

10/6/94

MEMORANDUM:

SUBJECT: PP#3F4187. Thiazopyr (MON13200) in/on Citrus Processed Commodities. Amendment of May 16, 1994. MRID#'s 426197-05, 432349-00, and 432349-01. CBTS #13770. DP Barcode #D203667.

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

THRU: Richard A. Loranger, Ph.D., Acting Chief  
Chemistry Branch/Tolerance Support  
Health Effects Division (7509C)

TO: Joanne Miller/Eugene Wilson, PM 23  
Fungicide/Herbicide Branch  
Registration Division (7505C)

and

Albin Kocialski  
Chemical Coordination Branch  
Health Effects Division

Monsanto Company has submitted a cover letter dated May 16, 1994, a revised Section F, and additional citrus processing data to support PP#3F4187. Previously the registrant requested the establishment of permanent tolerances for residues of the selective herbicide thiazopyr (ISO common name) [3-pyridine carboxylic acid, 2-(difluoromethyl)-5-(4,5-dihydro-2-thiazolyl)-4-(2-methylpropyl)-6-(trifluoromethyl)-, methyl ester] and its

metabolites determined as 3-pyridine carboxylic acid, 5-(aminocarbonyl)-2-(difluoromethyl)-4-(2-methylpropyl)-6-trifluoromethyl-, methyl ester and 3-pyridine carboxylic acid, 2-(difluoromethyl)-4-(2-methylpropyl)-5-(((2-sulfoethyl)amino)carbonyl)-6-trifluoromethyl and expressed as parent equivalents as follows:

| <u>Commodity</u>    | <u>Parts Per Million (ppm)</u> |
|---------------------|--------------------------------|
| Citrus, whole fruit | 0.05 ppm (group tolerance)     |
| Cottonseed          | 0.05 ppm                       |
| Cotton, forage      | 0.2 ppm                        |

The revised Section F now requests the following:

| <u>Commodity</u>        | <u>Parts Per Million (ppm)</u> |
|-------------------------|--------------------------------|
| Oranges, whole fruit    | 0.05 ppm                       |
| Grapefruit, whole fruit | 0.05 ppm                       |
| Cottonseed              | 0.05 ppm                       |
| Cotton, forage          | 0.2 ppm                        |

These changes have been requested by Monsanto because of an apparent concentration of thiazopyr residues in lemon oil, thus requiring the possible establishment of a 409 tolerance. TOX has classified thiazopyr as a Group C carcinogen (See memo of 05/25/94, P. Hurley, TOX), and, if a 409 tolerance is required, this classification causes a discontinuation of data review according to the current Agency policy of prioritization of actions subject to the Delaney Clause.

This memo is a review of citrus processing data for orange, grapefruit, and lemon for possible thiazopyr residues, and a discussion of concentration in citrus oil, and the possible need of a food additive tolerance.

#### Conclusions:

1. CBTS considers the metabolism of thiazopyr in citrus as adequately understood for these tolerance requests. 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). The residues to be regulated will be determined by the HED Metabolism Committee.

2. The residue analytical methodology RES-017-91 does not determine the parent per se, but only those thiazopyr metabolites convertible to the AA and SAA chemophores. This is acceptable methodology for the submitted field residue data, but this is not an acceptable proposed method for enforcement purposes.
- 3a. The data indicate that residues of thiazopyr and its metabolites convertible to SAA and AA are not likely to concentrate in the pulp (finisher), peel (wet and dry), and juice that had been processed from citrus fruits treated with a single broadcast application of the thiazopyr EC formulation at 5x the proposed maximum seasonal rate.
- 3b. The field residue data submitted for orange, grapefruit, and lemon oil show slight concentrations of thiazopyr residues in orange and grapefruit, and a larger concentration in lemon oil. Based on an average concentration of thiazopyr residues in orange and grapefruit of 10X, and based on the proposed 0.05 ppm tolerance on the RAC, a food additive tolerance of 0.5 ppm should be proposed.
- 3c. Residue data are still needed for citrus molasses. Also the need for additional residue data is dependent on the decisions of the HED Metabolism Committee.
4. Thiazopyr has now been classified as a Group C carcinogen (See memo of 05/25/94, P. Hurley, TOX). This classification causes a discontinuation of data review according to the current Agency policy of prioritization of actions subject to the Delaney Clause as a result of the need for a 409 tolerance for citrus oil.

