03/07/95

MEMORANDUM

SUBJECT: Request for a Metabolism Review of Thiazopyr (MON-13200) and Determination of Residue(s) to be Regulated.

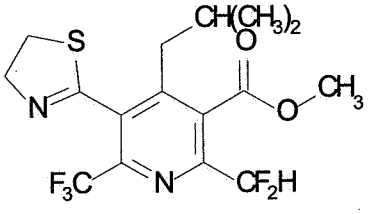
FROM: Jerry B. Stokes, Chemist
Chemistry Branch I/Tolerance Support
Health Effects Division (7509C)

THRU: Ed Zager, Acting Branch Chief
Chemistry Branch I/Tolerance Support
Health Effects Division (7509C)

TO: Metabolism Committee
Health Effects Division (7509C)

Thiazopyr {3-Pyridinecarboxylic acid, 2-(difluoromethyl)-5-(4,5-dihydro-2-thiazolyl)-4-(2-methylpropyl)-6-(trifluoromethyl)-, methyl ester} (also known as MON 13200) is a herbicide that is proposed for application for weed control in citrus orchards and cotton fields.

Structure:



Nature of the Residue in Plants and Animals

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Thiazopyr undergoes extensive and rapid degradation in plants and animals to a large number of polar metabolites, each present at low levels (<10% of TRR). Major routes of metabolism include sulfur oxidation, thiazoline ring opening and methyl ester hydrolysis, and transformation of the isobutyl side chain. More than 30 metabolites have been positively or tentatively identified. (See Supplementary Information, this memo for structures of metabolites).

The major residues in ruminant muscle and milk are thiazopyr and its unsaturated nitrile acid (metabolite #26). The major residues in fat are thiazopyr and its sulfone ester metabolite (metabolite #8). The major terminal residues in poultry are thiazopyr and its nitrile acid ester metabolite (metabolite #29).

Analytical Methodology:

The parent and most of the identified metabolites share a common moiety, 2-difluoromethyl-4-(2-methylpropyl)-6-trifluoromethyl pyridine carboxylate. The residues of thiazopyr and its metabolites can be converted to a sulfonic diacid (**SAA**), or an amide acid (**AA**). (See p.3 this memo, for structures of **SAA** and **AA**).

The registrant has supplied CBTS with two proposed analytical enforcement methods, but neither is an adequate enforcement method according to screening reviews by EPA laboratory personnel [Beltsville (BEAD, ACB, ACS)]. Four metabolites #15, #16, #5, and #14 are not converted to either the SAA or AA chemophores and the method must be altered to detect these metabolites assuming the latter are of toxicological concern. According to a conversation with a Monsanto analytical laboratory scientist, another **proposed** enforcement method in which all residues are converted to one common chemophore, a triacid with the fluorinated pyridine ring still intact, has been developed. The Monsanto company representative also stated that esterification of this triacid and analysis by GC/MS show conversion of more than 70% of the thiazopyr residues. This methodology is presently being evaluated by an independent laboratory. **CBTS has not received this method for review and does not know if this method will be an adequate enforcement method for thiazopyr and any thiazopyr metabolites in cotton or citrus commodities.** In

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addition, this chemical has now been sold to another company (Rohm Haas) and CBTS does not know if, or when, this proposed enforcement method will be submitted. **Therefore, CBTS does not have an adequate enforcement method for the proposed uses on cotton and citrus.** No methods have been submitted for livestock meat, meat by-products, and fat, and milk and eggs, because the petitioner the expected amounts of identifiable residues from the proposed use would not be finite (<0.01).

Crop Field Trials and Livestock Residues:

In cotton and citrus field trials, no residues of thiazopyr or its metabolites convertible to either **SAA** or **AA** were found to be greater than the lower limit of the method validation (0.025 ppm). Based upon the available data for the proposed uses, tolerances are not required for livestock tissues, milk, or eggs.

Request to Committee:

CBTS requests the Metabolism Committee to determine if only the parent thiazopyr should be regulated, or should additional metabolites be included in the tolerance expression and/or dietary risk assessment as proposed by the petitioner?

