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

OCT 21 1996

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

**MEMORANDUM:**

**SUBJECT:** PP#5F04456 - New Chemical - Chlorfenapyr/Pirate®/Alert® on Cotton. Evaluation of Product and Residue Chemistry Data Amendments. MRID Nos. 440840-01 and 440840-02. CBTS No. 17517. DP Barcode: D229319. Chemical No. 129093. Case No. 286152

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## Background

This submission includes a letter dated 8/13/96 in response to the deficiencies iterated in the last review of PP#5F04456 (see 2/6/96 memo of G. Otakie).

The American Cyanamid Company has petitioned for permanent tolerances for residues of the insecticide/miticide chlorfenapyr/Pirate®/Alert® (CL 303,630) [4-bromo-2-(chlorophenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-1H-pyrrole-3-carbonitrile] as follows:

| | |
|---|---|
| Cottonseed | 0.5 ppm |
| Milk | 0.01 ppm |
| Milk Fat | 0.15 ppm |
| Meat | 0.01 ppm |
| Meat By-Products | 0.10 ppm |

Under PP#3G4224 (see 1/26/94 review of G. Otakie) CBTS recommended in favor of a temporary tolerance for Pirate in/on cottonseed of 0.5 ppm, for a period of two years. Under PP#5G04507 (see 8/10/95 review of G. Kramer) CBTS recommended in favor of temporary tolerances for Pirate in/on oranges, orange oil, lemon oil and lemons of 0.50, 2.0, 2.0, and 0.50 ppm, respectively, and in milk fat (reflecting 0.01 ppm in whole milk), fat, meat, and meat by-products (cattle, goats, horses and sheep) of 0.25, 0.20, 0.01, and 0.05 ppm, respectively. Other temporary tolerances for Alert/Pirate have been proposed under PP#5G04523 and PP#5G04548 in/on lettuce and cabbage, respectively. Per PP#3G4224 (see 5/16/95 review of G. Otakie) a satisfactory EPA method trial for Pirate in/on cottonseed has been completed.

**Outstanding Deficiencies**

9b. CBTS concurs that the previous estimate of 10.00 ppm parent residues in cotton gin byproducts represented an unrealistic worst case. We note that in the new cottonseed processing study (see Deficiency 10a and b) parent residues in linters and linter motes were 1.80 and 2.13 ppm, respectively after processing delinted cottonseed with parent residues of <0.05 ppm. In the absence of the required cotton gin byproduct field trial data CBTS will use 2.00 ppm as a realistic worst case estimate of parent residues in cotton gin byproducts. The petitioner has committed to conduct six field trials during the 1997 season to obtain residue data on cotton gin byproducts.

11. A revised label containing the following crop rotation restrictions is required:

Do not plant root crops within 60 days of last application.

For all other crops do not plant within 30 days of last application.

12b. A revised Section F with time limited tolerances for chlorfenapyr in ruminant commodities of 0.01, 0.15, 0.01, 0.10 and 0.05 ppm, respectively for milk, milk fat, meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep is required (note: a tolerance for fat was not proposed). A note in the tolerance expression of the revised Section F is also required indicating that the parent is serving as a marker for metabolite residues in meat byproducts. For this reason the meat byproduct tolerance will be listed separately in the Code of Federal Regulations. The proposed and required permanent tolerances are summarized as follows:

| | Required | Proposed |
|---|---|---|
| Milk | 0.01 | 0.01 |
| Milk Fat | 0.15 | 0.15 |
| Meat of Cattle, Goats, Hogs, Horses, and Sheep | 0.01 | 0.01 |
| Fat of Cattle, Goats, Hogs, Horses and Sheep | 0.10 | none |
| Meat Byproducts of Cattle, Goats, Hogs, Horses and Sheep | 0.05 | 0.10 |

**Recommendations**

At this time CBTS recommends against establishing the proposed permanent tolerances of 0.50, 0.01, 0.15, 0.01, and 0.10 ppm for chlorfenapyr/Pirate/Alert in/on cottonseed, milk, milk fat, meat and meat by-products, respectively for the reasons cited in Deficiency Nos. 9b, 11 and 12b. Residue data requirements for cotton gin byproducts (i.e. Deficiency 9b) would not preclude the establishment of time limited tolerances provided the other deficiencies were resolved.

HED notes that the Food Quality Protection Act of 1996 has amended and strengthened the standard for establishing tolerances under the FFDCA. OPP is still assessing the full impact of this change in the law on the tolerance-setting process and plans to issue guidelines concerning the establishment of tolerances under the amended statute. All tolerance petitions have to meet the requirements of the FFDCA as amended by the FQPA and OPP may require additional data to determine if the terms of the amended statute are met.

Notes for PM

A note in the tolerance expression of the revised Section F and CFR for animal commodities is also required indicating that the parent is serving as a **marker** for metabolite residues in meat byproducts. For this reason the meat byproduct tolerance will be listed separately in the Code of Federal Regulations. Any time limited tolerances would be established to allow the petitioner time to submit residue data for cotton gin bybroducts (i.e. Deficiency 9b) once the other deficiencies are resolved.

