matrices, except egg white, were subjected to protease hydrolysis. Nonextractable residues remaining after protease hydrolysis measured 0.5% TRR (0.006 ppm) in liver, 3.9% TRR (0.045 ppm) in muscle, 34.2% TRR (0.059 ppm) in fat and 0.5% TRR (0.003 ppm) in egg yolk. The accountabilities ranged ~92-105% for all hen matrices, except fat (~132%)

No propazine was identified. Atrazine-desethyl-desisopropyl was the only identified metabolite in the matrices, accounting for a significant portion of the radioactivity. Atrazine-desethyl-desisopropyl was found to be a major metabolite, at 14.3% TRR (0.171 ppm) in liver, 18.3% TRR (0.212 ppm) in muscle, 48.1% (0.083 ppm) in fat, 35.3% TRR (0.236 ppm) in egg yolk, and 51.9% (0.170 ppm) in egg white. Seven identified unknown compounds were found in the matrices: A (RT 4.0-5.5 min.), B (RT 6.0-7.0 min.), C (RT 9.0-9.5 min.), E (RT 14.0 min.), F (RT 15.0-16.5 min.), G (RT 17.0-18.0 min.) and H (RT 25.0-26.0 min.). Compounds A, B, C, G and H were observed at >10% in various matrices.

Based on the study results, all of the metabolites which were observed in the study were more polar than propazine, indicating that propazine is readily metabolized in the laying hen to more polar metabolites. The petitioner determined that propazine was metabolized via dealkylation of the two isopropyl alkyl group, generating atrazine-desethyl-desisopropyl as a major metabolite.





Further degradation to the multiple polar metabolites was suggested to occur via oxidation and/or conjugation.

## **E. REFERENCES**

Memorandum of Understanding between HED and Griffin for Propazine (1/11/96, M. Metzger)

## **F. DOCUMENT TRACKING**

RDI: P.V. Shah (8/24/05), RAB1 Chemists (8/24/05)

G.F. Kramer:806T:CM#2:(703)305-5079:7509C:RAB1

Petition Number(s): 7F4837

DP#: 323273

PC Code: 080808

Template Version September 2003



APPENDIX I. Chemical Names and Structures of Reference Standards Used in Hen Metabolism Study.		
Common name. Company code	Chemical name	Chemical structure
Propazine (G-30028)	2-chloro-4,6-bis(1-methylethylamino)-s-triazine	
Atrazine-desctoy. (G-30033)	2-amino-4-chloro-6-(1-methylethylamino)-s-triazine	
Atrazine-desethyl desisopropyl (G-28273)	2,4-diamino-6-chloro-s-triazine	
Propazine-2-hydroxy (GS-11526)	2-hydroxy-4,6-bis(1-methylethylamino)-s-triazine	
Propazine-hydroxymethyl	2-chloro-4-(1-hydroxymethylethylamino)-6-(1-methylethylamino)-s-triazine	
Propazine-carboxymethyl	2-chloro-4-(1-carboxymethylethylamino)-6-(1-methylethylamino)-s-triazine	



APPENDIX I. Chemical Names and Structures of Reference Standards Used in Hen Metabolism Study.		
Common name, Company code	Chemical name	Chemical structure
Propazine-2,4-dihydroxy (GS-11957)	2,4-dihydroxy-6-(1-methylethylamino)-s-triazine	
Propazine-2-methylsulfinyl (GS-16141)	2,4-bis(1-methylethylamino)-6-methylsulfinyl-s-triazine	
Prometon (G-31435)	2-methoxy-4,6-bis(1-methylethylamino)-s-triazine	
Triazine-methyl-triamine (CGA-101248)	N-(1-methyl)-1,3,5-triazine-2,4,6-triamine	
Propazine-mercapturic acid	2-S-acetylcysteinyl-4,6-bis(1-methylethylamino)-s-triazine	
Atrazine-desethyl-2-hydroxy (GS-17794)	2-amino-4-hydroxy-6-(1-methylethylamino)-s-triazine	



<b>APPENDIX I. Chemical Names and Structures of Reference Standards Used in Hen Metabolism Study.</b>		
Common name: Company code	Chemical name	Chemical structure
Ammeline (GS-17791)	2,4-diamino-6-hydroxy-s-triazine	 <chem>Nc1nc(O)c(O)n1</chem>
Ammelide (G-35713)	2,4-diamino-6-amino-s-triazine	 <chem>Nc1nc(O)c(O)n1</chem>
Triazine-trihydroxy (G-28521)	2,4,6-trihydroxy-s-triazine	 <chem>Oc1nc(O)c(O)n1</chem>
Triazine-diamino-thione (CGA-236433)	2,4-diamino-1,3,5-triazine-2(1H)-thione	 <chem>Nc1nc(S)c(N)n1</chem>
Triazine-chloro-one	4-chloro-6-(1-methylethylamino)-1,3,5-triazine-2(1H)-one	 <chem>CC(C)Nc1nc(Cl)c(=O)n1</chem>



Primary Evaluator: \_\_\_\_\_

George F. Kramer, Ph.D., Chemist  
Registration Action Branch I (RAB1)  
Health Effects Division (HED) (7509C)

Date: 07-DEC-2005

Approved by: \_\_\_\_\_

P.V. Shah, Ph.D., Branch Senior  
Scientist/RAB1/HED (7509C)

Date: 07-DEC-2005

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This DER was originally prepared under contract by Dynamac Corporation (20440 Century Boulevard, Suite 100, Germantown, MD 20874; submitted 07/13/2005). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

### **STUDY REPORT:**

44184817 Thalacker, F. W. (1996) The Nature of the Residue of <sup>14</sup>C-Hydroxypropazine in Lactating Goats. Project Number: CHW 6641-104. Unpublished study prepared by Corning Hazelton Inc. 85 p

### **EXECUTIVE SUMMARY:**

Griffin Corporation has submitted a goat metabolism study with [<sup>14</sup>C]hydroxypropazine. The test substance, [U-<sup>14</sup>C]2-hydroxypropazine (specific activity 55.9 mCi/mmol), was administered orally to a single goat at 10.9 ppm in the diet. The goat was dosed once per day for three consecutive days. Milk was collected twice daily throughout the study, and tissues (muscle, fat, liver, and kidney) were collected at sacrifice. The in-life and analytical phases of the study were conducted by Corning Hazelton, Inc. (Madison, WI).

Total radioactive residues (TRR) were 0.025-0.029 ppm in milk, 0.006 ppm in muscle, 0.001 ppm in fat (renal and omental), 0.110 ppm in kidney, and 0.036 ppm in liver. Radioactivity was highest in kidney and lowest in fat. Residues in milk were at relatively constant levels during dosing.

Muscle and fat tissues were not extracted because of low radioactivity (<0.010 ppm). In milk, ~88-91% of TRR was retained in the aqueous fraction following acetone and hexane extraction, and the nonextractable residues were <7% TRR (0.001-0.002 ppm). The majority of radioactivity was extracted from kidney and liver with methanol/water, with ~40-43% TRR being retained in the aqueous fraction. In liver, 66% TRR (0.024 ppm) remained in the organic fraction, leaving <8% TRR (0.003 ppm) as nonextractable residues. In kidney, only ~34% TRR (0.038 ppm) remained in the organic fraction, and nonextractable residues were <0.05 ppm (26.5% TRR, 0.029 ppm). Accountabilities were ~93-114%. Residues were identified by high-performance liquid chromatography (HPLC) analysis, using 2D-thin-layer chromatography (TLC), a second HPLC method, and/or cation exchange chromatography for confirmation. These methods successfully identified the predominant residues in goat matrices. No supporting



storage stability data are required because milk and tissue samples from the subject goat metabolism study were stored frozen and analyzed within 6 months of collection.

Approximately 66-81% TRR were identified in goat milk, kidney, and liver. The test substance, hydroxypropazine, was found to be the major residue in all matrices, accounting for 63.5% TRR (0.069 ppm) in kidney, 77.2% TRR (0.028 ppm) in liver, and 65.0-69.4% TRR (0.017-0.020 ppm) in milk. The only other metabolite identified was desisopropyl hydroxypropazine, which was detected in minor amounts in all matrices: 2.9% TRR (0.003 ppm) in kidney, 3.6% TRR (0.001 ppm) in liver and 8.2-8.5% TRR (0.002 ppm) in milk. The remaining radioactivity was attributed to unknowns accounting for 10.3% TRR in kidney, 24.7% TRR in liver, and  $\leq$  14.8% TRR in milk; no individual peak unknown was present at  $>0.003$  ppm.

Based on the results of the study, hydroxypropazine is metabolized in goats by N-dealkylation to yield desisopropyl hydroxypropazine. Furthermore, hydroxypropazine, the polar metabolite of propazine, is likely rapidly excreted by lactating animals with little deposition into tissues.

#### **STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:**

Under the conditions and parameters used in the study, the goat metabolism data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision Document (TRED) for propazine.

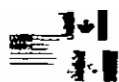
#### **COMPLIANCE:**

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**

Propazine (6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine) is a member of the chloro triazine class of herbicides. Other members of this pesticide class include atrazine, cyanazine, and simazine. Propazine is a selective herbicide that can be applied before planting, at planting, and after crop emergence for the preemergence control of annual broadleaf weeds. Currently, the only registered uses are for weed control of ornamental plants grown in containers under greenhouse conditions. There are presently no registered food/feed uses of propazine.