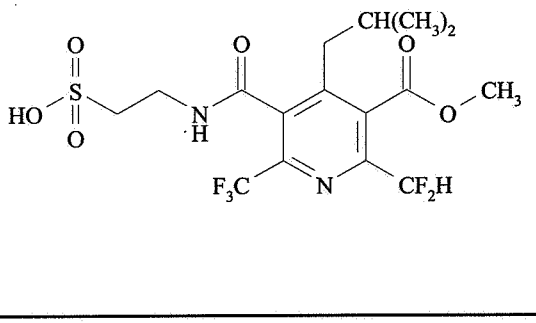
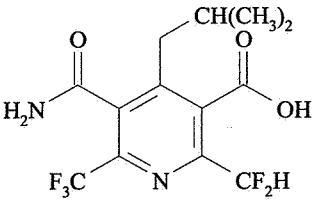
Supplementary Information:

Proposed Use:

The 2 lb a.i./gal EC formulation (22.3 % a.i.) is proposed for 1 to 3 preemergence surface applications to citrus crops with 2- to 3-month retreatment intervals and a maximum of 2 lb a.i./A/season. A 90-day PHI is proposed. The same formulation is proposed for use in all states except AZ and CA for 1 to 2 treatments as preplant incorporated or preemergence surface applications to cotton for a maximum of 0.375 lb a.i./A/season. No PHI is proposed.

Nature of the Residue in Plants and Animals

Thiazopyr undergoes extensive and rapid degradation in plants and animals to a large number of polar metabolites, each present at low levels (<10% of TRR). The parent and most of the identified metabolites share a common moiety, 2-difluoromethyl-4-(2-methylpropyl)-6-trifluoromethyl pyridine carboxylate. The residues of concern as proposed by the petitioner are thiazopyr and its metabolites that can be converted to the sulfonic diacid (**SAA**), 2-difluoromethyl-4-(2-methylpropyl)-5-[(2-sulfoethyl)aminocarbonyl]-6-trifluoromethyl-3-pyridine carboxylic acid, methyl ester, and the amide acid (**AA**), 2-difluoromethyl-4-(2-methylpropyl)-5-aminocarbonyl-6-trifluoromethyl-3-pyridine carboxylic acid.

	
SAA	**AA**

Plant Metabolism Studies:

Lemon trees grown in 5 gallon containers in a sandy loam soil were treated with thiazopyr labelled at the C4 position of the pyridine moiety at the maximum proposed label rate of 2 lb a.i./A and at twice the proposed maximum label rate using 4 lb a.i./A. Foliage and immature fruit were collected at 133 and 124 days, respectively, after treatment, and mature fruits were harvested 236 days after treatment. Only the mature fruit were analyzed and fractionated for determination of residues. The following table shows the distribution and identification of thiazopyr residues. For the metabolite structures and numbers refer to the metabolite identification table, p. 8 , this memo.

The low C14 thiazopyr activity in this metabolism study suggests that 1) thiazopyr metabolites containing the intact pyridine ring undergo negligible translocation from the soil to fruit, 2) under actual field conditions at the maximum proposed label rate of 2.0 lb a.i./A, residues of thiazopyr and its metabolites would be undetectable (<0.05 ppm). Most of the metabolites in the lemon tissues were partitioned into the aqueous layer. MON 13200 is relatively nonpolar and is water-insoluble. Several metabolites (#15 and #16) were partially distributed in the organic and the aqueous layers. The levels of organic-soluble residues (MON-13200, #3, #5, #6, and #8) totaled <4% TRR.

Quantification of Thiazopyr and Its Metabolites in Lemons (ppb in parent equivalents) (4 lb a.i./A treatment)								
Chemical Residue	Rind		Pulp		Juice		Whole Fruit	
	% TRR	ppb	% TRR	ppb	% TRR	ppb	% TRR	ppb
thiazopyr (parent recovered)	0.22	0.31	ND	ND	ND	ND	0.22	0.05
Metabolite No.								
3	0.07	0.09	ND	ND	ND	ND	0.07	0.02
4	2.7	3.8	1.3	1.7	1.3	1.1	5.3	2.0
5	0.09	0.13	ND	ND	ND	ND	0.09	0.03
6	1.1	1.5	0.03	0.04	0.05	0.04	1.2	0.43
7	6.3	8.8	0.34	0.46	0.88	0.71	7.5	2.8
8	0.13	0.18	<0.02	<0.03	ND	ND	0.13	0.05
10	3.6	5.0	0.39	0.52	0.65	0.53	4.6	1.7
11	3.3	4.7	0.28	0.37	0.60	0.49	4.2	1.6
15	5.9	8.33	2.1	2.8	2.4	1.9	10	3.9
16	1.0	1.4	0.74	0.99	0.95	0.77	2.7	1.0
19	4.3	6.1	0.40	0.54	0.69	0.56	5.4	2.0
20	5.4	7.6	0.78	1.0	0.94	0.77	7.1	2.7