Note for DRES

A DRES run may be initiated based on required tolerances for chlorfenapyr of 0.50 ppm in/on cottonseed and 0.01, 0.15, 0.01, 0.10 and 0.05 ppm, respectively for milk, milk fat, meat, **fat** and meat byproducts of cattle, goats, hogs, horses, and sheep. The permanent tolerance expression for chlorfenapyr in plant and animal commodities may be expressed in terms of parent only. However, for risk assessment purposes a ratio of 6X the proposed parent tolerance level in **ruminant** meat byproducts, is to be used to account for metabolite residues per the HED Metabolism Committee. Therefore, 0.3 ppm should be used in the DRES run for meat byproducts of cattle, goats, hogs, horses and sheep.

Tolerances for poultry commodities are **not** required based on the current proposed uses for chlorfenapyr. However, for future risk assessment purposes where a tolerance for **poultry** meat by-products is required a ratio of 10X the proposed parent tolerance is to be used to account for metabolite residues per the HED Metabolism Committee.

## Detailed Considerations

The numbering of Deficiencies follows the latest CBTS review under PP#5F04456 (see 2/6/96 memo of G. Otakie).

### Deficiency No. 1

Most product chemistry data requirements for the TGAI have been satisfied. Preliminary analysis data reflects pilot as well as large scale production. A revised CSF is required with certified limits for all impurities $\geq$0.1 w/w%. Pending submission of a revised CSF, adequate product chemistry data are available for the subject proposed permanent tolerances for Pirate in/on cottonseed and animal commodities. The petitioner should submit verification of an approved ANSI common name if one has been obtained.

### Petitioner's Response to Deficiency No. 1

Although our proposed common name, chlorfenapyr has been provisionally accepted by the ANSI K62 Committee, the British Standards Institute (BSI) has still not processed our request.

### CBTS's Comments/Conclusions re: Deficiency No. 1

This deficiency is resolved per the revised CSF dated 8/12/96 (see Confidential Appendix).

### Deficiency No. 2

CBTS notes that the maximum application rate has been reduced in the subject petition from 2.0 lbs ai/A/season in the temporary tolerance PP#3G4224 to 1.05 lbs ai/A/season. A revised label with a crop rotation statement not to plant to any food or feed crop within 60 days of the last application (except a 30 day plant back for leafy and legume vegetables) is required (see Conclusion 11).

### Petitioner's Response to Deficiency No. 2

The petitioner's response is presented under Deficiency No 11.

### CBTS's Comments/Conclusions re: Deficiency No. 2

This deficiency is no longer applicable since the required revised label for crop rotation is now addressed under deficiency No. 11.

**Deficiencies Nos. 3, 4 and 5**

The nature of the residue in cotton is adequately understood. Pending HED Metabolism Committee review, the residue of concern in cotton consists of the parent Pirate.

The nature of the residue in poultry is adequately understood and consists primarily of the parent in muscle and fat. In addition to the parent numerous Pirate metabolites have been identified. In eggs the parent and its N-dealkylation metabolite CL 303,268 [i.e. Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)-] are present at the highest level. In liver and kidney the parent, CL 303,268, CL 152,835/M-6 [i.e. Acetic acid, {[2-(p-chlorophenyl)-3-cyano-5-(trifluoromethyl)pyrrol-1-yl]methoxy}-) and CL 325,157/M-6A (i.e. Acetic acid, {[3-bromo-5-(p-chlorophenyl)-4-cyano-2-(trifluoromethyl)pyrrol-1-yl] methoxy}-) are present at the highest levels. In light of the low dietary burden for poultry from the proposed use on cotton a decision on which moieties should be regulated **if any** is deferred pending HED Metabolism Committee review.

The nature of the residue in ruminants is adequately understood and consists primarily of the parent in muscle, fat and milk. In addition to the parent numerous Pirate metabolites have been identified. In the liver and kidney the metabolites CL 325,195 [i.e. 2-Pyrrolidine-3-carbonitrile, 2-(p-chlorophenyl)-5-hydroxy-4-oxo-5-(trifluoromethyl)-] and CL 322,250 [ i.e. Pyrrole-2-carboxylic acid, 3-bromo-5-(p-chlorophenyl)-4-cyano-] were present at the highest level as well as the parent, other metabolites and conjugates. A decision on which moieties should be regulated is deferred pending HED Metabolism Committee review. The petitioner has proposed regulating only the parent for animal commodities.

**Petitioner's Response to Deficiencies Nos. 3, 4 and 5**

The petitioner welcomes HED Metabolism Committee's recent ruling that for plants (cottonseed/oranges/lemons/tomatoes/lettuce/cabbage/potatoes) and animals (poultry/ruminants) commodities the tolerance expression will be established in terms of parent only and that no tolerances are required at the present time for poultry commodities. The petitioner concurs with the Committee's decision that the residues of the parent will be used in assessments of dietary risk from plants (RAC and processed commodities) as well as ruminant meat and milk. Although the parent is the only moiety that needs to be regulated in meat byproducts, the relative contribution of two other metabolites will also be included in the dietary risk assessment. Consequently no further data nor residue methods for liver and kidney metabolites will be required.