Recommendations:

CBTS recommends against the establishment of permanent tolerances for residues of the selective herbicide thiazopyr [3-pyridine carboxylic acid, 2-(difluoromethyl)-5-(4,5-dihydro-2-thiazolyl)-

4-(2-methylpropyl)-6-(trifluoromethyl)-, methyl ester] and its metabolites determined as 3-pyridine carboxylic acid, 5-(aminocarbonyl)-2-(difluoromethyl)-4-(2-methylpropyl)-6-trifluoromethyl-, methyl ester and 3-pyridine carboxylic acid, 2-(difluoromethyl)-4-(2-methylpropyl)-5-(((2-sulfoethyl)amino)carbonyl)-6-trifluoromethyl and expressed as parent equivalents in/on oranges and grapefruit (whole fruit) at 0.05 ppm because of **conclusions 3b, 3c, and 4**. We also continue to recommend against tolerances in cottonseed for reasons stated in our 09/12/94 review of this petition. With respect to the Delaney clause impact on this petition, the petitioner has the option of deleting citrus commodities and pursuing a tolerance on cottonseed only.

#### Detailed Considerations:

##### Proposed Use:

The 2 lb a.i./gal EC formulation (22.3 % a.i.) is proposed for preemergence surface applications to citrus crops as a single treatment at 1.0-1.5 lb a.i./A, for two sequential applications at 0.125-0.375 lb a.i./A/application with a 2- to 3-month retreatment interval, or for up to three sequential applications at 0.125-0.25 lb a.i./A/application with a 2- to 3-month retreatment interval. A maximum of 2 lb a.i./A may be applied per year. Ground applications are to be made in volumes from 20 to 50 gal/A with a minimum of 20 gal/A. Application may be made alone or as a tank mix with other herbicides. A 90-day PHI is proposed.

In these field trials, the crops harvested for the processing study were from experiments conducted at a rate of 10 lb a.i./A (5X the proposed rate), and PHI's ranging from 89 to 92 days.

##### Nature of the Residue in Citrus: (MRID #422755-05)

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, specific activity: 28 mCi/mmol) at rates of 2 lb a.i./A (13 trees treated) and 4 lb a.i./A (26 trees treated). 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 mature whole lemon fruit was divided into three parts; rind, pulp, and juice. The solid matrices were macerated, combusted and radioactivity determined by liquid scintillation counting; the lemon juice was counted directly. The following results were for both a 2 lb a.i./A and a 4 lb a.i./A treatments:

Table 1. Radioactivity Distribution in Lemon Trees.

| Plant Portion | Uptake% of Applied Radioactivity | % TRR | ppm, (Thiazopyr equivalents) |
|---------------|----------------------------------|-------|------------------------------|
| 2 lb a.i./A   |                                  |       |                              |
| rind          | 0.14                             | 67    | 0.05                         |
| pulp          | 0.03                             | 13    | 0.01                         |
| juice         | 0.04                             | 21    | 0.01                         |
| fruit         | 0.21                             | 100   | 0.02                         |
| 4 lb a.i./A   |                                  |       |                              |
| rind          | 0.13                             | 68    | 0.10                         |
| pulp          | 0.02                             | 13    | 0.02                         |
| juice         | 0.04                             | 19    | 0.02                         |
| fruit         | 0.19                             | 100   | 0.04                         |

The low C14 thiazopyr activity in this metabolism study suggests that thiazopyr metabolites containing the intact pyridine ring undergo negligible translocation from the soil to fruit. This study also shows that 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). Mon 13200 is relatively nonpolar and is water-insoluble. Most of the metabolites in the lemon tissues were partitioned into the aqueous layer. Several metabolites were partially distributed in the organic and the aqueous layers. The levels of organic-soluble residues (including parent) totaled <4% TRR.