Total % TRR of whole fruit Identified/ Quantified	34	--	6.3	--	8.4	--	49	--
% TRR of whole fruit Contained In	68	--	13	--	19	--	100	--

TRR: 0.04 ppm (thiazopyr equivalents), 0.19 % of applied radioactivity
ND: Not detected above LOD

Cotton plants grown in sandy loam soil in individual greenhouse pots were divided into 4 treatment groups: untreated, treated with soil incorporation with unlabeled thiazopyr, soil incorporation treated with thiazopyr labeled in the pyridine or thiazoline rings, surface treatment with thiazopyr labeled in the pyridine or thiazoline rings. The pesticide was applied to each pot in an amount equivalent to 0.125 lbs a.i./A. The proposed maximum seasonal label rate is 0.375 lb a.i./A (0.5 lb a.i./A in AZ and CA). Cotton foliage was harvested at 56 days; cottonseed and cotton plant hay at 249 days after treatment. Residue levels were determined in plant matrices by combustion and the captured radioactivity was determined by LSC. Uptake of C14 thiazopyr was approximately 0.5% of the applied radioactivity. Residue levels for both ring labels were similar for both application methods.

The very low level of C14 radioactivity in cottonseed prohibited extraction and isolation of metabolites. The metabolism of thiazopyr in cotton was extensive, although some parent remained in crop tissues. In a representative experiment, 93.1% of the total radioactivity of the leaves was extractable. The organic extract had 42% of the initial radioactivity, and of this, 13.2% was resolved into 11 discrete peaks. The aqueous phase had 57.8% of the initial radioactivity. HPLC resolved 29% of the initial extract radioactivity into 26 discernable peaks. In all, of over 40 peaks present, nine significant metabolites were identified and characterized. (See Metabolite identification table, p. 8, this memo, for compound structures and numbers). Recoveries of the identified peaks ranged from 0.1% to 9.4% of the TRR.

Quantification of Thiazopyr and Its Metabolites in Cotton (0.125 lb a.i./A treatment; C14-pyridine label)		
Chemical Residue	Forage (56 days)	
	% TRR	ppb
thiazopyr (parent recovered)	2.1	1.7
Metabolite No.		
3	7.2	6.0
5	3.1	2.6
6	7.1	5.9
7	7.6	6.3
8	3.0	2.5

10	2.2	1.8
11	9.4	7.8
18	6.1	5.1
Total % TRR Identified/Quantified of whole plant	48	--
% TRR Contained of whole plant	93	--

In summary, thiazopyr undergoes extensive and rapid degradation in plants to a large number of polar metabolites, all found at low levels (<10% of the TRR). Major routes of metabolism include sulfur oxidation, thiazoline ring opening and methyl ester hydrolysis, and transformation of the isobutyl side chain. About 30 metabolites have been positively or tentatively identified. The complete breakdown of thiazopyr to many low-level polar metabolites closely resembles the metabolic pathways observed in other crops and soil metabolism. For example in cotton, 8 metabolites are found, 13 in peanuts, and 12 in lemons. (See the comparison table of metabolic pathways, p. 16, this memo). The submitted metabolic data for plants are adequate to support the proposed uses with citrus and cotton. No additional data are needed.

Animal Metabolism Studies:

Lactating Goat:

Two lactating goats were dosed orally for 4 consecutive days with 19.3 mg of C14/C13 thiazopyr (labeled with C13 and C14 in the C-4 position of the pyridine ring; specific activity, 16.1 mCi/mmole). One goat dosed with a placebo served as the control. The dosage administered to the animals was equivalent to 12 and 21 ppm in the diet, based on actual feed consumption. The "higher dosed" goat (21 ppm) is labelled goat #2 in this memo. After four days the animals were sacrificed, aliquots of tissues, feces, milk, and urine were combusted and counted for radioactivity by LSC. Other aliquots were extracted with acetonitrile/water, partitioned, and after sample cleanup were analyzed by HPLC with radiometric detection to identify metabolites. (See Metabolite identification table, p. 8, this memo, for compound structures and numbers). The total percentage

recoveries of administered radioactivity in goat #1 and goat #2 in blood, feces, milk, tissues, and urine were approximately 89 and 90, respectively. Radiolabeled residues plateaued in milk by day 3.