Propazine was previously registered for use on sorghum. The 5/19/87 Propazine Residue Chemistry Chapter along with the 12/88 Propazine Reregistration Standard (Guidance Document) identified several data deficiencies for the reregistration of propazine. Ciba-Geigy, which was then the basic manufacturer of propazine, elected to cancel its registrations of propazine. Another registrant, Griffin Corporation, is now supporting the previously-cancelled



uses of propazine on grain sorghum. The structure and nomenclature of propazine are presented in Table A.1. The physicochemical properties of propazine are listed in Table A.2.

<b>TABLE A.1. Propazine Nomenclature</b>	
PC Code 006308	
Chemical structure	
Common name	Propazine
Molecular Formula	C <sub>9</sub> H <sub>16</sub> N <sub>4</sub> Cl
Molecular Weight	229.7
IUPAC name	6-chloro- <i>N,N'</i> -di-isopropyl-1,3,5-triazine-2,4-diamine
CAS name	6-chloro- <i>N,N'</i> -bis(1-methylethyl)-1,3,5-triazine-2,4-diamine
CAS #	139-40-2

<b>TABLE A.2. Physicochemical Properties of Propazine</b>		
Parameter	Value	Reference
Melting point	217.7 °C	RD D219079, 9/26/95, S. Malak
pH	5.66	
Density, bulk density, or specific gravity	0.46 g/mL	
Water solubility	3.8 ppm at 25 °C	
Solvent solubility (at 25 °C)	14,252 ppm in acetone 4,696 ppm in 1-octanol	
Vapor pressure	2.9 x 10 <sup>-8</sup> mm Hg at 20 °C  2.98 x 10 <sup>-5</sup> Torr at 45 °C	Product Chemistry Chapter of the Propazine Reregistration Standard, 5/19/87  RD D219079, 9/26/95, S. Malak
Dissociation constant, pK	Not applicable; practically insoluble in water.	RD D219079, 9/26/95, S. Malak
Octanol/water partition coefficient	P = 1234.7 Log P = 3.08	



## B. EXPERIMENTAL DESIGN

### B.1. Livestock

Species	Breed	Age	Weight at study initiation (kg)	Health Status	Description of housing/holding area
Lactating goat	Toggenburg	5 years	61	Appeared healthy; no observable toxicological signs.	Individual bedded pen in a room with 12 hours of illumination where temperatures were maintained at $\geq 10^{\circ}\text{C}$ and humidity was ambient.

Composition of Diet	Feed consumption (kg/day)	Water	Acclimation period	Predosing
A grain-based milking ration (1.5 kg/day) and hay <i>ad libitum</i>	1.438-1.500 grain ration: 0.860-1.056 roughage	Not reported	10 days	None

Treatment Type	Feeding Level (ppm test material in food)	Vehicle	Timing/Duration
Oral	10.9	Capsule	Once daily for 3 consecutive days

### B.2. Test Materials

Chemical structure	
Radiolabel position	[U- $^{14}\text{C}$ ]2-hydroxypropazine
Lot No	3225-077
Purity	98.8% (radiochemical purity); 99.6% (chemical purity)
Specific activity	55.9 mCi/mmol; 137,700 dpm/ $\mu\text{g}$ (isotopically diluted test substance)





### B.3. Sampling Information

Milk collected	Urine, feces and cage wash collected	Interval from last dose to sacrifice	Tissues harvested and analyzed
Milk was collected twice daily, in the morning and evening (~ 10 hours later). Daily milk production during dosing (1429-1509 g) was similar to daily milk production during acclimation (~ 939-1792 g).	Not collected	23 hours	Muscle (round), liver, kidneys, and fat (renal and omental).

### B.4. Identification/Characterization of Residues

#### B.4.1. Sample Handling and Preparation

Milk was collected twice daily and stored frozen (-30°C to -10°C). The milk samples were combined into daily samples and homogenized. Tissue samples were rinsed with tap water, blotted dry, and stored frozen (-30°C to -10°C). Prior to analysis, the tissues were cut into small pieces and homogenized with dry ice.

The petitioner reported that all samples were stored in a freezer (-30°C to -10°C) or refrigerator (2°C to 8°C) before and after each analysis and that the time which samples were out of frozen storage was minimized. Samples of fat and muscle were not extracted for metabolite characterization because of low radioactivity (<0.01 ppm).

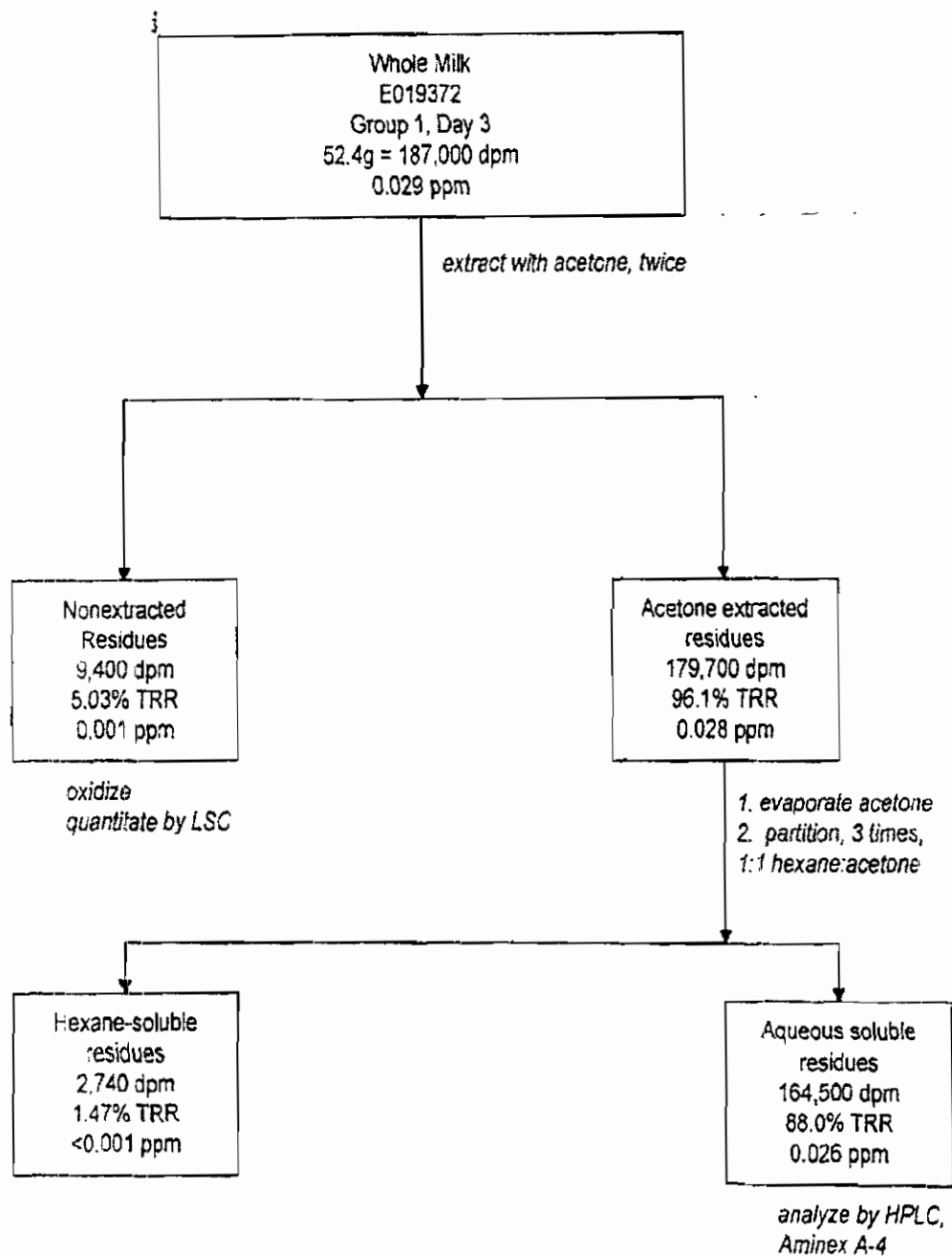
Milk: Daily milk subsamples were extracted twice with acetone, centrifuged, and the supernatants were combined. The acetone extract was evaporated to aqueous and partitioned (3x) with hexane. The hexane fractions were combined. The remaining aqueous fraction was concentrated for analysis by HPLC.

Kidney and liver: Subsamples of kidney and liver were extracted (3x) with methanol:water (80:20, v:v) in an ice bath, centrifuged, and the supernatants were combined. The extract was evaporated to aqueous and partitioned (3x) with chloroform. The chloroform fractions were combined, concentrated, and partitioned with water. All of the aqueous phases (from the chloroform and water partitions) were combined. The aqueous and chloroform fractions were reserved for analysis by HPLC.

The extraction procedures for the milk, kidney and liver samples are summarized in the flow charts below, which were copied without alteration from MRID 44184817.

