MEMORANDUM

SUBJECT: PP3P2947/FAP#3H5411: Chlorpyrifos in or on Wheat. Evaluation of analytical method and residue data. Accession No. 071865

TO: J. Ellenberger, PM 12
Registration Division (TS-767) and
Toxicology Branch
HED (TS-769)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
HED (TS-769)

FROM: V. Frank Boyd
Residue Chemistry Branch
HED (TS-769)

Dow Chemical Co. proposes the establishment of tolerances for combined residues of the insecticide chlorpyrifos (0,0-diethyl-O-(3,5,6-trichloro-2-pyridyl) phosphorothioate; trade name Lorsban™, and its metabolite 3,5,6-trichloro-2-pyridinol (TCP) in or on wheat grain at 0.6 ppm (of which no more than 0.3 ppm is chlorpyrifos) in or on wheat straw at 6 ppm (of which no more than 4 ppm is chlorpyrifos), in or on wheat forage at 3 ppm (of which no more than 2.5 ppm is chlorpyrifos). A feed additive tolerance is proposed under 21 CFR 561.98 for combined residues of 2 ppm (of which no more than 1 ppm is chlorpyrifos) in or on milling fractions (except flour) of wheat.

Tolerances for combined residues of chlorpyrifos and TCP have been established under 40 CFR 190.342 in or on various commodities, ranging from 0.05 to 15 ppm. Food additive tolerances are 1.5 to 10 ppm under 21 CFR 193.85, and feed additive tolerances combined under 21 CFR 561.98 range from 1 to 15 ppm. Tolerances for residues of chlorpyrifos and its metabolite TCP have been established at 0.5 ppm in milk fat (reflecting 0.02 ppm in whole milk), 2 ppm in meat, fat, and meat byproducts of goats, horses, and sheep; 0.5 ppm in meat, fat, and meat byproducts of hogs and poultry (including turkeys); and 0.1 ppm in eggs.

A temporary tolerance for wheat was established in connection with PP#1G2438.
Conclusions:

1. The metabolism of chlorpyrifos in plants and animals is adequately understood. The residue of concern in both plants and animals consists of chlorpyrifos and its metabolite 3,5,6-trichloro-2-pyridinol.

2. Adequate analytical methods are available for enforcement purposes for chlorpyrifos and 3,5,6-trichloro-2-pyridinol.

3a. The residue data are inadequate in the number of studies submitted for us to draw a conclusion on the adequacy of the proposed tolerances for wheat, grain, forage and straw. A total of eight studies are submitted for grain and straw and five studies are submitted for forage. No studies are submitted for the eastern U.S. Additional residue studies should be submitted for the major wheat growing areas and some data should also be submitted for the East. The data already submitted for wheat do show that the now proposed tolerances for grain and straw are not adequate and that higher tolerances need to be proposed.

b. Because we cannot draw a conclusion on the adequacy of the proposed tolerance for wheat grain, we can also draw no conclusion on the adequacy of the proposed food additive tolerances for wheat milling fractions. However, the milling studies are adequate for us to conclude that the petitioner should propose food additive tolerances for wheat milling fractions (except flour) at a level 3x the tolerance level needed for wheat grain.

4. Because we can draw no conclusion as to appropriate tolerance levels for wheat (grain, forage, straw, milling fractions), we cannot draw a conclusion on the adequacy of the existing meat, milk, poultry and egg tolerances to cover secondary residues resulting in these commodities from the proposed use.

5. It should be called to the attention of the petitioner that the coloring agent previously cleared for the Lorsban F (EPA Reg. No. 466-404), [REDACTED] is RFR'ed currently as a potential oncogen. A change may be required dependent on FDA assessment of the data.

6. There are no Codex, Mexican or Canadian tolerances for chlorpyrifos in wheat. Codex limits are established for other commodities based on the residue as chlorpyrifos only. We cannot recommend for the Codex limits because the U.S. tolerances are expressed in terms of parent and the metabolite, because TCP may be a significant part of the residue.