CBTS considers the metabolism of thiazopyr in citrus 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 amide acid (AA) and the sulfonic diacid (SAA). The residues to be regulated will be determined by the HED Metabolism Committee.

#### Residue Analytical Method

Monsanto Company (MRID #42619712) has submitted residue data from five field trials using Method RES-017-91 for analysis of thiazopyr residues. Thiazopyr and its major metabolites are converted into amide acid (AA) and sulfonic diacid (SAA) chemophores.

Table 2. Method Recoveries of AA and SAA from Fortified Samples of Whole Citrus Fruit and Its Processed Commodities.

| Commodity                    | Fortified Level (ppm) | Percent Recovery |             |
|------------------------------|-----------------------|------------------|-------------|
|                              |                       | AA               | SAA         |
| Orange, whole fruit          | 0.025                 | 60, 71, 94       | 83, 88, 92  |
|                              | 0.100                 | 71, 78, 85       | 83, 89, 90  |
| Grapefruit, whole fruit      | 0.025                 | 78               | 87          |
|                              | 0.100                 | 73               | 79          |
| Lemon, whole fruit           | 0.025                 | 81, 90           | 75          |
|                              | 0.100                 | 73, 80           | 87          |
| Orange juice                 | 0.025                 | 64, 89           | 64, 88, 121 |
|                              | 0.100                 | 66, 78, 80       | 72, 89, 98  |
| Citrus oil (from oranges)    | 0.025                 | 88               | 93          |
|                              | 0.050                 | --               | 85          |
|                              | 0.100                 | 70               | --          |
|                              | 0.200                 | 70               | --          |
|                              | 0.400                 | --               | 74          |
| Grapefruit juice             | 0.025                 | 62               | 102         |
|                              | 0.100                 | 74               | 95          |
| Citrus oil (from grapefruit) | 0.100                 | 85               | --          |
|                              | 0.200                 | --               | 85          |

| Commodity      | Fortified Level (ppm) | Percent Recovery |     |
|----------------|-----------------------|------------------|-----|
|                |                       | AA               | SAA |
| Lemon juice    | 0.025                 | 57, 61           | --  |
|                | 0.100                 | 64, 69           | 85  |
| Lemon wet peel | 0.025                 | 90               | 138 |
|                | 0.100                 | 82               | 92  |
| Lemon dry peel | 0.025                 | 80               | 146 |
|                | 0.100                 | 69               | 70  |
| Lemon oil      | 0.025                 | 71               | --  |
|                | 0.500                 | --               | 78  |
|                | 2.000                 | --               | 93  |

The lower limit of the method validation in whole citrus fruit and the processed commodities is reported at 0.025 ppm for both the AA and SAA chemophores. However, in the analyses of the field trial samples listed in Table 3 the limits of detection and quantitation for AA metabolites were reported as 0.003 ppm and 0.037 ppm, and for SAA metabolites were 0.013 ppm and 0.017 ppm, respectively. The following rationale is given by the petitioner to explain the determination of the limits of detection and the limits of quantitation:

"The limit of detection (LOD) for both the sulfonic acid acid (SAA) and amide ester (AE) chemophores was operationally defined as the maximum recovery-corrected amount "found" in check samples. This value reflects an approximate upper bound on false positive concentrations. Concentrations exceeding this maximum value are considered "detected". A total of 41 check samples were analyzed for SAA and 40 check samples were analyzed for AE. The maximum values and, hence, the LODs for SAA and AE were 0.013 ppm and 0.003 ppm, respectively.