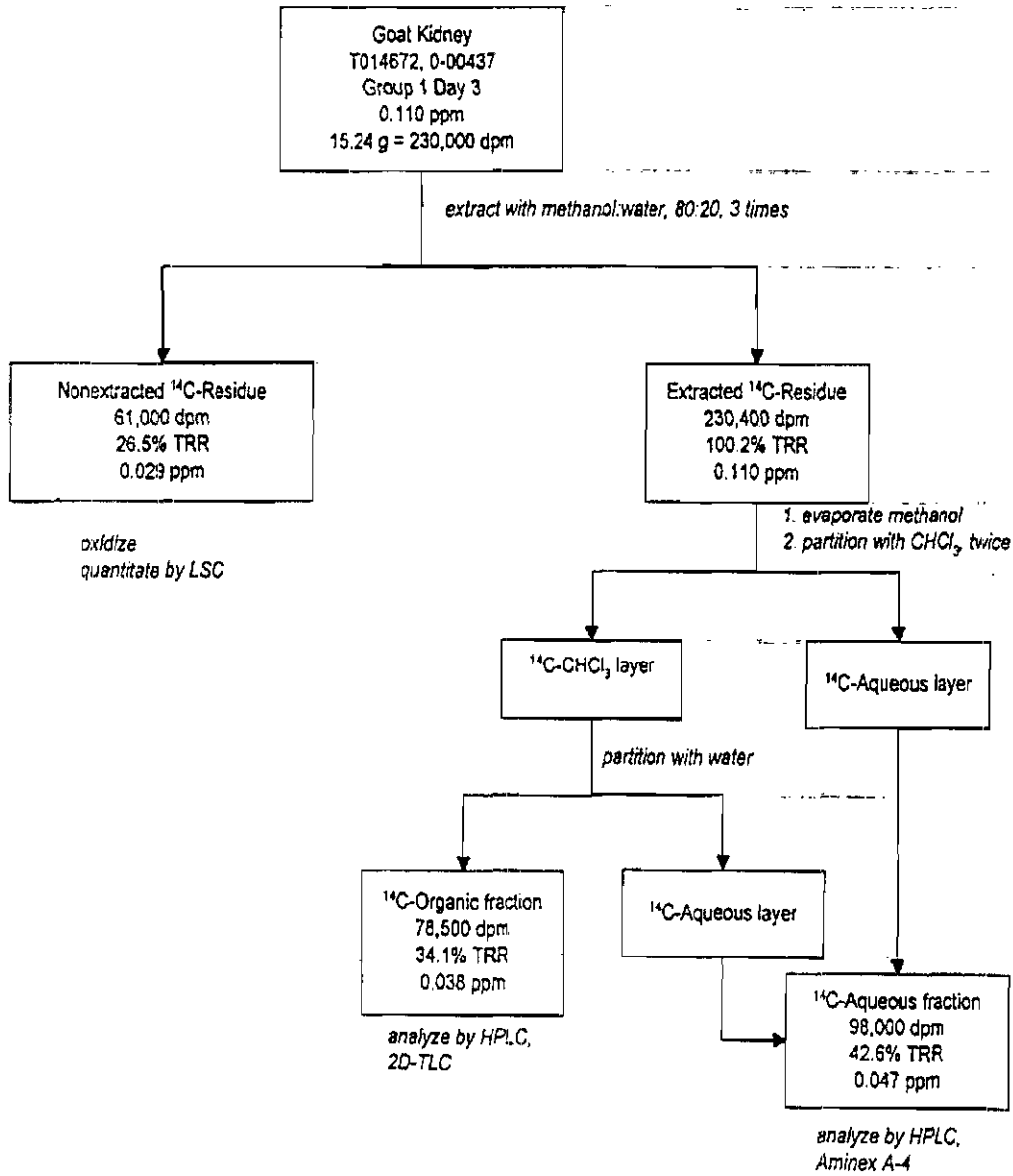


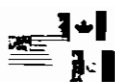
### Extraction procedures for milk:



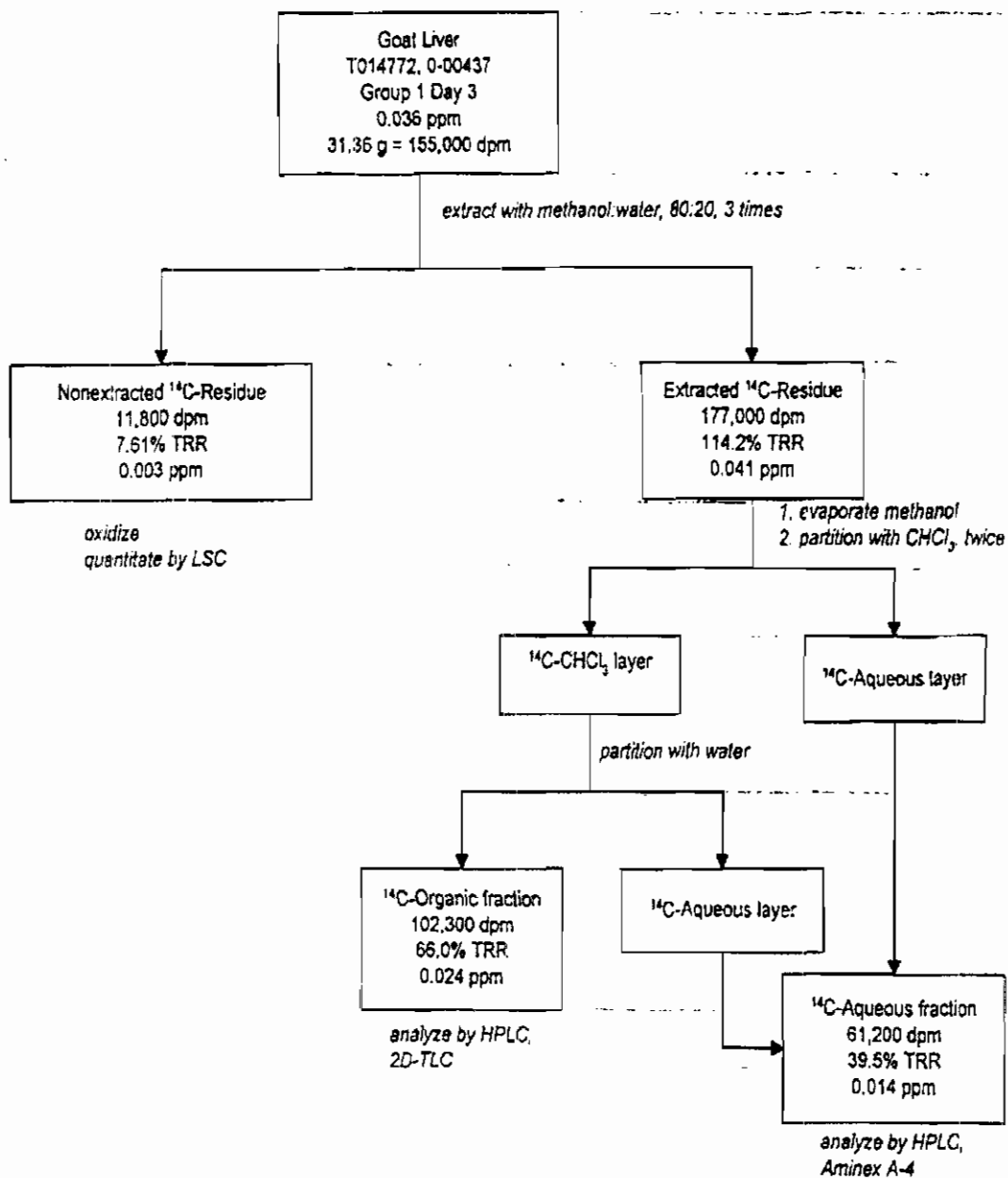


### Extraction procedures for kidney:





### Extraction procedures for liver:





#### **B.4.2. Analytical Methodology**

Total radioactive residues were measured in the milk samples by liquid-scintillation counting (LSC) in triplicate. Tissue samples, except fat, were radioassayed by combustion/LSC (in triplicate); fat samples were digested overnight prior to direct LSC analysis. Radioactivity in the extracts was determined by LSC, and radioactivity in the nonextractable/solids was determined by combustion/LSC. The limits of detection (LODs) for TRR determination were 0.001 ppm for milk, 0.0005 ppm for fat, and 0.001 ppm for kidney, liver and muscle.

The organic and/or aqueous extracts were analyzed by HPLC using a system equipped with an ultraviolet (UV) detector (240 nm), a fraction collector, and one of the following column/gradient mobile phase combinations: (Method I) C18 (ODS) column with water and acetonitrile (ACN), each containing 1% acetic acid or (Method II) Partisil PAC and Spherex SCX in-line columns with ACN:0.1 M ammonium formate (pH 7; 94:6, v:v) and ACN:0.1 M ammonium formate (pH 7):methanol (70:20:10, v:v:v). Metabolites were identified by comparison of retention times or co-chromatography with reference standards; the chemical names and structures of the reference standards used in this study are presented in Appendix I. Using fraction collection and LSC analysis for radioactivity, Method I was used for quantitation of metabolites in the aqueous extracts, and Method II was used for quantitation of metabolites in the organic extracts.

Identification of hydroxypropazine and desisopropyl hydroxypropazine was confirmed in the aqueous extracts of milk, liver and kidney using Aminex A-4 cation exchange chromatography. The cation exchange columns were eluted with an ammonium formate linear mobile phase followed by 0.1 M ammonium hydroxide. Isolated compounds from Aminex A-4 cation exchange chromatography were identified by HPLC (Method I) co-chromatography with reference standards.

Identification of hydroxypropazine and desisopropyl hydroxypropazine was confirmed in the organic extracts of liver and kidney using a second HPLC system (Method I) and two-dimensional TLC. 2D-TLC analyses were conducted using silica gel 60 F254 plates and a first solvent system of chloroform:methanol:formic acid:water (75:20:4:2, v:v:v:v) followed by a second solvent system of butanol:acetic acid:water (80:11:11, v:v:v). Radioactive compounds were quantified using a radioanalytic imaging system, and non-radiolabeled reference standards were observed with UV light and/or iodine staining.