**CBTS's Comments/Conclusions re: Deficiency Nos. 3, 4 and 5**

Per the HED Metabolism Committee Meeting of 6/20/96 (see PP#5F04456 7/10/96 memo of G. Otakie) the following conclusions were made:

1. For **plant** commodities there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. Use of only parent residues is acceptable for chlorfenapyr dietary risk assessments on plant commodities based on the parent comprising such a high percentage of the residue.

2. For **ruminant** commodities (**excluding meat byproducts**) there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. Use of only parent residues is acceptable for chlorfenapyr dietary risk assessments on ruminant commodities (excluding meat byproducts).

3. For **ruminant meat byproducts** there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. However, chlorfenapyr dietary risk assessments on ruminant meat byproducts should include the two metabolites CL 303,268 and CL 325,195 as well as the parent (CL 303,630). Although the metabolites have different acute toxicities and CL 303,268 has a lower $LD_{50}$ than the parent, the metabolites were detected in the rat metabolism study and are therefore included in the toxicology endpoints. For risk assessment, the three moieties are assumed to have comparable toxicity taking into account their relative residue levels. The ruminant meat byproduct risk assessment will use a factor (i.e. ratio parent plus metabolites/parent) multiplied by the parent based tolerance determined from the residue levels of the three moieties in the ruminant metabolism studies.

4. The metabolism decisions for ruminant commodities are not fully applicable to poultry commodities. It was noted that based on the current proposed uses tolerances on poultry commodities are not required. However, poultry was addressed in the event that future proposed uses for this new chemical require tolerances on poultry commodities.

5. For **poultry** commodities (**excluding meat byproducts**) there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. Use of only parent residues is acceptable for

chlorfenapyr dietary risk assessments on poultry commodities (excluding meat byproducts).

6. For **poultry meat byproducts** there is no scientific objection to establishing the chlorfenapyr permanent tolerance expression in terms of parent only. However, chlorfenapyr dietary risk assessments on poultry meat byproducts should include the four metabolites CL 303,268, CL 325,195, CL 152,835 and CL 325,157 as well as the parent (CL 303,630). Although the metabolites have different acute toxicities and CL 303,268 has a lower $LD_{50}$ than the parent the metabolites were detected in the rat metabolism study and are therefore included in the toxicology endpoints. For risk assessment the five moieties are assumed to have comparable toxicity taking into account their relative residue levels. The poultry meat byproduct risk assessment will use a factor (i.e. ratio parent plus metabolites/parent) multiplied by the parent based tolerance determined from the residue levels of the five moieties in the poultry metabolism studies.

**Ruminants**

In accordance with the HED Metabolism Committee, the ruminant meat byproduct risk assessment for chlorfenapyr will use a factor (i.e. ratio parent plus metabolites/parent) multiplied by the parent based tolerance determined from the residue levels of the three moieties in the ruminant metabolism studies (two metabolites CL 303,268 and 325,195 as well as the parent (303,630)). The estimate is as follows:

The first goat metabolism studies (see PP#3G4224 1/26/94 memo of G. Otakie) indicated the highest residues occurred in pyrrole label study with the following results:

| | residue (ppm) | |
|---|---|---|
| | liver | kidney |
| parent CL 303,630 | 0.04 | 0.06 |
| metabolite CL 303,268 | 0.02 | 0.02 |
| metabolite CL 325,195 | 0.20 | <0.01 |
| total | 0.26 | 0.09 |

liver ratio = 0.26/0.04 = 6.5
kidney ratio = 0.09/0.06 = 1.5

Additional characterization data was also included in the second goat metabolism studies (see PP#5F4456 5/30/96 memo of G. Otakie) which will be used for the calculation.

| | Ruminant Residue (ppm) | |
|---|---|---|
| | liver | kidney |
| parent CL 303,630 | 0.15 | 0.02 |
| metabolite CL 303,268 | 0.09 | 0.03 |
| metabolite CL 325,195 | 0.46 | 0.10 |
| total | 0.70 | 0.15 |

liver ratio = 0.70/0.15 = 4.7
kidney ratio = 0.15/0.13 = 1.2

Since the highest ratios (parent plus metabolites of concern/parent) result in liver rather than kidney the average of the liver ratios from the goat metabolism studies will be used. Accordingly, the ratio for residue value to be used for risk assessment for chlorfenapyr in ruminant byproducts is 6 times the ruminant byproduct tolerance established for the parent (6.5 + 4.7/2 = 6).