Residues in Tissues, Fluids, and Milk (Percentages of dose, thiazopyr equivalents)				
Matrix	Goat #1		Goat #2	
	% of dose	ppm	% of dose	ppm
liver	0.30	0.193	0.48	0.375
kidney	<0.01	0.023	0.02	0.112
renal fat	<0.01	0.013	0.02	0.034
omental fat	<0.01	0.011	0.02	0.026
muscle	0.06	0.006	0.02	0.013
milk	0.06	0.02	0.12	0.013
bile	0.02	0.477	0.20	6.629

The tissues of goat #2 were extracted and the extracts analyzed by HPLC. Total accountabilities ranged from 98 to 100, except for omental fat at 113%.

Thiazopyr and Its Metabolites Found in Tissues and Milk in Goat #2 (% of tissue radioactivity: ppm, thiazopyr equivalents)												
No.	liver		kidney		renal fat		omental fat		muscle		milk	
thiazopyr	1.9	0.007	-	ND	18	0.006	23	0.006	8.9	0.001	-	ND
2	-	ND	-	ND	-	-	-	-	9.8	0.001	-	ND
3	5.9	0.022	-	ND	8.5	0.003	12	0.003	-	ND	9.2	0.003
4	4.1	0.015	-	ND	-	-	-	-	-	ND	9.2	0.003
5	19	0.071	-	ND	7.8	0.003	11	0.003	-	ND	-	ND
6	-	ND	-	ND	6.2	0.002	13	0.003	-	ND	-	ND

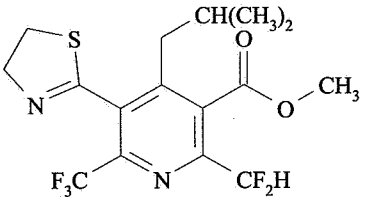
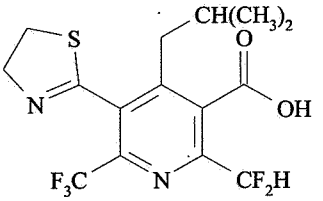
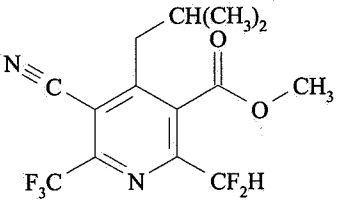
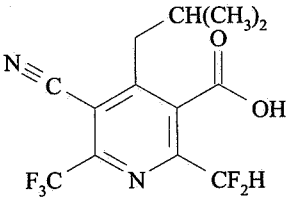
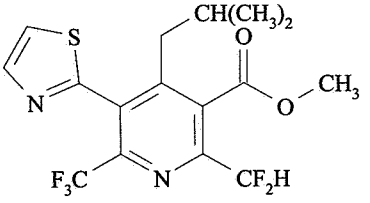
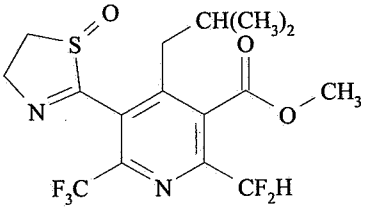
8	-	ND	-	ND	9.2	0.003	21	0.005	-	ND	-	ND
14	3.7	0.014	-	ND	-	-	-	-	-	ND		ND
24	12	0.045	21	0.024	-	-	-	-	7.8	0.001	-	ND
25	6.0	0.023	-	ND	-	-	-	-	-	ND	-	ND
26	-	ND	31	0.035	-	-	-	-	24	0.003	44	0.015
29	-	ND	-	ND	-	-	-	-	10	0.001	-	ND
unext.	14	0.053	6.8	0.008	3.5	0.001	4.1	0.001	19	0.002	8.6	0.003
undefined	33	0.125	41	0.046	47	0.016	20	0.005	40	0.005	29	0.004

ND: not detected (Limit of detection: <0.0019 ppm)

Unext.: unextracted radioactivity

Undefined: Residues undefined/residues lost in extraction interfaces

Compound Numbers, Names, and Structures of Isolated Metabolites.