### **C. RESULTS AND DISCUSSION**

TRR in goat milk and tissues are reported in Table C.2.1. TRR were 0.025-0.029 ppm in milk, 0.006 ppm in muscle, 0.001 ppm in fat (renal and omental), 0.110 ppm in kidney and 0.036 ppm in liver from a goat dosed orally with [<sup>14</sup>C]2-hydroxypropazine at 10.9 ppm in the diet for three consecutive days. Radioactivity was highest in kidney and lowest in fat. Residues in milk were constant during dosing. Excreta was not collected.



The distribution of radioactivity in goat matrices is presented in Table C.2.2.; muscle and fat were not extracted because of low radioactivity (<0.010 ppm). The majority of the radioactivity (~88-91%) in the milk was retained in the aqueous fraction with hexane extraction, and nonextractable residues were <7% TRR (0.001-0.002 ppm). The majority of the radioactivity was extracted from kidney and liver with methanol/water, with ~40-43% TRR being retained in the aqueous fraction. In liver, 66% TRR (0.024 ppm) remained in the organic fraction, leaving <8% TRR (0.003 ppm) as nonextractable residues. In kidney, only ~34% TRR (0.038 ppm) remained in the organic fraction and nonextractable residues were <0.05 ppm (26.5% TRR, 0.029 ppm). Accountabilities were ~93-114%. Residues were identified by HPLC analysis, using 2D-TLC, a second HPLC method, and/or cation exchange chromatography for confirmation. These methods successfully identified the predominant residues in goat matrices.

The characterization and identification of residues in goat matrices is summarized in Table C.2.3. Approximately 66-81% TRR were identified in goat milk, kidney, and liver. The test substance, hydroxypropazine, was found to be the major residue in all matrices, accounting for 63.5% TRR (0.069 ppm) in kidney, 77.2% TRR (0.028 ppm) in liver, and 65.0-69.4% TRR (0.017-0.020 ppm) in milk. The only other metabolite identified was desisopropyl hydroxypropazine, which was detected in minor amounts in all matrices: 2.9% TRR (0.003 ppm) in kidney, 3.6% TRR (0.001 ppm) in liver and 8.2-8.5% TRR (0.002 ppm) in milk. The remaining radioactivity was attributed to unknowns accounting for 10.3% TRR in kidney, 24.7% TRR in liver, and ≤14.8% TRR in milk; no individual peak was present at >0.003 ppm.

### C.1. Storage Stability

Samples of goat matrices were stored frozen (-30°C to -10°C) throughout the study period, except that tissue samples were briefly stored in a refrigerator (2 °C to 8 °C) for six days after two days of frozen storage following collection (these samples were returned to frozen storage after being refrigerated). Actual study dates were not provided; however, based on the study completion date the maximum storage interval from collection to analysis was ~4.5 months for milk and tissue samples. No supporting storage stability data are required because samples appear to have been stored mostly frozen for <6 months from collection to analysis.

We note for future studies, the actual study dates, including extraction and analysis dates should be provided for each sample.

Matrix	Storage Temp (°C)	Actual Storage Duration	Interval of Demonstrated Storage Stability
Milk	-30 to -10	63-66 days based on experimental termination date	None required.
Tissues <sup>1</sup>		~4.5 months based on study completion date	None required.

<sup>1</sup> Tissue samples were stored frozen for 2 days following collection, then refrigerated for 6 days, and returned to frozen storage for the remainder of the study.



## C.2. Identification, Characterization, and Distribution of Residues

**TABLE C.2.1. Total Radioactive Residues (TRR) in Milk and Tissues.**

Matrix	Collection Timing	[U- <sup>14</sup> C]2-hydroxypropazine	
		ppm	% of Administered Dose
Milk	Day 1	0.025	0.06
	Day 2	0.029	0.06
	Day 3	0.029	0.07
	Subtotal	NA	0.19
Muscle (round)	At sacrifice	0.006	0.14 <sup>1</sup>
Fat, renal	At sacrifice	0.001	0.01 <sup>1</sup>
Fat, omental	At sacrifice	0.001	
Kidneys	At sacrifice	0.110	0.03
Liver	At sacrifice	0.036	0.06

<sup>1</sup> Calculated by the petitioner based on 26% and 14% of body weight for muscle and fat and assuming that body composition is similar in goats to dairy cattle.

**TABLE C.2.2. Distribution of the Parent and the Metabolites in Goat Matrices Following Dosing with [U-<sup>14</sup>C]2-Hydroxypropazine at 10.9 ppm in the Diet.<sup>1</sup>**

Metabolite Fraction <sup>2</sup>	Milk (Day 1)		Milk (Day 2)		Milk (Day 3)		Kidney		Liver	
	TRR = 0.025 ppm		TRR = 0.029 ppm		TRR = 0.029 ppm		TRR = 0.110 ppm		TRR = 0.036 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Acetone	94.9	0.024	95.8	0.028	96.1	0.028				
-Hexane	0.58	<0.001	1.17	<0.001	1.47	<0.001				
-Aqueous	88.9	0.022	90.8	0.026	88.0	0.026				
Hydroxypropazine	69.4	0.017	67.7	0.020	65.0	0.019				
Desisopropyl hydroxypropazine	8.3	0.002	8.2	0.002	8.5	0.002				
Others <sup>3</sup>	11.3	0.003	14.8	0.004	14.5	0.004				
Methanol/water							100.2	0.110	114.2	0.041
-Chloroform							34.1	0.038	66.0	0.024
Hydroxypropazine							31.3	0.034	58.5	0.021
Desisopropyl hydroxypropazine							0.2	<0.001	0.5	<0.001
Others <sup>3</sup>							2.5	0.003	7.0	0.003
-Aqueous							42.6	0.047	39.5	0.014
Hydroxypropazine							32.2	0.035	18.7	0.007
Desisopropyl hydroxypropazine							2.7	0.003	3.1	0.001
Others <sup>3</sup>							7.8	0.009	17.7	0.006
Nonextractable	6.37	0.002	6.15	0.002	5.03	0.001	26.5	0.029	7.61	0.003

<sup>1</sup> Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.



Only % TRR values were provided for the extractions; the ppm values were calculated by the study reviewer using the % TRR  
 Summation of all radioactivity not associated with characterized peaks: no individual peak area was >0.003 ppm.

**TABLE C.2.3. Summary of Characterization and Identification of Radioactive Residues in Goat Matrices Following Dosing with [U-<sup>14</sup>C]2-Hydroxypropazine at 10.9 ppm in the Diet.**

Compound	Kidney		Liver		Milk (Day 1)		Milk (Day 2)		Milk (Day 3)	
	TRR = 0.110 ppm		TRR = 0.036 ppm		TRR = 0.025 ppm		TRR = 0.029 ppm		TRR = 0.029 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Hydroxypropazine	63.5	0.069	77.2	0.028	69.4	0.017	67.7	0.020	65.0	0.019
Desisopropyl hydroxypropazine	2.9	0.003	3.6	0.001	8.3	0.002	8.2	0.002	8.5	0.002
Others	10.3	0.011	24.7	0.009	11.3	0.003	14.8	0.004	14.5	0.004
Total identified	66.4	0.072	80.8	0.029	77.7	0.019	75.9	0.022	73.5	0.021
Total characterized	10.3	0.011	24.7	0.009	11.3	0.003	14.8	0.004	14.5	0.004
Total extractable <sup>2</sup>	76.7	0.084	105.5	0.038	89.5	0.022	92.0	0.027	89.5	0.026
Unextractable (PES) <sup>3</sup>	26.5	0.029	7.61	0.003	6.37	0.002	6.15	0.002	5.03	0.001
Accountability <sup>4</sup>	103		114		96.0		100		93.1	

<sup>1</sup> Summation of all radioactivity not associated with characterized peaks; no individual peak area was >0.003 ppm.

<sup>2</sup> The sum of the aqueous fraction and organic fraction.

<sup>3</sup> Residues remaining after exhaustive extractions

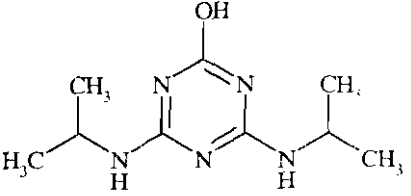
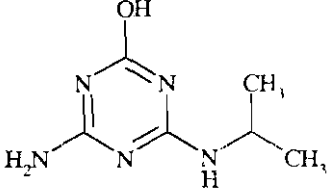
<sup>4</sup> Accountability = (Total extractable + Total unextractable) / TRR from combustion analysis; see TABLE C.2.1) \* 100.





### C.3. Proposed Metabolic Profile

A flowchart of the metabolic profile of hydroxypropazine in goats was not provided.

Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
2- Hydroxypropazine	2-hydroxy-4,6-bis(isopropylamino)-s-triazine	
Desisopropyl hydroxypropazine	4-amino-2-hydroxy-6-isopropylamino-triazine	

### D. CONCLUSION

Total radioactive residues in goat milk and tissues were 0.025-0.029 ppm in milk, 0.006 ppm in muscle, 0.001 ppm in renal and omental fat, 0.110 ppm in kidney and 0.036 ppm in liver from a goat dosed orally with [U-<sup>14</sup>C]2-hydroxypropazine, a metabolite of propazine, at 10.9 ppm in the diet for 3 consecutive days. Excreta was not collected.