**Poultry**

CBTS notes that based on the **current** proposed uses tolerances for chlorfenapyr in/on poultry commodities are not required. However, in accordance with the HED Metabolism Committee, any **future** poultry meat byproduct risk assessment for chlorfenapyr will use a factor (i.e. ratio parent plus metabolites/parent) multiplied by the parent based tolerance determined from the residue levels of the five moieties in the poultry metabolism studies (four metabolites CL 303,268, 325,195, 152,835, and 325,157 as well as the parent (303,630)). The estimate is as follows:

The first poultry metabolism studies (see PP#3G4224 1/26/94 memo of G. Otakie) failed to identify one of the major metabolites (i.e. M-6A or 312,157) found in the second poultry metabolism studies and accordingly will not be used. Characterization data included in the second poultry metabolism studies (see PP#5F4456 5/30/96 memo of G. Otakie) will be used for the calculation as follows:

| | Poultry Residue (ppm) liver | kidney |
|---|---|---|
| parent CL 303,630 | 0.18 | 0.10 |
| metabolite CL 303,268 | 0.19 | 0.07 |
| metabolite CL 325,195 | 0.05 | 0.01 |
| metabolite CL 152,835 (M-6) | 0.52 | 0.49 |
| metabolite CL 325,157 (M-6A) | 0.79 | 0.92 |
| total | 1.73 | 1.59 |

liver ratio = 1.73/0.18 = 9.6
kidney ratio = 1.59/0.10 = 16

Since tolerances are not established specifically for residues in poultry kidney a 10X factor based on the liver ratio will be used to account for metabolites in poultry meat byproducts.

**Summary re: Chlorfenapyr Metabolism**

The permanent tolerance expression for chlorfenapyr in plant and animal commodities may be expressed in terms of parent only. However, for risk assessment purposes ratios of 6X and 10X the proposed parent tolerance level in ruminant and poultry meat byproducts, respectively will be used to account for metabolite residues (note: tolerances for poultry commodities are not required based on the current proposed uses).

**Deficiency No. 6a and b**

a. Adequate analytical methods for Pirate in/on cottonseed are available to support the proposed permanent tolerance pending completion of HED Metabolism Committee review.

b. Pending review by FDA multiresidue data for the parent Pirate appear adequate. Additional multiresidue data for metabolites may be needed pending HED Metabolism Committee review.

**Petitioner's Response to Deficiency No. 6a and b**

Since the HED Metabolism Committee has agreed that the parent is the only moiety that needs to be regulated, the proposed enforcement method for chlorfenapyr in/on cottonseed (M2216) has been validated, and the multiresidue data has been accepted by FDA, adequate analytical methods are available to support the proposed permanent tolerance.

**CBTS's Comments/Conclusions re: Deficiency No. 6a and b**

Since the HED Metabolism Committee has agreed that the parent is the only moiety that needs to be regulated (i.e., included in the tolerance expression), this deficiency is resolved.

**Deficiency No. 7**

Pending completion of a successful EPA Method Validation, submission of a revised method including a procedure for analyzing Pirate in milk fat, adequate method radiovalidation data, and HED Metabolism Committee review and agreement to regulate only the parent, adequate analytical methods for Pirate in animal commodities are available to support the proposed permanent tolerances.

**Petitioner's Response to Deficiency No. 7**

Radiovalidation results show good agreement between GC and radiotracer analyses. The following is a summary of the radiovalidation data provided:

| Tissue | % of TRR as Parent | ppb as parent (Radiotracer) | ppb as parent GC Analysis |
|---|---|---|---|
| Milk | 68 | 40 | 38 |
| Muscle | 52 | 30 | 43 |
| Fat | 78 | 276 | 247 |
| Liver | 7 | 45 | 59 |

**MRID No. 440840-01: CL 303,630: GC Determinative and GC/MS Confirmatory Method for CL 303,630 Residues in Cattle Muscle, Fat and Milkfat, 8/1/96 (M 2398.01)**

A revised analytical method (i.e. M 2398.01) was submitted which included the analytical procedures for milkfat. Method recovery for milkfat fortified with 10.0 ppb parent was 74%.

**CBTS's Comments/Conclusions re: Deficiency No. 7**

Per PP#5G04456 (see 5/9/96 memo of G. Otakie) three methods for chlorfenapyr in animal commodities have been validated (M 2405 for cattle liver, M 2398 for cattle muscle and M 2395.01 for cow's milk). In the current submission the analytical procedures for milkfat have been added to the method for cattle muscle and fat with the revised method identified as M 2398.01.

This deficiency has been resolved.

**Deficiency No. 8e**

e. Additional data on the storage stability of the parent and any metabolites which need to be regulated are needed before a

determination of the stability of parent and metabolite residues in muscle and fat samples can be made.

**Petitioner's Response to Deficiency No. 8e**

Freezer storage stability data for the parent in cottonseed, processed cottonseed commodities and ruminant milk have already been demonstrated. Additional data from the ruminant feeding study were provided to indicate the fat and muscle samples were analyzed within 42 rather than 90 days.

**CBTS's Comments/Conclusions re: Deficiency No. 8e**

Since the HED Metabolism Committee has decided that only the parent needs to be regulated, storage stability data on metabolites are not required.