Recommendations:

We recommend against the establishment of the proposed tolerances for the reasons stated in conclusions 3a, 3b and 4. The petitioner should also be made aware of conclusion 5.
For a favorable recommendation, the petitioner needs to submit:

1. Additional residue data for wheat grain, forage and straw from the major growing areas and also some data from the eastern states. Higher tolerances should be proposed for these commodities as needed. The existing data show that the proposed tolerances are not adequate for grain and straw.

2. Food additive tolerances should be proposed for wheat milling fractions (except flour) at a level 3x that deemed necessary for wheat grain. These food additive tolerances will be established under both 21 CFR 193 and 21 CFR 581 since both human and animal commodities are involved.

Upon resolution of the above question, the adequacy of the existing meat, milk, poultry and egg tolerances will need to be determined.

**DETAILED CONSIDERATIONS**

**Formulation:**

The formulation proposed for use on wheat is Lorsban 4E Insecticide, EPA Reg. No. 464-448, an emulsifiable liquid containing 40.7% of the active ingredient chlorpyrifos and 22.8% of the active ingredient aromatic petroleum derivative solvent. The inert ingredients and the petroleum solvents in this formulation are cleared under 40 CFR 180.1001. However, [has been evaluated by FDA as a carcinogen by chronic ingestion, placing its exempt status in jeopardy (memo D. Ritter/O.E. Baynter, 3/18/83)].

We have previously concluded that no residue problems are expected from the manufacturing impurities (A. Smith, 5/3/74, FP4F1445).

**Proposed Use**

Apply Lorsban 4E at 0.25 to 1.0 lb ai/A by ground or air as a broadcast foliar spray to control aphids, armyworms, cutworms, and grasshoppers in wheat. Do not apply more than 1.5 lbs ai/A, per season. Do not apply within 28 days of a harvest at rates up to 0.5 lb act/A. At rates over 0.5 lb act/A, a 42-day PHI is to be observed. These PHI's would be applicable to harvest of grain and straw. There is also a restriction against grazing or otherwise feeding treated wheat forage within 14 days of application.

**Nature of the Residue:**

The metabolism of chlorpyrifos in plants and animals has been previously discussed in our reviews of PP3F1306 (corn, beans), PP0F2281 (apples, soybeans), PP1F2575 (citrus), and PP2F2584 (grapes). In view of the TOX conclusion (PP0F2281, W. Dykstra, 10/21/81) that unidentified metabolites found in the apple and soybean studies are not of toxicological significance, we reiterate our previous conclusion that the metabolism of chlorpyrifos in plants is adequately understood and the residue of concern consists of chlorpyrifos and its metabolite 3,5,6-trichloro-2-pyridinol (TCP).
In animal metabolism studies involving rats, cows and goats, the major metabolites were parent chlorpyrifos and TCP (and conjugates of TCP). We consider the metabolism of chlorpyrifos in animals is adequately understood and the residue of concern consists of chlorpyrifos and its metabolite TCP.

Analytical Methods:

The analytical method for chlorpyrifos, entitled "Determination of Residues of O,O-Diethyl O-(3,5,6-Trichloro-2-Pyridyl)Phosphorothionate in Sugar Beets and Solid Process Fractions by Gas Chromatography" (J. H. Wetters, Method ACR 73.5) is essentially similar to Method I in PAM II. In principle, the method for chlorpyrifos in wheat forage involves extraction by blending with methanol, transfer to hexane after evaporation of the methanol, and partitioning with acetonitrile. The residue is transferred back to hexane and cleaned up on a deactivated silica gel column. Quantitation is by gas chromatography using a flame photometric detector. A study is included in this petition demonstrating that a single polytron homogenization with methanol has an efficiency of >99%.

The analytical method for 3,5,6-trichloro-2-pyridinol is Method VII in PAM II. The TCP is extracted with methanolic sodium hyroxide, to hydrolyze any chlorpyrifos to TCP. An aqueous solution of the hydrolyzate is washed with benzene (discard), and then acidified, and the residue extracted into benzene. After cleanup on acidic alumina oxide column and additional cleanup by partition with sodium bicarbonate, the residue is derivatized with N,O-bis(trimethylsilyl) acetamide to form the trimethylsilyl derivative of pyridinol, which is quantitated by electron capture GC.