Compound Number	Simplified Name [a]	Structure
1	thiazopyr; MON-13200	
2	monoacid	
3	nitrile ester	
4	nitrile acid	
5	thiazole ester	
6	sulfoxide ester	

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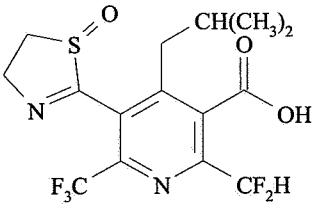
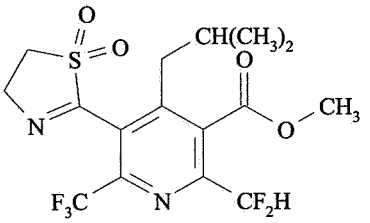
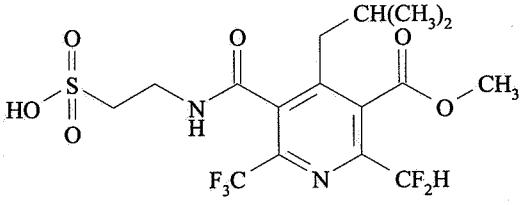
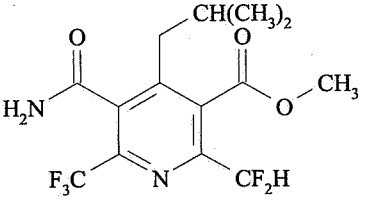
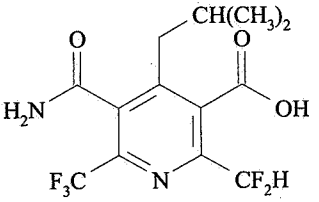
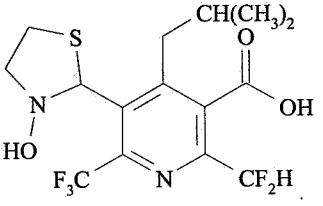
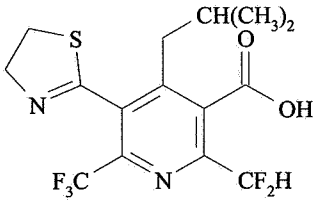
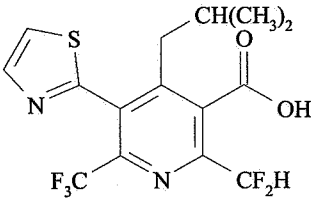
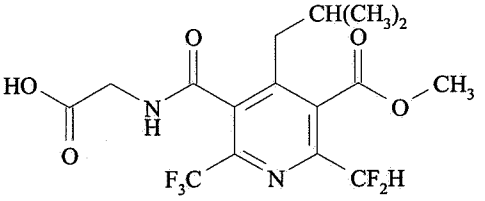
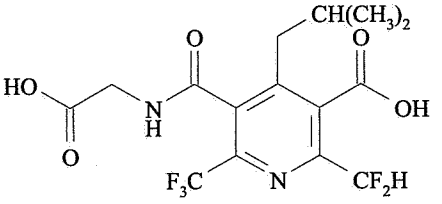
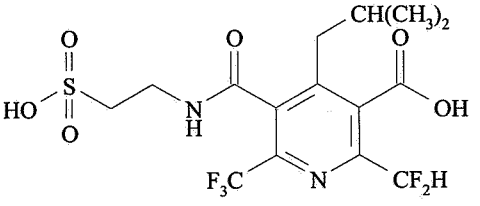
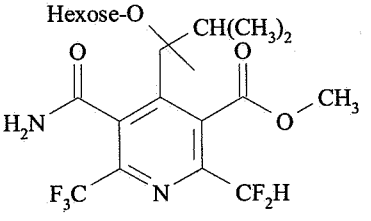
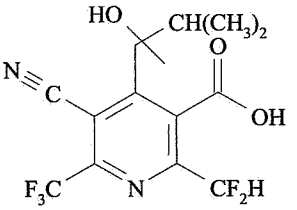
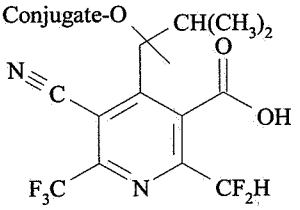
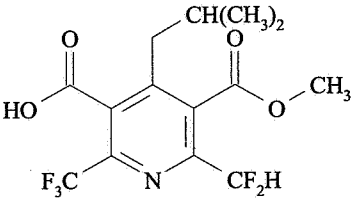
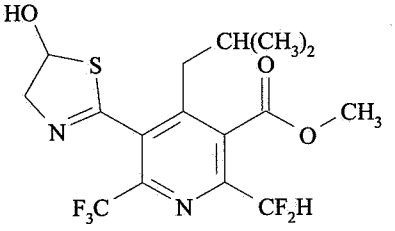
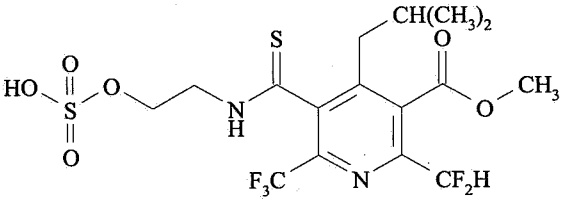
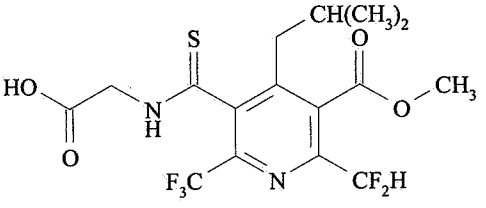
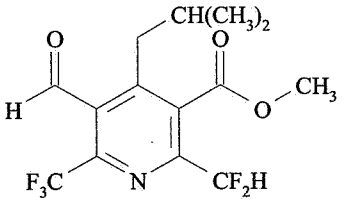
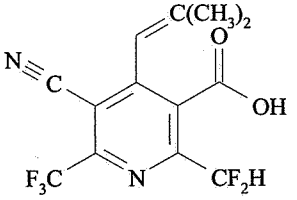
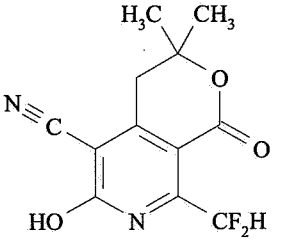
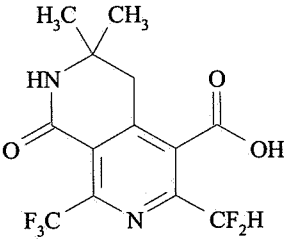
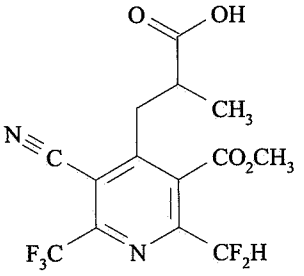
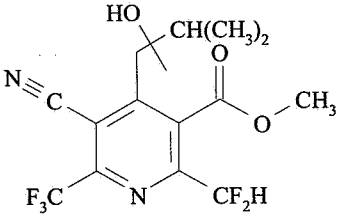
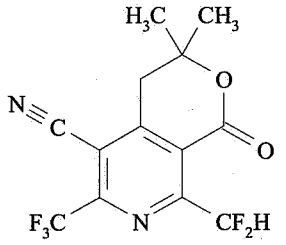
Compound Number	Simplified Name [a]	Structure
7	sulfoxide acid	
8	sulfone ester	
9	sulfonic acid ester	
10	amide ester	
11	amide acid (**AA**)	
12	NA [b]	