The goat metabolism study (see PP#5F04456 2/6/96 memo of G. Otakie) included a C-14 radioactivity profile of HCl digest of liver after 8 months of storage which indicated a similar profile after the 8 month interval with only a 20% lower dpm.

This deficiency is resolved.

**Deficiency No. 9b**

Per Table II (September 1995) residue data on cotton gin byproducts (RAC) are required for Pirate. At least 3 field trials for each type of harvesting (stripper and picker) are needed, for a total of 6 field trials. These data may be provided on a conditional basis. Based on $^{14}C$ residue data CBTS anticipates a tolerance above 0.5 ppm for Pirate in/on cotton gin by-products will be required.

**Petitioner's Response to Deficiency No. 9b**

The petitioner has committed to conduct six field trials during the 1997 season to obtain residue data on cotton gin byproducts. They believe the estimate of 10.00 ppm parent in/on cotton gin by-products, even as a worst case is a gross exaggeration. Although, they agree with the extrapolation used by CBTS for a parent residue as high as 5.1 ppm in cotton leaves 21 days after application, cotton gin byproducts include the plant residues from ginning cotton and consist of burrs leaves, stems, lint, immature seeds, and sand and dirt. Therefore, any residue in the leaves will be considerably diluted by all the other matrices (many of which contribute significantly to the sample weight but not in total residue, i.e. stems, sand and dirt) and therefore they do not expect residue levels in the gin trash to be significantly higher than in the undelinted seed. In addition, although Table II lists that cotton gin byproducts constitute up

to 20% of the diet of beef and dairy cattle, the petitioner believes that only a fraction (ca. 9%) of the gin trash is actually available for feed. Therefore, the petitioner contends that time-limited tolerances on ruminant commodities should be at levels already proposed and reassessed after the results from the cotton gin trash RAC studies are available.

**CBTS's Comments/Conclusions re: Deficiency No. 9b**

CBTS concurs that the previous estimate of 10.00 ppm parent residues in cotton gin byproducts represented an unrealistic worst case. We note that in the new cottonseed processing study (see Deficiency 10a and b) parent residues in linters and linter motes were 1.80 and 2.13 ppm. In the absence of the required cotton gin byproduct field trial data CBTS will use 2.00 ppm as a realistic worst case estimate of parent residues in cotton gin byproducts. The petitioner has committed to conduct six field trials during the 1997 season to obtain residue data on cotton gin byproducts.

This deficiency remains unresolved.

**Deficiency No. 10a and b**

a. An additional cottonseed processing study is required to resolve questions concerning the diminution of the parent during processing. The dark color of the refined oil from the original processing study may indicate excessive temperatures during refining and accordingly for the new processing study a lower and consistent temperature during oil recovery is suggested (i.e. 165-175°F).

b. A final decision on the need for feed/food additive tolerances for Pirate is deferred pending the submission of an acceptable cotton seed processing study.

**Petitioner's Response to Deficiency No. 10a and b**

MRID No. 440840-02; Cl 303,630:Process Study Cl 303,630 Residues in processed Cotton Seed after Multiple Applications of AC 303,630 3SC Insecticide to Cotton in Mississippi; August 1, 1996.

In brief, the field portion of the study was conducted in Greenville, Mississippi with Pirate applied in five weekly applications beginning 42 days before normal harvest and ending 14 days before normal harvest at a rate of 0.4 lb ai/A in 10.8 to 13.0 gallons of spray mixture per acre (i.e. total of 2.0 lb ai/A or 2X). Samples of cottonseed were collected 1, 2 and 14 days after the fifth (last application). Ginned cottonseed samples were analyzed by Method M 2216.01 and processed samples analyzed

by Method M 2274 with the Limit of Quantitation (LOQ) of 0.05 ppm for each method.

The apparent parent residues in ginned cottonseed averaged 0.67 ppm immediately after treatment (1-2 DAT) and 0.36 ppm at 14 DAT. Unginned cottonseed was sampled at 14DAT and processed at Texas A&M to produce processed commodities. Ginned seed with approximately 11-15% remaining lint was saw-delinted in a Carver delinter to remove most of the remaining lint; after delinting, approximately 3% of the lint remained with the seed. The samples were processed to simulate commercial practice as closely as possible except they were processed by batch as opposed to continuously, as in commercial practice.

The highest temperatures reported was as the material moved through the expander, steam was injected directly into it and the temperature range of the material (collets) as it exited the expander was 180-235°F. The crude oil was recovered at a temperature range of 163-194°F. The parent residues from the processing study were: 0.30 ppm (avg.) in ginned cottonseed, <0.05 ppm in delinted cottonseed, 1.80 ppm in linters (avg.), 2.13 ppm (avg.) in linter motes, 0.16 ppm in hull, 0.07 ppm in crude oil, 0.07 ppm in recovered refined oil and below the LOQ in delinted cottonseed, kernel material, toasted meal, extracted collets, and desolventized soapstock.