The limit of quantitation (LOQ) for both the SAA and AE chemophores was defined to be the lowest fortification level for which the standard deviation, relative to the fortification level, was 15% or less. This definition implies that:

$$(1) \quad 0.15 = (\text{Standard Deviation})/\text{LOQ}$$

or

(2) 
$$LOQ = (\text{Standard Deviation})/0.15$$

The recovery samples for the lowest fortification level (0.025 ppm), which were background corrected for the amount found in the check, were used to determine the standard deviation to use in (2) above. Although the standard deviation does decrease with fortification level, the recovery corrected value obtained from the 0.025 ppm samples should be a close approximation to the standard deviation at the LOQ. The average SAA recovery was 83.1% and the average AE recovery was 79.0%. These recovery values are reported in Table 2 of this report. A total of 14 samples were fortified at 0.025 ppm for SAA and 16 samples were fortified at 0.025 ppm for AE. The standard deviation in the equations below has been corrected for the appropriate percent recovery. The LOQ for SAA was calculated from (2) as:

(3) 
$$LOQ = \text{Standard Deviation}/0.15 = 0.0024876/0.15 = 0.017 \text{ ppm}$$

Similarly, the LOQ for AE is:

(4) 
$$LOQ = 0.0056074/0.15 = 0.037 \text{ ppm}$$

Each LOQ should be interpreted as the approximate fortification level at which the relative standard deviation becomes 15%, the desired limit of acceptable precision.<sup>1</sup>

#### Magnitude of the Residues:

Residues of thiazopyr and its metabolites convertible to AA and SAA in/on orange, grapefruit, and lemon following a single soil broadcast application at 2 lb a.i./A or two sequential soil broadcast applications each at 1 lb a.i./A/application of the 2 lb a.i./gal EC formulation (MRID #42641401) are presented in Table 3. (Residues were not corrected for method recoveries.)

---

<sup>1</sup> [Administrative Materials for the Registration of Thiazopyr Technical Active Ingredient and the End Use Product, MON-13211, for Use on Citrus and Cotton and Petitions for Tolerances for Residues of Thiazopyr and Metabolites on Citrus and Cotton Commodities, p 299, dated December, 29, 1992, (No MRID#)]. Note: AE is the ester of the amide acid AA.



Table 3. Thiazopyr Residues in Citrus.

| Total Rate<br>(lb<br>a.i./A) | Number<br>of<br>Appl. | PHI,<br>in<br>days | Test<br>Sites<br>(no. of<br>samples) | Residues in ppm   |                  |                      |
|------------------------------|-----------------------|--------------------|--------------------------------------|-------------------|------------------|----------------------|
|                              |                       |                    |                                      | AA <sup>a</sup>   | SAA <sup>a</sup> | Combined<br>Residues |
| Orange                       |                       |                    |                                      |                   |                  |                      |
| 2                            | 1                     | 90-98              | FL (12)                              | <0.003-<br>0.0042 | <0.013           | <0.016-<br><0.0172   |
| 2                            | 2                     | 90-98              | FL (12)                              | <0.003-<br>0.0052 | <0.013           | <0.016-<br><0.0182   |
| 2                            | 1                     | 32-92              | CA (8)                               | <0.003-<br>0.0039 | <0.013           | <0.016-<br><0.0169   |
| 2                            | 2                     | 32-92              | CA (8)                               | <0.003            | <0.013           | <0.016               |
| 2                            | 1                     | 65                 | AZ (2)                               | <0.003            | <0.013           | <0.016               |
| 2                            | 2                     | 65                 | AZ (2)                               | <0.003            | <0.013           | <0.016               |
| Control                      | --                    | --                 | FL, CA,<br>AZ (22)                   | <0.003            | <0.013           | <0.016               |
| Grapefruit                   |                       |                    |                                      |                   |                  |                      |
| 2                            | 1                     | 90-98              | FL (6)                               | <0.003-<br>0.0051 | <0.013           | <0.016-<br>0.0181    |
| 2                            | 2                     | 90-98              | FL (6)                               | <0.003-<br>0.006  | <0.013           | <0.016-<br>0.019     |
| 2                            | 1                     | 89, 91             | CA (4)                               | <0.003            | <0.013           | <0.016               |
| 2                            | 2                     | 89, 91             | CA (4)                               | <0.003            | <0.013           | <0.016               |
| 2                            | 1                     | 91                 | AZ (2)                               | <0.003            | <0.013           | <0.016               |
| 2                            | 2                     | 91                 | AZ (2)                               | <0.003            | <0.013           | <0.016               |
| Control                      | --                    | --                 | FL, CA,<br>AZ (12)                   | <0.003            | <0.013           | <0.016               |
| Lemons                       |                       |                    |                                      |                   |                  |                      |
| 2                            | 1                     | 55, 85             | CA (4)                               | <0.003-<br>0.0042 | <0.013           | <0.016-<br>0.0172    |
| 2                            | 2                     | 55, 85             | CA (4)                               | <0.003-<br>0.0108 | <0.013           | <0.016-<br>0.0238    |
| 2                            | 1                     | 91                 | AZ (2)                               | <0.003,<br>0.0043 | <0.013           | <0.013,<br><0.0173   |
| 2                            | 2                     | 91                 | AZ (2)                               | <0.003            | <0.013           | <0.016               |
| Control                      | --                    | --                 | CA, AZ<br>(6)                        | <0.003            | <0.013           | <0.016               |