Muscle and fat were not extracted because of low radioactivity (<0.010 ppm). The majority of the radioactivity (~88-91%) in the milk was retained in the aqueous fraction with hexane extraction, and nonextractable residues were <7% TRR. The majority of the radioactivity was extracted from kidney and liver with methanol/water, with ~40-43% TRR being retained in the aqueous fraction. In liver, 66% TRR remained in the organic fraction, leaving <8% TRR as nonextractable residues. In kidney, only ~34% TRR remained in the organic fraction and nonextractable residues were <0.05 ppm (26.5% TRR). Accountabilities were ~93-114%.

Approximately 66-81% TRR were identified in goat milk, kidney, and liver. The test substance, hydroxypropazine, was found to be the major residue in all matrices, accounting for 63.5% TRR in kidney, 77.2% TRR in liver, and 65.0-69.4% TRR in milk. The only other metabolite identified was desisopropyl hydroxypropazine, which was detected in minor (2.9-8.5% TRR) amounts in all matrices. The remaining radioactivity was attributed to unknowns accounting for 10.3-24.7% TRR in kidney, liver, and milk; no individual peak was present at >0.003 ppm.



Based on the results of the study, the petitioner concluded that hydroxypropazine is metabolized in goats by N-dealkylation to yield desisopropyl hydroxypropazine. Furthermore, the petitioner stated that hydroxypropazine, the polar metabolite of propazine, is likely rapidly excreted by lactating animals with little deposition into tissues.

## **E. REFERENCES**

None.

## **F. DOCUMENT TRACKING**

RDI: P.V. Shah (8/24/05), RAB1 Chemists (8/24/05)  
G.F. Kramer:806T:CM#2:(703)305-5079:7509C:RAB1  
Petition Number(s): 7F4837  
DP#: 323273  
PC Code: 080808

Template Version: September 2003



<b>APPENDIX I. Chemical Names and Structures of Reference Standards Used in Goat Metabolism Study.</b>		
Common name: Company code	Chemical name	Chemical structure
2-Hydroxypropazine	2-hydroxy-4,6-bis(isopropylamino)-s-triazine	 <chem>CC(C)Nc1nc(O)c(NC(C)C)n1</chem>
Desisopropyl hydroxypropazine	4-amino-2-hydroxy-6-isopropylamino-triazine	 <chem>CC(C)Nc1nc(O)c(N)n1</chem>
4,6-Diamino-2-hydroxy-s-triazine		 <chem>Nc1nc(O)c(N)n1</chem>



Primary Evaluator: George F. Kramer  
George F. Kramer, Ph.D., Chemist Date: 07-DEC-2005  
Registration Action Branch 1 (RAB1)  
Health Effects Division (HED) (7509C)

Approved by: P.V. Shah  
P.V. Shah, Ph.D., Branch Senior Date: 07-DEC-2005  
Scientist/RAB1/HED (7509C)

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This DER was originally prepared under contract by Dynamac Corporation (20440 Century Boulevard, Suite 100; Germantown, MD 20874; submitted 07/13/2005). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

### **STUDY REPORT:**

44287316 Bookbinder, M. (1997) Magnitude of the Residue of Propazine (2-Chloro-4,6-bis(isopropylamino)-s-triazine) and its Metabolites in/on Grain Sorghum Forage, Grain, and Stover Harvested after Preemergence Ground Application of Milo-Pro 4L Herbicide: Final Report: Lab Project Number: 6641-106: MGB 94001: 94001. Unpublished study prepared by Corning Hazleton, Inc. 362 p.

### **EXECUTIVE SUMMARY:**

Griffin Corporation has submitted field trial data on sorghum with propazine. A total of 13 sorghum trials were conducted in Regions 2 (GA; 1 trial), 4 (AR and MO; 2 trials), 5 (IL, KS, and NE; 3 trials), 6 (OK and TX; 4 trials), 7 (SD; 1 trial), and 8 (CO and TX; 2 trials) during the 1994 growing season. Geographic representation of residue data is adequate since the number and locations of field trials are in accordance with OPPTS Guideline 860.1500.

The field study was designed to include three plots at each field trial site. Plot 1 was untreated to provide control samples. Two additional plots each received a single preemergence broadcast application of the 4 lb/gal flowable concentrate (FIC) formulation at low rates (Treatment Plot 2) or high rates (Treatment Plot 3). Nominal "low rates" of ~0.75, 1.5, or 2.4 lb ai/A were applied in plots with soil described as coarse-, medium-, or fine-textured, respectively. Nominal "high rates" of ~1.5, 3.0, or 4.8 lb ai/A were also applied in plots with soil described as coarse-, medium-, or fine-textured, respectively. Soil analysis was not conducted before application of propazine, and the principal study investigator 'estimated' the soil texture designation by direct examination and by using available information sources; the target application rates for each soil texture were based on these estimates. Application was made in 10-17 gal/A of water using ground equipment. Samples of sorghum forage (whole green plants) were collected at the late or hard dough stage at a 69- to 117-day PHI, and samples of sorghum grain and stover were collected at normal harvest for each test location with a PHI range of 85 to 152 days.

Following treatment, soil samples from each treatment plot were sent to Agvise Laboratories (Northwood, ND) for texture characterization. The results of soil analysis showed discrepancies



between the field investigator's "estimates" and the laboratory determinations of soil texture. It was reported that the actual applied rates ranged from 60.4-320% of target rates. Consequently, the study submission only reported residue data from treatment rates bracketing the application rate of 1.2 lb ai/A, which is the maximum single application rate the petitioner wishes to support (see 6/30/2004 Propazine Use Closure Memo) and the rate approved for Section 18 (96-TX-02, dated 1/31/96) use on sorghum for all soil types.

Samples of sorghum forage, grain, and stover were analyzed by a Corning Hazelton analytical method (CHW 6641-106, Method J, Rev. 1) entitled "Determination of Propazine, Desethyl Atrazine (DEA), and Diamino Atrazine (DAA) in Forage, Grain, and Stover using Capillary Gas Chromatography with Mass-Selective Detection and Nitrogen-Phosphorous Detection," dated 10/16/96. The method determines residues of propazine and the chlorometabolite DEA (aka G-30033) by gas chromatography/mass-selective detector (GC/MSD) while residues of DAA (aka G-28273) are quantitated by GC/nitrogen-phosphorus detector (NPD). The limit of quantitation (LOQ) for propazine, DEA, and DAA in all sorghum matrices is 0.05 ppm for each analyte. Overall, the method is adequate for data collection based on acceptable concurrent method recovery data.

Samples were stored frozen for 25.7-26.6 months prior to residue analysis. The petitioner stated that a storage stability study has been initiated and will be submitted in a separate report upon completion. In the interim, the petitioner cited the storage stability data submitted in conjunction with a sorghum metabolism study (MRID 44184814). These data indicate that the metabolic profiles of select sorghum extracts are reasonably unchanged after 25 months of freezer storage. The petitioner has also cited the available storage stability data (MRID 41258601) for corn matrices which indicate that residues of DEA and DAA are stable for at least 24 months.

Following a single preemergence broadcast application of a representative FIC formulation of propazine at 1.47-2.43 lb ai/A, the results of the sorghum field trials indicate the following: In **sorghum forage** harvested at a PHI range of 69-117 days, residues of propazine and DEA (G-30033) were each less than the LOQ (<0.05 ppm) in/on 26 treated samples. Residues of DAA (G-28273) ranged 0.050-0.087 ppm in/on four treated forage samples but were <0.05 ppm in/on 22 treated samples. In **sorghum grain and stover** harvested at a PHI range of 86-152 days, residues of propazine, DEA (G-30033), and DAA (G-28273) were each <0.05 ppm in/on 26 treated samples.



## STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the sorghum field trial data are classified as scientifically acceptable pending submission of an ongoing storage stability study to validate sample storage conditions and intervals. The acceptability of this study for regulatory purposes is addressed in the forthcoming Residue Chemistry Summary for the Tolerance Reassessment Eligibility Decision Document (TRED) for propazine.

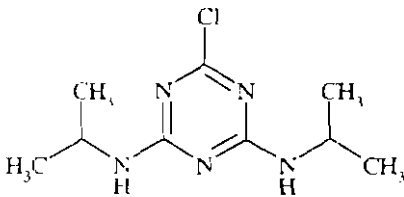
## COMPLIANCE:

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

Propazine (6-chloro-*N,N'*-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine) is a member of the chloro triazine class of herbicides. Other members of this pesticide class include atrazine, cyanazine, and simazine. Propazine is a selective herbicide that can be applied before planting, at planting, and after crop emergence for the preemergence control of annual broadleaf weeds. Currently, the only registered uses are for weed control of ornamental plants grown in containers under greenhouse conditions. There are presently no registered food/feed uses of propazine.

Propazine was previously registered for use on sorghum. The 5/19/87 Propazine Residue Chemistry Chapter along with the 12/88 Propazine Reregistration Standard (Guidance Document) identified several data deficiencies for the reregistration of propazine. Ciba-Geigy, which was then the basic manufacturer of propazine, elected to cancel its registrations of propazine. Another registrant, Griffin Corporation, is now supporting the previously-cancelled uses of propazine on grain sorghum. The structure and nomenclature of propazine are presented in Table A.1. The physicochemical properties of propazine are listed in Table A.2.