The percent of total parent accounted for in each processed commodity (expressed as a percent of ginned cottonseed) was linters 24.6%, linter motes 69.4%, hulls 1.9% and crude oil 2.1%, for a total parent mass balance of 98%. There was no concentration of apparent parent residues in any of the animal feed cottonseed commodities(meal and hull), nor in the crude or refined cottonseed oils.

A letter dated 6/11/96 from M. Gerngross, Head of GLP Processing Program, of Texas A&M addressed previous CBTS concerns about the dark cottonseed oil from the first processing study as follows:

> "On occasion we do produce a darker colored, refined oil. Through conversations with a commercial processor, I have discovered that they also, on occasion, produce a darker colored oil. Since commercial processors refine large quantities of oil on a continuous basis, they have the luxury of combining darker oil with lighter oil for sale purposes..... It is my opinion and experience that production of an occasional darker oil is a combined result of a NaOH/crude oil contact reaction during miscella refining, presence of dark pigmentation in the gossypol gland of glanded cottonseed kernels and quality variation of kernel material from the field.....Please understand we keep our processing parameters within or below the

commercial conditions, because I agree with EPA's worst case scenario approach.

**CBTS's Comments/Conclusions re: Deficiency No. 10a and b**

Since the major portion of the parent was left in linters and linter motes, Malcolm Gerngross of Texas A & M University was called at 409-845-2741 to determine their composition. He indicated that linters consist of lint removed from the delinter and linter motes are delinter trash consisting of little pieces of lint, hull and seed from the continuous brushing of the delinter blades (i.e. similar to cotton gin trash from cotton ginning but in smaller amounts)'. A mass balance accounting for 98% of the parent was provided and the cottonseed processing study is acceptable. No concentration of parent residues (average level of 0.30 ppm in ginned cottonseed) occurred in crude/refined cottonseed oil or hulls from the second chlorfenapyr processing study. Accordingly, separate tolerances for cottonseed processed commodities are not required.

These deficiencies are resolved.

**Deficiency No. 11**

The confined crop rotation study indicates that residues of Pirate and or metabolites CL 312,094 and CL 325,195 at 0.01-0.02 ppm are possible in rotated crops with a 30 day plant back interval. However, since the study was conducted at approximately 2X the current proposed use rate of 1.05 lb ai/A/season with application made to bare ground (a worst case), at a plant back interval of 60 days or later all residue components in all rotated crops should be less than 0.01 ppm. Accordingly, at the current proposed use rate of 1.05 lb ai/A/season field rotational crop studies are not required provided a revised label specifying a 60 day plant back interval for all rotated food/feed crops is submitted.

**Petitioner's Response to Deficiency No. 11**

The petitioner agrees with the reviewer comments that the confined crop rotation study represents a worst case scenario since it was conducted at approximately 2X the current proposed use rate of 1.05 lb ai/A/season with applications made to bare ground which realistically results in residues considerably higher than 2X. This is due to the fact that, that under normal use rates, a major portion of the residue would be intercepted by a developed canopy.

Data in the final confined crop rotation report and summarized on pages 95-110 were provided (MRID No. 43492851). Residue data were generated for lettuce, carrot, barley, and soybean follow crops at plant back intervals of 31, 60, 119, and 364 days after the fifth treatment. Residues of the parent ranged from 0.02-0.07 ppm in barley forage and carrots at the 31 day plant back period and therefore they have submitted a revised label recommending a 60 day plant back interval for small grains and root crops. However, as the residues in lettuce and soybeans follow crops were a maximum of 0.01 ppm after a 31 day plant back, a 60 day plant back restriction is too conservative for these latter rotational crops, since residues under real world scenarios at maximum application rates of 1.05 lb ai/A/season would be considerably lower than 0.01 ppm.

**CBTS's Comments/Conclusions re: Deficiency No. 11**

Per Guidelines: Confined Accumulation in Rotational Crops (8/96)

> An appropriate rotational crop restriction can be set at the shortest interval where no TRR is ≥ 0.01 ppm, provided the registrants are willing to include this interval on the label. If the TRR is **<0.01 ppm** in all three crops at the 1-month interval, then no plantback restriction will be needed on the label. However, if the minimum intervals at which the TRR is less than 0.01 ppm differ in the three confined studies, the rotational crop restrictions will be set at the interval appropriate to each tested crop group with the **longest** interval being applied to all other (untested) rotated crops.

and per Guidelines: Field Accumulation in Rotational Crops (8/96)

> If no residues above the LOQ are observed in RAC's in the limited field trials, no tolerances will be needed. However, plantback restrictions will normally be needed unless the confined study shows no residues of concern at a 30-day plant back interval.