Compound Number	Simplified Name [a]	Structure
13	NA	
14	thiazole acid	
15	glycine amide ester	
16	glycine amide acid	
17	sulfonic diacid (**SAA**)	
18	amide ester, hexose conjugate	

Compound Number	Simplified Name [a]	Structure
19	hydroxy nitrile acid	
20	nitrile acid conjugate	
21	NA	
22	NA	
23	sulfate ester	
24	glycine thioamide ester	

Compound Number	Simplified Name [a]	Structure
25	aldehyde ester	
26	unsaturated nitrile acid	
27	NA	
28	NA	
29	nitrile acid ester	
30	hydroxy nitrile ester	

16

Compound Number	Simplified Name [a]	Structure
31	nitrile lactone	

[a] Assigned by company for discussion of metabolism studies.

[b] NA: Not assigned a simplified name by company.

Thiazopyr in a lactating ruminant and plants undergoes metabolic degradation to a large number of polar metabolites, all found at low levels. Milk contained 3 identifiable metabolites, liver had 7 metabolites including the parent, kidney had 2, and renal and omental fat had 5, and muscle had 5. In all, parent plus 11 individual metabolites were identified in goat tissues and milk. Of these, 6 were identical to plant metabolites and 2 others were very similar. The major residues in ruminant muscle and milk are thiazopyr and its unsaturated nitrile acid (compound #26). The major residues in fat are thiazopyr and its sulfone ester metabolite (compound #8). (See the comparison table of metabolic pathways (thiazopyr in plants, animals, and soil), p. 16, this memo.

Poultry:

Laying hens were dosed orally for 4 days with either 1.3 mg (Group #'s 6 and 7) or 10.4 mg (Group #4) of labeled thiazopyr (C14/C13 in the C-4 position of the pyridine ring). The administered dosages based on actual feed consumption, were equivalent to 12 and 78 ppm in the diet in the low and high dose diet, respectively. After four days the animals were sacrificed, aliquots of tissues, excreta, and eggs were combusted and counted for radioactivity by LSC. Other aliquots were extracted with acetonitrile/water, partitioned, and analyzed after sample cleanup by HPLC with radiometric detection to identify metabolites. (See Metabolite identification table, p. 8, this memo, for compound structures and numbers).