<sup>a</sup> The limits of detection for AA and SAA are 0.003 ppm and 0.013 ppm, respectively.

The available data indicate that residues of thiazopyr and its metabolites convertible to AA and SAA are not likely to exceed the proposed tolerance of 0.05 ppm in/on citrus fruits harvested 32-98 days following a single soil broadcast application of the 2 lb a.i./gal EC formulation at 2 lb a.i./A or two sequential soil broadcast applications at 1 lb a.i./A/application for a maximum seasonal rate of 2 lb a.i./A. Apparent residues of AA and SAA metabolites in/on 40 untreated samples of citrus fruits were nondetectable (<0.003 ppm and <0.013 ppm, respectively).

#### Citrus Fruit Processed Commodities

These comments were presented previously in a CBTS review (See memo of 09/12/94, J. Stokes).

"Monsanto Company submitted data (MRID #42619705) depicting the potential for concentration of residues of thiazopyr and its metabolites convertible to AA and SAA in citrus processed commodities. In five tests conducted in CA(1) and FL(4), citrus fruits (orange, grapefruit, and lemon) were harvested 89-92 days following a single soil broadcast application of the 2 lb a.i./gal EC formulation at 10 lb a.i./A/application (5x the proposed maximum seasonal rate) using ground equipment."

"Treated and control samples from the FL and CA sites were harvested and delivered to the University of Florida, Citrus Research Center and Education Center (Lake Alfred, FL) or to California State Polytechnic University (Pomona, CA), respectively, for processing. Samples were cooled (4-7 C) prior to processing. Citrus fruits were processed and untreated fruits, washed fruits, finisher pulp, wet peel, dry peel, juice, molasses, and cold-pressed oil were collected using a simulated commercial procedure. The processed fractions were shipped frozen (temperature unspecified) by freezer trucks to the analytical laboratory (Monsanto Company, St. Louis, MO). Samples were stored frozen at -24 to -23 C for up to 428 days for oranges, 369 days for grapefruit, 504 days for lemons, 511 days for orange juice, 414 days for grapefruit juice, 651 days for lemon juice, and 531 days for wet and dry lemon peel prior to analysis. Untreated control and treated samples were analyzed for residues of AE and SAA using Method RES-017-91, which has a

lower limit of method validation of 0.025 ppm for both AE and SAA."