TABLE A.1. Propazine Nomenclature	
PC Code 006308	
Chemical structure	
Common name	Propazine
Molecular Formula	C <sub>9</sub> H <sub>16</sub> N <sub>5</sub> Cl
Molecular Weight	229.7
IUPAC name	6-chloro- <i>N,N'</i> -di-isopropyl-1,3,5-triazine-2,4-diamine

**TABLE A.1. Propazine Nomenclature**

CAS name	6-chloro- <i>N,N'</i> -bis(1-methylethyl)-1,3,5-triazine-2,4-diamine
CAS #	139-40-2

**TABLE A.2. Physicochemical Properties of Propazine**

Parameter	Value	Reference
Melting point	217.7 °C	RD D219079, 9/26/95, S. Malak
pH.	5.66	
Density, bulk density, or specific gravity	0.46 g/mL	
Water solubility	3.8 ppm at 25 °C	
Solvent solubility (at 25 °C)	14,252 ppm in acetone 4,696 ppm in 1-octanol	Product Chemistry Chapter of the Propazine Reregistration Standard. 5/19/87
Vapor pressure:	2.9 x 10 <sup>-8</sup> mm Hg at 20 °C  2.98 x 10 <sup>-5</sup> Torr at 45 °C	
Dissociation constant, pK	Not applicable; practically insoluble in water.	RD D219079, 9/26/95, S. Malak
Octanol/water partition coefficient	P = 1234.7 Log P = 3.08	

## B. EXPERIMENTAL DESIGN

### B.1. Study Site Information

**TABLE B.1.1. Trial Site Conditions.**

Trial Identification (County, State, Year)	Treatment plot <sup>1</sup>	Soil characteristics				Meteorological data	
		Type	%OM	pH	CEC (meq/g)	Total rainfall (inches) <sup>1</sup>	Overall average temperature range (°C)
Crittenden, AR: 1994 (AR)	2	Clay loam	1.6	5.6	22.3	1.32-5.31 (1)	11.7-32.6
	3	Clay	2.0	5.8	31.8		
Weld, CO: 1994 (COE)	2	Sandy loam	0.9	6.5	17.0	0.20-3.00	6.2-31.1
	3	Sandy loam	0.7	7.2	19.2		
Mitchell, GA: 1994 (GA)	2	Sandy loam	1.1	6.8	7.3	3.10-11.90 (1)	19.2-30.7
	3	Sandy loam	0.9	6.8	7.3		
Henderson, IL: 1994 (IL)	2	Sandy loam	2.1	5.8	14.8	0.00-4.65 (1)	12.8-29.3
	3	Sandy loam	2.6	5.7	17.1		



**TABLE B.1.1. Trial Site Conditions.**

Trial Identification (County, State, Year)	Treatment plot <sup>1</sup>	Soil characteristics				Meteorological data	
		Type	%OM	pH	CEC (meq/g)	Total rainfall (inches) <sup>2</sup>	Overall average temperature range (°C)
Chautauqua, KS: 1994 (KSW)	2	Loam	2.2	5.8	16.9	0.00-7.40	3.9-36.4
	3	Loam	2.2	5.9	14.6		
Pemscot, MO: 1994 (MO)	2	Loamy sand	0.5	6.0	7.0	0.13-2.18	11.3-31.3
	3	Sandy loam	2.0	6.2	14.2		
York, NE: 1994 (NEW)	2	Silty clay loam	2.5	5.7	21.3	1.4-4.45 (i)	11.1-31.4
	3	Silt loam	3.0	5.6	19.5		
Caddo, OK: 1994 (OKE)	2	Sandy loam	0.7	5.0	8.3	0.1-2.3	16.2-35.6
	3	Sandy loam	1.0	5.2	8.8		
Custer, OK: 1994 (OKW)	2	Sandy loam	0.6	4.9	8.3	0.00-1.80 (i)	4.4-38.9
	3	Sandy loam	0.3	5.6	7.9		
Tripp, SD: 1994 (SDE)	2	Clay	2.3	7.8	47.2	0.60-3.49	6.8-29.5
	3	Clay	1.6	7.8	48.2		
Waller, TX: 1994 (TXE)	2	Sandy loam	0.7	5.9	5.8	0.36-2.83 (i)	22.2-34.2
	3	Sandy loam	1.0	6.0	6.0		
Willacy, TX: 1994 (TXS)	2	Sandy clay loam	1.4	8.0	31.6	0.10-3.65 (i)	17.2-36.9
	3	Sandy clay loam	1.1	8.1	32.1		
Lubbock, TX: 1994 (TXW)	2	Sandy loam	0.5	7.9	20.0	0.10-1.90 (i)	10.2-38.1
	3	Sandy loam	0.4	8.0	17.8		

<sup>1</sup> Treatment rates were based on soil texture. Treatment Plot 2 ("low rate") with soil described as coarse-, medium-, or fine-textured received one preemergence broadcast application at 0.75, 1.5, or 2.4 lb ai/A, respectively. Treatment Plot 3 ("high rate") received 1.5, 3.0, or 4.8 lb ai/A, respectively.

<sup>2</sup> (i) indicates that supplemental irrigation was received

The actual temperature recordings are: (i) similar to the corresponding 10-year average for SDE and TXS trials; (ii) slightly below the corresponding 10-year average for the AR, GA, MO, OKE, OKW trials; (iii) slightly above the corresponding 10-year average for COE, IL, KSW, NEW, TXW trials; and (iv) several degrees below the corresponding 10-year average maxima and several degrees above the corresponding 10-year average minima for TXE. Precipitation (4.7-33.30 inches) and irrigation totaled approximately 35-338% of the 10-year average for all plots. Irrigation was used to supplement as needed.





**TABLE B.1.2. Study Use Pattern.**

Location (City, State, Year)	EP <sup>1</sup>	Treatment Plot <sup>2</sup>	Application					Tank Mix Adjuvants
			Method; Timing	Vol. (GPA <sup>3</sup> )	Rate (lb ai/A)	RTI <sup>4</sup> (days)	Total Rate (lb ai/A)	
Crittenden, AR. 1994 (AR)	4 lb/gal FIC	2 (fine/fine)	1. Broadcast; preemergence	10.00	2.40	NA <sup>5</sup>	2.40	None
	4 lb/gal FIC	3 (fine/fine)	1 Broadcast; preemergence	10.10	4.80	NA	4.80	None
Weld, CO: 1994 (COE)	4 lb/gal FIC	2 (fine/coarse)	1. Broadcast; preemergence	14.12	2.38	NA	2.38	None
	4 lb/gal FIC	3 (fine/coarse)	1. Broadcast; preemergence	14.19	4.79	NA	4.79	None
Mitchell, GA: 1994 (GA)	4 lb/gal FIC	2 (coarse/coarse)	1. Broadcast; preemergence	10.00	0.75	NA	0.75	None
	4 lb/gal FIC	3 (coarse/coarse)	1. Broadcast; preemergence	10.00	1.49	NA	1.49	None
Henderson, IL. 1994 (IL)	4 lb/gal FIC	2 (fine/coarse)	1. Broadcast; preemergence	14.96	2.40	NA	2.40	None
	4 lb/gal FIC	3 (fine/coarse)	1. Broadcast; preemergence	15.07	4.83	NA	4.83	None
Chautauqua, KS 1994 (KSW)	4 lb/gal FIC	2 (medium/medium)	1. Broadcast; preemergence	16.80	1.68	NA	1.68	None
	4 lb/gal FIC	3 (medium/medium)	1 Broadcast; preemergence	16.90	3.39	NA	3.39	None
Pemiscot, MO: 1994 (MO)	4 lb/gal FIC	2 (coarse/coarse)	1 Broadcast; preemergence	12.00	0.75	NA	0.75	None
	4 lb/gal FIC	3 (coarse/coarse)	1. Broadcast; preemergence	12.30	1.54	NA	1.54	None
York, NE: 1994 (NEW)	4 lb/gal FIC	2 (medium/ medium)	1. Broadcast; preemergence	10.19	1.48	NA	1.48	None
	4 lb/gal FIC	3 (medium/medium)	1 Broadcast; preemergence	10.16	2.95	NA	2.95	None
Caddo, OK: 1994 (OKE)	4 lb/gal FIC	2 (coarse/coarse)	1. Broadcast; preemergence	15.00	0.78	NA	0.78	None
	4 lb/gal FIC	3 (coarse/coarse)	1. Broadcast; preemergence	14.90	1.50	NA	1.50	None
Custer, OK: 1994 (OKW)	4 lb/gal FIC	2 (medium/coarse)	1. Broadcast; preemergence	15.80	1.64	NA	1.64	None
	4 lb/gal FIC	3 (medium/coarse)	1 Broadcast; preemergence	14.90	3.10	NA	3.10	None
Tripp, SD: 1994 (SDE)	4 lb/gal FIC	2 (medium/fine)	1. Broadcast; preemergence	14.50	1.51	NA	1.51	None
	4 lb/gal FIC	3 (medium/fine)	1. Broadcast; preemergence	13.98	2.90	NA	2.90	None



Location (City, State; Year)	EP <sup>1</sup>	Treatment Plot <sup>2</sup>	Application				Tank Mix Adjuvants	
			Method; Timing	Vol. (GPA <sup>3</sup> )	Rate (lb ai/A)	RTI <sup>4</sup> (days)		Total Rate (lb ai/A)
Waller, TX; 1994 (TXE)	4 lb/gal FIC	2 (coarse/coarse)	1. Broadcast; preemergence	12.39	0.77	NA	0.77	None
	4 lb/gal FIC	3 (coarse/coarse)	1. Broadcast; preemergence	12.01	1.49	NA	1.49	None
Willacy, TX; 1994 (TXS)	4 lb/gal FIC	2 (fine/medium)	1. Broadcast; preemergence	10.56	2.43	NA	2.43	None
	4 lb/gal FIC	3 (fine/medium)	1. Broadcast; preemergence	12.25	5.17	NA	5.17	None
Lubbock, TX; 1994 (TXW)	4 lb/gal FIC	2 (medium/coarse)	1. Broadcast; preemergence	14.53	1.47	NA	1.47	None
	4 lb/gal FIC	3 (medium/coarse)	1. Broadcast; preemergence	15.15	3.07	NA	3.07	None

<sup>1</sup> EP = End-use Product.