Residues in Poultry Tissues and Excreta (Percentages of dose, thiazopyr equivalents)						
Matrix	Group #6, low dose (12 ppm)		Group #7, low dose (12 ppm)		Group #4. high dose (78 ppm)	
	% of dose	ppm	% of dose	ppm	% of dose	ppm
liver	0.17	0.222	0.24	0.298	0.12	1.112
kidney	<0.01	0.047	0.01	0.052	0.01	0.501
abdominal fat	0.03	0.123	0.06	0.173	0.09	1.417
skin with fat	0.03	0.049	0.08	0.097	0.05	0.488
muscle, thigh	0.01	0.010	0.01	0.008	0.02	0.086
muscle, breast	0.01	0.004	0.01	0.005	0.01	0.033
egg yolk	0.03	0.124	0.04	0.132	0.03	1.06
egg white	0.02	0.027	0.02	0.026	0.02	0.163
blood	<0.01	0.016	<0.01	0.021	<0.01	0.097
GI tract	0.19	0.134	0.21	0.153	0.19	0.933
excreta	94.31	-	90.08	-	92.73	-
Totals	95	-	91	-	93	-

Residues in eggs in the low dose groups plateaued by day 4. In the high dose birds the residues had not plateaued by day 4. Since normal egg formation requires 7 days, the low dose may not really be a plateau, but a variation of residues from day to day.

Tissues of group 3 hens were extracted and the extracts subjected to HPLC. Total accountabilities ranged from 92 to 114% (ave: 104%).

Thiazopyr and Its Metabolites Found in Tissues and Eggs in Poultry Dosed Orally at 12 ppm/day (Groups #'s 6 and 7) (% of tissue radioactivity: ppm, thiazopyr equivalents)												
No.	liver		kidney		skin with fat		abdominal fat		muscle		egg yolk	
thiazopyr	0.5	0.002	-	ND	2.7	0.003	2.7	0.005	1.5	0.0001	2.0	0.002
3	1.4	0.004	2.3	0.001	59	0.057	69	0.119	16	0.0011	24	0.018
5	6.7	0.020	-	ND	7.6	0.007	7.9	0.014	1.9	0.0001	2.8	0.002
29	41	0.122	57	0.029	4.2	0.004	-	-	9.9	0.0007	11	0.008
31	-	-	-	-	3.4	0.003	7.0	0.012	3.2	0.0002	-	-
10	2.5	0.008	4.2	0.002	-	-	-	-	1.4	0.0001	-	-
26	-	-	-	-	-	-	-	-	-	-	7.7	0.006
unext.	23	0.068	30	0.015	7.2	0.007	8.6	0.015	19	0.0013	31	0.023
undefined	25	0.075	9	0.005	16	0.016	5	0.009	47	0.003	22	0.016

ND: not detected (Limit of detection: <0.0019 ppm)
Unext.: unextracted radioactivity
Undefined: Residues undefined/residues lost in extraction interfaces

Comparison chart of metabolic pathways for plants and animals.

Compd. No.	aerobic soil	anaerobic soil	cotton/peanut	citrus	rotational crops	rat	lactating goat	laying hen	bluegill sunfish
1:Thiazopyr	✓	✓	✓	✓	✓	✓	✓	✓	✓
2	✓	✓					✓		
3	✓	✓	✓	✓	✓	✓	✓	✓	✓
4	✓			✓	✓		✓		✓
5	✓	✓	✓	✓	✓	✓	✓	✓	✓
6	✓	✓	✓	✓	✓		✓		
7	✓	✓	✓	✓	✓				
8	✓		✓	✓	✓		✓		✓
9	✓	✓	✓ (peanut only)		✓				
10	✓	✓	✓	✓	✓			✓	✓
11	✓	✓	✓	✓	✓				
12		✓							
13		✓							
14			✓(peanut only)			✓	✓		
15			✓(peanut only)	✓					
16			✓(peanut only)	✓	✓				
17			✓(peanut only)						
18			✓						
19				✓					
20				✓					
21					✓				

Comparison chart of metabolic pathways for plants and animals.