"Residues of AA metabolites were nondetectable (<0.025 ppm) in/on 6 samples of whole oranges, 2 samples of whole grapefruit, 4 samples of whole lemons, 6 samples of orange juice, 2 samples of grapefruit juice, 3 samples of lemon juice, 2 samples of lemon wet peel, and 2 samples of lemon dry peel; residues of AA metabolites were 0.064 ppm in one sample of lemon juice.

Residues of SAA metabolites were nondetectable (<0.025 ppm) in/on 6 samples of whole oranges, 2 samples of whole grapefruit, 2 samples of whole lemons, 6 samples of orange juice, 2 samples of grapefruit juice, 2 samples of lemon juice, 2 samples of lemon wet peel, and 2 samples of lemon dry peel. Apparent residues of AA and SAA metabolites were nondetectable (<0.025 ppm each) in/on 6 samples of whole oranges, 2 samples of whole grapefruit, 4 samples of whole lemons (2 samples for SAA analysis), 6 samples of orange juice, 2 samples of grapefruit juice, 4 samples of lemon juice (2 samples for SAA analysis), 2 samples of lemon wet peel, and 2 samples of lemon dry peel. Analyses of the molasses was not performed because residues less than the level of quantitation (<0.025 ppm) of AA and SAA were found in whole citrus and peel. **Note:** Residue data for processed citrus oil has recently been submitted and are currently in review (Barcode DP D203667). Residue data for citrus molasses is still needed."

"The data indicate that residues of thiazopyr and its metabolites convertible to AA and SAA are not likely to concentrate in the pulp (finisher), peel (wet and dry), and juice that had been processed from citrus fruits treated with a single broadcast application of the thiazopyr EC formulation at 5x the proposed maximum seasonal rate."

In this submission (MRID#432349-01), analyses for citrus oil from field treated samples are as follows:

Table 4. Thiazopyr Residues Measured as the AA Chemophore in Whole Fruit and Citrus Oil  
After Exaggerated Rate of 10 lb a.i./A (5X).

| Location          | Residues in Whole fruit, ppm |        |         |        | Residues in Citrus oil, ppm |       |         |        |
|-------------------|------------------------------|--------|---------|--------|-----------------------------|-------|---------|--------|
|                   | Treated                      |        | Control |        | Treated                     |       | Control |        |
|                   | Uncorr.                      | Corr.  | Uncorr. | Corr.  | Uncorr.                     | Corr. | Uncorr. | Corr.  |
|                   | Uncorr.                      | Corr.  | Uncorr. | Corr.  | Uncorr.                     | Corr. | Uncorr. | Corr.  |
| Orange            |                              |        |         |        |                             |       |         |        |
| Immokalee, FL     | 0.0071                       | <0.025 | 0.0037  | <0.025 | 0.047                       | 0.062 | 0.004   | <0.025 |
| "                 | 0.0092                       | <0.025 | 0.0056  | <0.025 | 0.053                       | 0.069 | 0.004   | <0.025 |
| "                 | 0.0084                       | <0.025 | 0.0098  | <0.025 | 0.086                       | 0.113 | 0.000   | <0.025 |
| "                 | 0.0113                       | <0.025 | 0.0076  | <0.025 | 0.098                       | 0.129 | 0.000   | <0.025 |
| Frost Proof, FL   | 0.0090                       | <0.025 | 0.0100  | <0.025 | 0.025                       | 0.033 | 0.000   | <0.025 |
| "                 | 0.0100                       | <0.025 | 0.0130  | <0.025 | 0.024                       | 0.031 | 0.000   | <0.025 |
| ave.              | 0.0092                       | <0.025 | 0.0083  | <0.025 | 0.055                       | 0.073 | 0.001   | <0.025 |
| Grapefruit        |                              |        |         |        |                             |       |         |        |
| Haines City, FL   | 0.0066                       | <0.025 | 0.0061  | <0.025 | 0.014                       | 0.016 | 0.001   | <0.025 |
| "                 | 0.0089                       | <0.025 | 0.0093  | <0.025 | 0.025                       | 0.030 | 0.001   | <0.025 |
| ave.              | 0.0078                       | <0.025 | 0.0077  | <0.025 | 0.019                       | 0.023 | 0.001   | <0.025 |
| Lemon             |                              |        |         |        |                             |       |         |        |
| Valley Center, CA | 0.0158                       | <0.025 | 0.0111  | <0.025 | 0.388                       | 0.550 | 0.006   | <0.025 |
| "                 | 0.0193                       | <0.025 | 0.0059  | <0.025 | 0.362                       | 0.513 | 0.006   | <0.025 |
| "                 | 0.0267                       | <0.025 | 0.0155  | <0.025 | --                          | --    | --      | --     |