<sup>2</sup> Plot 1 is untreated control plot. Treatment Plot 2 ("low rate") with soil described as coarse-, medium-, or fine-textured received one preemergence broadcast application at ~0.75, 1.5, or 2.4 lb ai/A, respectively. Treatment Plot 3 ("high rate") received one preemergence broadcast application at ~1.5, 3.0, or 4.8 lb ai/A, respectively. Treatment rates were based on soil texture listed in parentheses. The first description is based on the Principal Field Investigator's estimate of the test plot soil texture class and the second description is based on a laboratory determination of soil texture and composition.

<sup>3</sup> GPA = Gallons per acre

<sup>4</sup> RTI = Retreatment Interval

<sup>5</sup> NA = Not applicable



**TABLE B.1.3. Trial Numbers and Geographical Locations.**

NAFTA Growing Region	Sorghum		
	Submitted	Requested	
		Canada	US
1			
1A			
2	1		1
3			
4	2		1
5	3		4
5A			
5B			
6	4		2
7	1		1
7A			
8	2		3
9			
10			
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
21			
Total	13		12

**B.2. Sample Handling and Preparation**

Duplicate control and duplicate treated samples of sorghum forage, grain, and stover were harvested from each test plot of each trial site. The harvested samples were frozen within 7 hours of collection. Samples of sorghum forage (whole green plants) were collected at the late dough or hard dough stage, and samples of sorghum grain and stover were collected at normal harvest. The frozen samples were stored frozen for 0-95 days at the field location prior to shipment via freezer truck to Griffin Corporation (Valdosta, GA). Originally, the analytical phase of the study was to be performed by Griffin Corporation; however, in order to expedite the completion of the study, the sponsor opted to send the frozen crop samples to Corning Hazelton,



Inc. (CHI, Madison, WI) for residue analysis. All samples were maintained under frozen conditions (-27.8 °C to -2.2 °C) until they were homogenized, extracted, and analyzed.

### **B.3. Analytical Methodology**

Samples were analyzed for residues of propazine and its chlorometabolites using GC/MSD and NPD method (CHW 6641-106, Method 1, Rev. 1) entitled "Determination of Propazine, Desethyl Atrazine (DEA), and Diamino Atrazine (DAA) in Forage, Grain, and Stover using Capillary Gas Chromatography with Mass-Selective Detection and Nitrogen-Phosphorous Detection," dated 10/16/96. A complete description of the method was included in the submission.

Briefly, a representative sample is soxhlet-extracted with acetone, concentrated by rotary evaporation, and diluted with acetone. An aliquot is extracted with ethyl acetate and saturated sodium chloride. The organic layer is reserved, and the water layer is reextracted. The organic layers are combined and evaporated to dryness. Residues are redissolved in water and cleaned up on a Chem-Elut column. Residues are eluted with 15% ethyl acetate/hexane for isolation of propazine and DEA (Fraction A). The eluate is evaporated to dryness, redissolved in ethyl acetate, and analyzed for propazine and DEA using GC/MSD.

A second aliquot is taken for isolation of DEA. The aliquot is evaporated to dryness and redissolved in water. The water solution is centrifuged and cleaned up on a Chem-Elut column. Residues of DAA are eluted with 50% ethyl acetate/hexane (fraction B). The eluate is evaporated to dryness, redissolved in acetone, and cleaned up on a LC-SCX column. Residues are eluted with 1 N ammonium hydroxide:methanol (1:3, v:v). The eluate is mixed with phosphate buffer (pH 6.5) and ethyl acetate. The organic layer is reserved, and the water layer is reextracted. The organic layers are combined and evaporated to dryness. Residues are redissolved in ethyl acetate and analyzed for DAA using GC/NPD. The limit of quantitation (LOQ) for propazine, DEA, and DAA in all commodities is 0.05 ppm.

Method verification was performed prior to analysis of sorghum samples. The analytical method was validated for propazine and DAA in/on sorghum forage, grain, and stover by analyzing two samples fortified with one compound at 0.05 ppm, 0.10 ppm, and 0.500 ppm. The analytical method was validated for DEA in/on sorghum forage, grain, and stover by analyzing two samples fortified with one compound at 0.0575 ppm, 0.115 ppm, and 0.575 ppm. Recoveries of propazine ranged 88-118% with an average recovery of 103% ± 12.6 for sorghum forage (n=6), 63.9-133% with an average recovery of 89.7% ± 27.4 for sorghum grain (n=6), and 92.5-136% with an average recovery of 125.1% ± 16.8 for sorghum stover (n=6). Recoveries of DEA ranged 89.7-109% with an average recovery of 98.3% ± 7.3 for sorghum forage (n=6), 7.34-130% with an average recovery of 111% ± 19.9 for sorghum grain (n=6), and 87.8-126% with an average recovery of 109% ± 15.5 for sorghum stover (n=6). Recoveries of DAA ranged 37.2-138% with an average recovery of 89.5% ± 42.8 for sorghum forage (n=6), 46.8-70.6% with an average recovery of 61.9% ± 10.3 for sorghum grain (n=5), and 59.6-102% with an average recovery of 78.2% ± 15.2 for sorghum stover (n=6).



## C. RESULTS AND DISCUSSION

Concurrent method recovery data are presented in Table C.1. Apparent residues of propazine, DEA, and DAA were each below the method LOQ (<0.05 ppm) in/on all untreated samples of sorghum forage, grain, and stover.

Sample storage conditions and intervals are summarized in Table C.2. The maximum storage intervals of crop samples from harvest to analysis for residues of propazine and DEA were 809 days (26.6 months) for sorghum forage, 779 days (25.9 months) for sorghum grain, and 787 days (25.9 months) for sorghum stover. The maximum storage intervals of crop samples from harvest to analysis for residues of DAA were 809 days (26.6 months) for sorghum forage, 784 days (25.8 months) for sorghum grain, and 782 days (25.7 months) for sorghum stover. The petitioner indicated that a storage stability study has been initiated and will be submitted in a separate report. In addition, to support sample storage conditions and intervals, the petitioner provided storage stability data for sorghum forage, grain, and fodder submitted in conjunction with the sorghum metabolism study (MRID 44184814). These data indicate that residues of propazine, DEA, and DAA are stable in/on frozen fodder for up to 24 months. Additionally, the available storage stability data (MRID 41258601) for commodities of corn show that residues of DEA and DAA are stable for at least 24 months.

Residue data from the sorghum field trials are reported in Table C.3. A summary of propazine residue data for sorghum is presented in Table C.4. Residues of propazine and DEA were each less than the LOQ (<0.05 ppm) in/on sorghum forage, grain, and stover harvested 69-117 days (forage) and 85/86-152 days (grain and stover) following a single broadcast preemergence application of the 4 lb/gal FIC formulation at a rate of 1.47-2.43 lb ai/A. Residues of DAA were less than the LOQ (<0.05 ppm) to 0.087 ppm in/on sorghum forage and less than the LOQ (<0.05 ppm) in/on sorghum grain and stover harvested 69-117 days (forage) and 85/86-152 days (grain and stover) following a single broadcast preemergence application of the 4 lb/gal FIC formulation at a rate of 1.47-2.43 lb ai/A.



<b>TABLE C.1. Summary of Concurrent Recoveries of Propazine and its Chlorometabolites, DEA and DAA from Sorghum.</b>				
Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean $\pm$ std dev
<b>Propazine</b>				
Sorghum forage	0.0500	11	93.4, 101, 108, 111, 111, 113, 114, 114, 120, 124, 133	109 $\pm$ 11.8
	0.100	2	94.5, 99.0	
	0.475	1	95.0	
Sorghum grain	0.0500	2	90.8, 124	124.0 $\pm$ 14.9
	0.100	11	69.5, 70.5, 83.5, 83.5, 88.5, 94.5, 101, 101, 102, 107, 110	
	0.500	1	96.8	
Sorghum stover	0.0500	7	86.2, 108, 109, 111, 113, 125, 129	129 $\pm$ 16.3
	0.100	7	83.0, 86.5, 109, 110, 115, 117, 118	
	0.500	2	69.8, 102	
<b>DEA</b>				
Sorghum forage	0.0575	11	87.0, 87.8, 103, 106, 110, 116, 120, 123, 126, 131, 134	109 $\pm$ 16.8
	0.115	2	86.1, 93.0	
	0.575	1	96.3	
Sorghum grain	0.0575	2	85, 96.5	95.3 $\pm$ 17.0
	0.115	11	63.9, 72.6, 77.0, 88.7, 92.2, 98.3, 103, 112, 115, 117, 119	
	0.575	1	93.4	
Sorghum stover	0.0575	8	94.8, 98.8, 114, 119, 122, 123, 126, 128	105 $\pm$ 18.5
	0.115	7	81.3, 81.7, 83.5, 96.5, 111, 114, 121	
	0.575	1	71.3	
<b>DAA</b>				
Sorghum forage	0.0500	10	56.6, 80.0, 98.6, 99.6, 100, 102, 105, 118, 141, 142, 178	108 $\pm$ 29.7
	0.100	2	95.0, 105	
	0.500	1	88.6	
Sorghum grain	0.0500	2	79.2, 140	82.3 $\pm$ 25.6
	0.100	11	33.1, 64.0, 65.5, 69.0, 76.5, 83.5, 85.5, 87.0, 95.0, 102, 112	
	0.500	1	60.0	
Sorghum stover	0.0500	7	101, 116, 120, 120, 124, 126, 127	96.9 $\pm$ 27.3
	0.100	7	49.2, 61.0, 67.0, 88.5, 89.5, 108, 111	
	0.500	2	48.8, 94.0	