In brief, data in the confined crop rotation study (final report) reflecting a 2X application rate indicated the following:

| | DAT | TRR (ppm) | Parent (ppm) |
|---|---|---|---|
| mature carrot | 31 | 0.02-0.18 | 0.02-0.07 |
| | 60 | 0.01-0.02 | <0.01 |
| mature lettuce | 31 | 0.08-0.19 | 0.01 |
| | 60 | 0.02-0.03 | <0.01 |
| barley forage | 31 | 0.39-0.66 | 0.01-0.02 |
| | 60 | 0.04-0.16 | <0.01 |
| barley straw | 31 | 0.56-0.65 | 0.01 |
| | 60 | 0.04-0.16 | <0.01 |
| barley grain | 31 | 0.05 | <0.01 |
| soybean forage | 31 | 0.08-0.09 | 0.01-<0.01 |
| | 60 | 0.04-0.15 | <0.01 |
| soybean seed | 31 | 0.02 | <0.01 |

CBTS agrees that the confined crop rotation study with application at a 2X rate to bare ground would result in rotational crop residue levels higher than expected from the approved maximum application rate on a developed canopy. Although, parent residues in/on barley forage up to 0.02 ppm were identified at 31 days DAT, considering the 2X rate to bare ground, parent residues at or above 0.01 ppm are not expected under commercial use conditions. However, significant TRR's and the above CBTS policies preclude the use of a crop rotation interval of less than 30 days (i.e: and 60 days for root crops), without field crop rotation studies.

Accordingly, a revised label containing the following crop rotation restrictions is required:

> Do not plant root crops within 60 days of last application.
>
> For all other crops do not plant within 30 days of last application.

This deficiency remains unresolved.

**Deficiency No. 12b**

b. The ruminant feeding study is tentatively acceptable pending HED Metabolism Committee review and adequate muscle and fat storage stability data as referenced under Conclusion 8e.

**Petitioner's Response to Deficiency No. 12b**

Since the HED Metabolism Committee's decision that the parent is the only moiety that needs to be regulated in ruminants and the stability of parent residues in frozen animal tissues has been adequately demonstrated, it is concluded that the ruminant feeding study is acceptable.

**CBTS's Comments/Conclusions re: Deficiency No. 12b**

Since the HED Metabolism Committee has concluded that the parent is the only moiety that needs to be regulated in tolerances for ruminants and storage stability concerns have been resolved (see Deficiency 9b) the ruminant feeding study is acceptable.

This deficiency has been resolved.

**Deficiency No. 13a, b and c**

a. Using the data from the seven day poultry metabolism study one would estimate the highest residue in poultry at 0.005 ppm which would likely not be detectable. Therefore, CBTS concludes that residues of Pirate are not likely to be found in poultry commodities, based on the feeding levels of the metabolism studies and the resulting residues. Therefore, a poultry feeding study and tolerances on poultry commodities are tentatively not required for the proposed use on cotton, pending HED Metabolism Committee review.

b. Based on a best estimate of possible residues in cotton gin byproducts tolerances for Pirate in ruminant commodities of 0.05, 0.75, 0.02, 0.50 and 0.05 ppm, respectively for milk, milk fat, meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep are required. A final determination of the secondary residues in meat, milk, poultry and eggs must be deferred pending HED Metabolism Committee review. If other deficiencies in this petition are resolved, the ruminant tolerances could be made conditional on the submission of the required residue data on cotton gin byproducts.

c. A revised Section F is needed proposing the animal commodity tolerances listed above.

**Petitioner's Response to Deficiency No. 13a, b and c**

The petitioner agrees that poultry commodities do not need to be regulated for residues of the parent. However, they disagree with Agency assumptions for a revised Section F based on a totally unrealistic exposure scenario of parent residues of 10.0 ppm in cotton gin byproducts. Following rationale discussed in Deficiency 9b above, the petitioner requests that the Agency defer revising tolerances on animal commodities until more definitive data are available regarding the residue levels in cotton gin trash.

**CBTS's Comments/Conclusions re: Deficiency No. 13a, b and c**

Given the potential residue contribution to the ruminant diet from cotton gin byproducts their exclusion from the animal diet in determining required tolerances is not acceptable. However, per Deficiency 9b (In the absence of the required cotton gin byproduct field trial data CBTS will use 2.00 ppm as a realistic worst case estimate of parent residues in cotton gin byproducts.) CBTS concurs that the previous estimate and assumptions represent an unrealistic worst case which is revised as follows:

Previous Estimate

**Worst Case Dietary Burden:** The maximum dietary burden associated with this proposed tolerance in dairy cows results from diet comprised of cottonseed, meal, hulls, and cotton gin byproducts:

| Feed Item | % Diet | proposed Tolerance* | % DM | ppm in Diet |
|---|---|---|---|---|
| undelinted seed | 25 | 0.5 ppm | 88 | 0.14 |
| meal | 20 | 0.5 | 89 | 0.11 |
| hulls | 15 (20 for beef cattle) | 0.5 | 90 | 0.08 |
| cotton gin by products | 20 | 10.0 ppm-worst case estimate | 90 | 2.22 |
| alfalfa hay | 20 | 0 | n/a | 0 |
| Total | 100 | | | **2.55** |