|      |        |        |        |        |       |       |       |        |
|------|--------|--------|--------|--------|-------|-------|-------|--------|
| "    | 0.0133 | <0.025 | 0.0083 | <0.025 | --    | --    | --    | --     |
| ave. | 0.0188 | <0.025 | 0.0102 | <0.025 | 0.375 | 0.532 | 0.006 | <0.025 |

Table 5. Thiazopyr Residues Measured as the SAA Chemophore in Whole Fruit and Citrus Oil After Exaggerated Rate of 10 lb a.i./A (5X).

| Location          | Residues in Whole fruit, ppm |        |         |        | Residues in Citrus oil, ppm |       |         |        |
|-------------------|------------------------------|--------|---------|--------|-----------------------------|-------|---------|--------|
|                   | Treated                      |        | Control |        | Treated                     |       | Control |        |
|                   | Uncorr.                      | Corr.  | Uncorr. | Corr.  | Uncorr.                     | Corr. | Uncorr. | Corr.  |
| Orange            |                              |        |         |        |                             |       |         |        |
| Immokalee, FL     | 0.000                        | <0.025 | 0.000   | <0.025 | 0.127                       | 0.152 | 0.000   | <0.025 |
| "                 | 0.000                        | <0.025 | 0.000   | <0.025 | 0.144                       | 0.171 | 0.000   | <0.025 |
| "                 | 0.000                        | <0.025 | 0.000   | <0.025 | 0.078                       | 0.094 | 0.007   | <0.025 |
| "                 | 0.000                        | <0.025 | 0.000   | <0.025 | 0.088                       | 0.105 | 0.007   | <0.025 |
| Frost Proof, FL   | 0.000                        | <0.025 | 0.000   | <0.025 | 0.050                       | 0.059 | 0.000   | <0.025 |
| "                 | 0.000                        | <0.025 | 0.000   | <0.025 | 0.061                       | 0.073 | 0.000   | <0.025 |
| ave.              | 0.000                        | <0.025 | 0.000   | <0.025 | 0.091                       | 0.109 | 0.002   | <0.025 |
| Grapefruit        |                              |        |         |        |                             |       |         |        |
| Haines City, FL   | 0.000                        | <0.025 | 0.0011  | <0.025 | 0.004                       | 0.004 | 0.000   | <0.025 |
| "                 | 0.000                        | <0.025 | 0.000   | <0.025 | 0.026                       | 0.030 | 0.000   | <0.025 |
| "                 | --                           | --     | --      | --     | 0.006                       | 0.007 | 0.000   | <0.025 |
| ave.              | 0.000                        | <0.025 | 0.006   | <0.025 | 0.012                       | 0.014 | 0.000   | <0.025 |
| Lemon             |                              |        |         |        |                             |       |         |        |
| Valley Center, CA | 0.000                        | <0.025 | 0.000   | <0.025 | 1.495                       | 1.752 | 0.000   | <0.025 |
| "                 | 0.000                        | <0.025 | 0.000   | <0.025 | 1.518                       | 1.779 | 0.000   | <0.025 |