**TABLE C.2. Summary of Storage Conditions.**

Matrix (RAC or Extract)	Analyte	Storage Temp. (°C)	Actual Storage Duration <sup>1</sup>	Interval of Demonstrated Storage Stability
Sorghum forage	Propazine	-32 to 22 at Griffin	755-809 days (24.8-26.6 months)	The petitioner indicated that a storage stability study has been initiated and will be submitted in a separate report.  In addition, the petitioner provided storage stability data for sorghum forage, grain, and fodder submitted in conjunction with the sorghum metabolism study (MRID 00414814). These data indicate that the metabolic profiles of select sorghum extracts are reasonably unchanged after 25 months of freezer storage.  Additionally, the available storage stability data (MRID 41258601) for RAC's of corn show that residues of DEA and DAA are stable for at least 24 months.
	DEA	-27.8 to -2.2 at Corning	729-809 days (24.0-26.6 months)	
	DAA	Hazelton		
Sorghum grain	Propazine	-32 to 22 at Griffin	693-779 days (22.8-25.6 months)	
	DEA	-27.8 to -2.2 at Corning	694-784 days (22.8-25.8 months)	
	DAA	Hazelton		
Sorghum stover	Propazine	-32 to 22 at Griffin	695-787 days (22.9-25.9 months)	
	DEA	-27.8 to -2.2 at Corning	698-782 days (23.0-25.7 months)	
	DAA	Hazelton		

<sup>1</sup> Actual storage duration from collection to analysis. All samples were analyzed 2-8 days of extraction.

**TABLE C.3. Residue Data from Crop Field Trials with Propazine.**

Trial ID (County, State; Year)	Region	Crop Variety	Commodity or Matrix	Treatment Plot <sup>1</sup>	Total Rate (lb. a/A)	PHI (days)	Residues (ppm)			
							Propazine	DEA	DAA	Total
Crittenden, AR; 1994 (AR)	4	Sorghum; Cherokee	forage	2 (fine/fine)	2.40	84	NQ, NQ <sup>2</sup>	NQ, NQ	NQ, NQ	NQ, NQ
			grain				136	NQ, NQ	NQ, NQ	NQ, NQ
			stover				136	NQ, NQ	NQ, NQ	NQ, NQ
Weld, CO; 1994 (COE)	8	Sorghum; 577	forage	2 (fine/coarse)	2.38	96	NQ, NQ	NQ, NQ	0.050, 0.059	<0.150, <0.159
			grain				135	NQ, NQ	NQ, NQ	NQ, NQ
			stover				135	NQ, NQ	NQ, NQ	NQ, NQ
Mitchell, GA; 1994 (GA)	2	Sorghum; DK 64	forage	3 (coarse/coarse)	1.49	76	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			grain				108	NQ, NQ	NQ, NQ	NQ, NQ
			stover				108	NQ, NQ	NQ, NQ	NQ, NQ



**TABLE C.3. Residue Data from Crop Field Trials with Propazine.**

Trial ID (County, State, Year)	Region	Crop: Variety	Commodity or Matrix	Treatment Plot <sup>1</sup>	Total Rate (lb ai/A)	PHI (days)	Residues (ppm)				
							Propazine	DEA	DAA	Total	
Henderson, IL: 1994 (IL)	5	Sorghum: Patriot 8703	forage	2 (fine/ coarse)	2.40	89	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ	
			grain				125	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				125	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
Chautauqua, KS: 1994 (KSW)	5	Sorghum: Hogemeyer 688	forage	2 (medium/ medium)	1.68	117	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ	
			grain				152	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				152	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
Pemiscot, MO: 1994 (MO)	4	Sorghum: Agratech 6K4613C	forage	3 (coarse/ coarse)	1.54	85	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ	
			grain				133	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				133	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
York, NE: 1994 (NEW)	5	Sorghum: NK 1210	forage	2 (medium/ medium)	1.48	95	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ	
			grain				126	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				126	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ





Trial ID (County, State: Year)	Region	Crop: Variety	Commodity or Matrix	Treatment Plot <sup>1</sup>	Total Rate (lb ai/A)	PHI (days)	Residues (ppm) <sup>2</sup>				
							Propazine	DEA	DAA	Total	
Caddo, OK: 1994 (OKE)	6	Sorghum: W-632-W	forage	3 (coarse/ coarse)	1.50	92	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ	
			grain				112	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				112	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
Custer, OK: 1994 (OKW)	6	Sorghum: NK KS714Y	forage	2 (medium/ coarse)	1.64	92	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ	
			grain				127	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				127	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
Tripp, SD: 1994 (SDE)	7	Sorghum: Pioneer 8855	forage	2 (medium/ fine)	1.51	77	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ	
			grain				132	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				132	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
Waller, TX: 1994 (TXE)	6	Sorghum: GSA-1290	forage	3 (coarse/ coarse)	1.49	69	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ	
			grain				85	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				86	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
Willacy, TX: 1994 (TXS)	6	Sorghum: RS200-E	forage	2 (fine/ medium)	2.43	76	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ	
			grain				97	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				97	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
Lubbock, TX: 1994 (TXW)	8	Sorghum: ORD- Bonus	forage	2 (medium/ coarse)	1.47	78	NQ, NQ	NQ, NQ	0.068, 0.087	<0.168, <0.187	
			grain				125	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ
			stover				125	NQ, NQ	NQ, NQ	NQ, NQ	NQ, NQ

<sup>1</sup> Plot 1 is untreated control plot. Treatment Plot 2 ("low rate") with soil described as coarse-, medium-, or fine-textured received one preemergence broadcast application at ~0.75, 1.5, or 2.4 lb ai/A, respectively. Treatment Plot 3 ("high rate") received one preemergence broadcast application at ~1.5, 3.0, or 4.8 lb ai/A, respectively. Treatment rates were based on soil texture listed in parentheses. The first description is based on the Principal Field Investigator's "estimate" of the test plot soil texture class and the second description is based on a laboratory determination of soil texture and composition.

<sup>2</sup> NQ = Not quantifiable, less than the LOQ (<0.05 ppm)



TABLE C.4. Summary of Residue Data from Crop Field Trials with Propazine.										
Commodity	Analyte	Total Applic Rate (lb ai/A)	PHI (days)	Residue Levels (ppm) <sup>1</sup>						
				n	Min	Max.	HAFT <sup>2</sup>	Median	Mean	Std. Dev.
Sorghum forage	Propazine	1.47-2.43	69-117	26	<0.05	<0.05	<0.05	<0.05	<0.05	--
	DEA			26	<0.05	<0.05	<0.05	<0.05	<0.05	--
	DAA			26	<0.05	0.087	0.078	0.05	0.052	0.008
	Total			26	<0.15	<0.187	<0.178	0.150	0.152	0.008
Sorghum grain	Propazine	1.47-2.43	85-152	26	<0.05	<0.05	<0.05	<0.05	<0.05	--
	DEA			26	<0.05	<0.05	<0.05	<0.05	<0.05	--
	DAA			26	<0.05	<0.05	<0.05	<0.05	<0.05	--
	Total			26	<0.15	<0.15	<0.15	<0.15	<0.15	--
Sorghum stover	Propazine	1.47-2.43	86-152	26	<0.05	<0.05	<0.05	<0.05	<0.05	--
	DEA			26	<0.05	<0.05	<0.05	<0.05	<0.05	--
	DAA			26	<0.05	<0.05	<0.05	<0.05	<0.05	--
	Total			26	<0.15	<0.15	<0.15	<0.15	<0.15	--

<sup>1</sup> For the determination of minimum, maximum, HAFT, median, mean, and standard deviation values, the LOQ (<0.05 ppm) was used for residues reported as nonquantifiable (NQ) in Table C.3.

<sup>2</sup> HAFT = Highest Average Field Trial.

#### D. CONCLUSION

The submitted sorghum field trial data reflect the use of propazine at a total rate of 1.47-2.43 lb ai/A with a 69- to 117-day PHI for sorghum forage, and a 85/86- to 152-day PHI for sorghum grain and stover. A single broadcast preemergence application of the 4 lb/gal FIC formulation was made at 1.47-2.43 lb ai/A. An acceptable method was used for quantitation of residues in/on sorghum commodities.

#### E. REFERENCES

44184814 Jalali, K; Saber, A; O'Neal, S. *et al.* (1996) [<sup>14</sup>C]Propazine: Metabolic Fate and Distribution in Grain Sorghum: Lab Project Number: CHW 6641-104: AM-067: GP96-018. Unpublished study prepared by Corning Hazleton Inc. 317 p.

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## **F. DOCUMENT TRACKING**

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