*Covered by RAC tolerance

"CBTS notes that residue data are not currently available on Pirate in cotton gin byproducts. High residues of Pirate were reported on cotton foliage from the cotton metabolism study. For example 48.3, 102.9 and 131.8 ppm TRR were reported at day zero after an application rate of 2 lb ai/A phenyl C14 (i.e. 2X the current proposed rate) in cotton foliage following the first, third and fifth treatments, respectively. Approximately 59-68% of the TRR in **cottonseed** was identified as parent. Pirate field dissipation residue data have also been submitted to EFED (re: MRID No. 434928-14) which indicates Pirate residues on cotton leaves (upper canopy) after a single late season application of 0.4 lb ai/A (0.4X) were 6.9 and 3.3 ppm, at 14 and 28 days after application, respectively. Assuming a linear residue dissipation Pirate residues 21 days after application (the proposed PHI) would be 5.1 ppm at 0.4X. Accordingly, in the absence of field trial data a **worst** case estimate of 10.0 ppm Pirate in/on cotton gin by-products appears reasonable."

New Estimate

Accordingly, CBTS in the absence of the required data will use the parent residue data in the new cottonseed processing study (i.e. parent residue in linters and linter motes of 1.80 and 2.13 ppm, respectively). Expressed as a percentage of the ginned cottonseed the linters and linter motes from the processing study accounted for 94% of the parent mass balance. Accordingly, CBTS will use 2.0 ppm as the estimated parent residue in cotton gin byproducts resulting in the following tolerances on animal commodities:

**Realistic Worst Case Dietary Burden:** The maximum dietary burden associated with this proposed tolerance in dairy cows results from diet comprised of cottonseed, meal, hulls, and cotton gin byproducts:

| Feed Item | % Diet | proposed Tolerance* | % DM | ppm in Diet |
|---|---|---|---|---|
| undelinted seed | 25 | 0.5 ppm | 88 | 0.14 |
| meal | 20 | 0.5 | 89 | 0.11 |
| hulls | 15 (20 for beef cattle) | 0.5 | 90 | 0.08 |
| cotton gin by products | 20 | 2.0 ppm-realistic worst case estimate | 90 | 0.44 |
| alfalfa hay | 20 | 0 | n/a | 0 |
| Total | 100 | | | 0.77 |

*Covered by RAC tolerance

**RESIDUES OF PIRATE IN RUMINANT COMMODITIES**

| MATRIX | PROPOSED PERMANENT TOLERANCE (ppm) | MAX. RESIDUE IN LOW DOSE CATTLE FEEDING STUDY (i.e. 0.66 ppm Pirate dosage group) | MAX. RESIDUE EXPECTED AFTER ADJUSTMENT TO REALISTIC WORST CASE EXPOSURE [required tolerance] (ppm) |
|---|---|---|---|
| MILK | 0.01 | <0.010 | 0.01 |
| MILK FAT | 0.15 | Residue data on milk fat not collected. 15X concentration factor proposed by petitioner. | 0.15 |
| MEAT* | 0.01 | <0.010 | 0.01 |
| MEAT BY-PRODUCTS* | 0.10 | <0.050 | 0.05 since is LOQ |
| FAT* | Not currently proposed | 0.067 | 0.10 |

*=CATTLE, GOATS, HOGS, HORSES AND SHEEP.

A 15X concentration factor for parent residues in milkfat/fat was discussed under PP#5F04456 (see page 33 of 2/6/96 memo of G. Otakie). Accordingly, based on a realistic worst case estimate of possible residues in cotton gin byproducts a revised Section F with time limited tolerances for Pirate in ruminant commodities of 0.01, 0.15, 0.01, 0.10 and 0.05 ppm, respectively for milk, milk fat, meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep is required.

**Required Revised Section F**

The proposed permanent tolerances for chlorfenapyr in/on animal commodities from the proposed use on cotton should be revised as follows:

| | |
|---|---|
| Milk | 0.01 |
| Milk Fat | 0.15 |
| Meat of Cattle, Goats, Hogs, Horses, and Sheep | 0.01 |
| Fat of Cattle, Goats, Hogs, Horses and Sheep | 0.10 |
| Meat Byproducts of Cattle, Goats, Hogs, Horses and Sheep | 0.05 |

A note in the tolerance expression of the revised Section F and CFR for animal commodities is also required indicating that the parent is serving as a **marker** for metabolite residues in meat byproducts. For this reason the meat byproduct tolerance will be listed separately in the Code of Federal Regulations.

This deficiency is not resolved. A revised Section F as specified above is required.

Attachment 1- Confidential Appendix - Revised Product Chemistry for Chlorfenapyr/Pirate/Alert

7509C:CBTS:CM#2:Rm 800:305-6991:G.Otakie:10/11/96

CBI
cc with all attachments including **Attachment 1 (Confidential Appendix)**: PM 19-Dennis Edwards, Reviewer-Otakie, PP#5F04456.

NON-CBI
cc **without Attachment 1 (Confidential Appendix)**: DRES, RF, Circu, E. Haeberer.

RDI: RLoranger:10/17/96 EHaeberer 10/21/96