22						✓			
23						✓		✓	
24						✓	✓		✓
25						✓	✓		
26						✓	✓	✓	
27						✓			
28						✓			
29							✓	✓	
30								✓	
31								✓	

Thiazopyr in laying hens and plants undergoes metabolic degradation to a large number of polar metabolites, all found at low levels. Liver had 5 metabolites including the parent (4 of which were found as plant metabolites), while kidney had 3 (2 of which are plant metabolites). Egg yolk had 5 (3 of which are plant metabolites) and muscle had 6 (4 of which are plant metabolites). In all, 8 individual metabolites were identified in hen tissue, eggs, and excreta. Of these, 4 were identical to plant metabolites. The major terminal residues in poultry are thiazopyr and its nitrile acid ester metabolite (compound #29).

CBTS considers the metabolism of thiazopyr in plants and animal as adequately understood. The petitioner has proposed that tolerances be established for thiazopyr and those metabolites that can be converted to two common entities, referred to as the sulfonic diacid (SAA) and the amide acid (AA).

Residue Analytical Methods, Crop Field Trials and Livestock Residues:

CBTS previously noted that the residue analytical method proposed with the petition (Method RES-017-91) appeared to be suitable for generating the residue data reported as the result of field trials with thiazopyr. However, CBTS considered the method to be too complex and lengthy for use as an enforcement method, and the Agency Laboratory (ACL) at Beltsville concurred.

In Method RES-017-91, thiazopyr and its major metabolites (nitrile ester, #3; sulfoxide ester, #6 ; sulfoxide acid, #7; amide ester, AE (#10); and amide acid, AA (#11) are transformed into sulfonic diacid (SAA) and amide acid (AA) chemophores. The AA chemophore is derivatized to its methyl ester (AE) and then quantitated. Metabolites #15, #16, #5, and #14 are not converted to either the SAA or AA chemophores using method RES-017-91, but these metabolites can be determined using a slight modification of the GC/MS analysis for the AA chemophore. The GC/MS analysis of the AA chemophore involves the conversion of the AA (amide acid) to AE (amide ester). Likewise #16 (GAA: glycine amide acid) is converted to #15 (GAE: glycine amide ester), and #14 (TA: triazole acid) to #5 (TE: triazole ester). AE, GAE, and TE are quantitated using multiple ion detection. Based upon the metabolism studies, the #15/#16 pair can represent a combined residue total of 12%, while the #5/#14 pair is <2%.

The petitioner notes that the AA chemophore metabolites account for the largest portion of the metabolite profile in terms of the **number** of metabolites. However, based on endogenous validations and metabolism studies, the concentration of the AA chemophore is approximately equal to or greater than the SAA chemophore in cotton and citrus. In cotton and citrus RAC studies (crop field trials), no residues of either chemophore were found to be greater than the lower limit of method validation (LLOMV) which is set at 0.025 ppm. Therefore, a rapid screening procedure for the AA chemophore would eliminate the need to routinely monitor for the SAA chemophore. If residue levels of the AA chemophore were above the LLOMV, then additional analyses for the SAA chemophore would be conducted using the more complex residue data collection method RES-017-91. The proposed enforcement method RES-041-92 submitted in this petition addresses this point. The validated limit of detection is 0.025 ppm for cottonseed and citrus commodities.

The recoveries of AA from samples of cottonseed and grapefruit using Method RES-041-92 are adequate. However, both ACL and CBTS agreed that the method as proposed would not be sufficient since it does not determine the parent compound thiazopyr. Samples must be fortified with compound #3 for the validation test. The major problem with this proposed methodology is that the parent cannot be analyzed using this procedure. Only those thiazopyr metabolites convertible to the AA chemophore are measured;

thiazopyr is converted to the SAA chemophore. According to the petitioner, Monsanto will submit another enforcement method in which all residues are converted to one common chemophore, a triacid with the fluorinated pyridine ring still intact. This methodology is presently undergoing an independent validation. According to a conversation with the company, esterification of this triacid and analysis by GC/MS show conversion of more than 70% of the thiazopyr residues.

Since tolerances for livestock meat, meat by-products, and fat, and milk and eggs are not required for thiazopyr residues based upon the proposed use and analytical methodology for such residues in these rac's will not be needed at this time. The need for additional analytical methodology is dependent on the decision of the residues to be regulated. However, if future uses show combined thiazopyr residues (>0.025 ppm) in these rac's, then analytical methodology will be needed in addition to tolerances for these rac's.

cc: J. Stokes (CBTS); thiazopyr S.F.; R.F.; Circu
RDI:Perrico:12/20/94:RLoranger:01/03/95
7509C:CBTS:CM#2:Rm803:JStokes:js:305-7561:03/07/95