14

|      |       |        |       |        |       |       |       |        |
|------|-------|--------|-------|--------|-------|-------|-------|--------|
| "    | 0.000 | <0.025 | 0.000 | <0.025 | 1.437 | 1.683 | --    | --     |
| ave. | 0.000 | <0.025 | 0.000 | <0.025 | 1.483 | 1.738 | 0.000 | <0.025 |

The above residue data for orange, grapefruit, and lemon [whole fruit (uncorrected values)] show "detectable" residues (>0.003 ppm) of the AA chemophore, but none for the SAA chemophore. In fact, in many cases the samples from the treated areas show residues similar to the controls. Corrected values for all AA chemophore residues were <0.025 ppm, the lower limit of the method validation. Likewise, corrected values for the SAA chemophore showed residues <0.025 ppm. Since this fruit was collected from field trials run at 5X the proposed rate, the expected residues would be even lower.

On the other hand, citrus oil from orange, grapefruit, and lemon show measurable AA and SAA residues not only above the limits of detection (0.003 ppm, AA; 0.013 ppm SAA), but also above the lower limit of the method validation (0.025 ppm) for each chemophore. Thus "real" thiazopyr residues (including metabolites) were apparently found in the citrus oil. Therefore using the combined average AA and SAA residues, both uncorrected and corrected, concentration factors for thiazopyr residues in citrus are determined in Table 6.

Table 6. Concentration Factors for citrus oils

| Crop   | Whole Fruit | Oil   | Concentration Factor |
|--|-------------|-------|----------------------|
| Uncorrected Thiazopyr Residues<br>(Combined Average AA and SAA Residues), in ppm |             |       |                      |
| orange   | 0.0092      | 0.146 | 16X                  |
| grapefruit   | 0.0078      | 0.031 | 4X                   |
| lemon  | 0.0188      | 1.858 | 100X                 |
| Corrected Thiazopyr Residues<br>(Combined Average AA and SAA Residues), in ppm   |             |       |                      |
| orange   | <0.050      | 0.182 | 4X                   |
| grapefruit   | <0.050      | 0.037 | 0.7X                 |
| lemon  | <0.050      | 2.27  | 45X                  |



The petitioner has stated that apparently the high values for the lemon samples are a result of field contamination or possible spray drift during application. The petitioner has submitted a revised Section F to change from the request for a group tolerance for citrus to orange and grapefruit only because of the conflict in the possible establishment of a 409 tolerance as a result of the concentration of residues in lemon oil, and thiazopyr being classified as a Group C carcinogen.

Therefore, CBTS will only direct its comments in regards to the need for a 409 tolerance to orange and grapefruit. CBTS policy (See memo of 11/17/88, C. Trichilo) dictates that if the highest practical exaggerated rate is less than the theoretical concentration (1000X for citrus oil), then samples from the highest practical exaggerated rate studies should be processed. If processed commodities **do contain** detectable residues, then a food/feed additive tolerance is required. Based on the above concentration factors for orange and grapefruit, it appears that thiazopyr residues concentrate in the citrus oil, slightly more in orange than grapefruit. Although the observed concentration is far less than the theoretical concentration of 1000X, it is observed as evidenced by the residue data in Tables 4, 5, and 6. Since tolerances are established on citrus oil, and not the individual citrus fruit, the concentration used to determine the value of the 409 tolerance for citrus oil would be the average for orange (16X) and grapefruit (4X). This is 10X, and based on the proposed 0.05 ppm tolerance on the RAC, a food additive tolerance of 0.5 ppm should be proposed.

This of course is a problem since thiazopyr has now been classified as a Group C carcinogen (See memo of 05/25/94, P. Hurley, TOX), and this classification causes a discontinuation of data review according to the current Agency policy of prioritization of actions subject to the Delaney Clause.

cc: J. Stokes (CBTS); Chris Gillis (PSPS, 7501C); PP#3F4147;  
R.F.; Circu  
RDI:Perrico:09/29/94:RLoranger:10/05/94  
7509C:CBTS:CM#2:Rm803:JStokes:js:305-7561:10/06/94