The PAM II Method II is essentially the procedure used in Norton, E. J., 1980 "Residues of Chlorpyrifos and 3,5,6-Trichloro-2-Pyridinol in Wheat Grain, Straw, and Milling and Baking Fractions."

These methods using flame photometric detection for chlorpyrifos and electron capture detection for TCP were employed for analysis of all wheat samples. The lower sensitivities in wheat were 0.01 ppm (grain) and 0.05 ppm (forage, straw and milling and baking fractions) for chlorpyrifos, and 0.05 ppm (all fractions) for TCP.

Recovery from fortified samples averaged 98% chlorpyrifos and 90% TCP for grain (concentration range of 0.01 to 1.0 ppm), 97% chlorpyrifos and 85% TCP for straw (concentration range of 0.05 to 2.0 chlorpyrifos and 90% TCP ppm), 93% chlorpyrifos and 90% TCP for green forage (concentration range of 0.05 to 20.0 ppm), and 84% chlorpyrifos and 77% TCP for milling and baking fractions (concentration range of 0.05 to 2.0 ppm). These average recoveries were found in samples fortified at the time of freezer storage and analyzed as indications of storage stability at time of analysis of treated samples.

We conclude that adequate methods are available for enforcement purposes.
Residue Data

Studies were conducted in nine states (CA, ID, IL, KS, MI, ND, OR TX & WA) containing approximately 63% of all the wheat acreage in the U.S. (according to Agric. Statistics). Eight studies were submitted for grain and five were submitted for forage.

Maximum residues found in or on wheat following application of 0.5 to 1.0 lbs ai/A (max. 1.5 lb ai/A per season) of chlorpyrifos as Lorsban 4E, are summarized in the following table:

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Location</th>
<th>Method of Application</th>
<th>PHI (Days)</th>
<th>Residue Found (ppm)</th>
<th>Chlorpyrifos TCP</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grain</td>
<td>Oregon</td>
<td>Air</td>
<td>28</td>
<td>0.23 (0.3)</td>
<td>0.38</td>
<td>0.61 (0.6)</td>
</tr>
<tr>
<td>Straw</td>
<td>Oregon</td>
<td>Air</td>
<td>28</td>
<td>4.2 (4.0)</td>
<td>1.6</td>
<td>5.8 (6.0)</td>
</tr>
<tr>
<td>Forage</td>
<td>Texas</td>
<td>Ground</td>
<td>14</td>
<td>2.3 (2.5)</td>
<td>0.23</td>
<td>2.5 (3.0)</td>
</tr>
</tbody>
</table>

Milling and Baking Fractions

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Location</th>
<th>Method of Application</th>
<th>PHI (Days)</th>
<th>Residue Found (ppm)</th>
<th>Chlorpyrifos TCP</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grain</td>
<td>Illinois</td>
<td>Ground</td>
<td>14</td>
<td>0.55 (0.3)</td>
<td>0.25</td>
<td>0.80 (0.6)</td>
</tr>
<tr>
<td>Grain</td>
<td>Illinois</td>
<td>Ground</td>
<td>14</td>
<td>1.5 (1.0)</td>
<td>0.63</td>
<td>2.1 (2.0)</td>
</tr>
<tr>
<td>Straight Grade Flour</td>
<td>Illinois</td>
<td>Ground</td>
<td>14</td>
<td>0.08 (-)</td>
<td>0.06</td>
<td>0.14 (-)</td>
</tr>
<tr>
<td>Break shorts</td>
<td>Illinois</td>
<td>Ground</td>
<td>14</td>
<td>1.0 (1.0)</td>
<td>0.42</td>
<td>1.4 (2.0)</td>
</tr>
<tr>
<td>Red shorts</td>
<td>Illinois</td>
<td>Ground</td>
<td>14</td>
<td>1.4 (1.0)</td>
<td>0.62</td>
<td>2.0 (2.0)</td>
</tr>
<tr>
<td>Red Dog</td>
<td>Illinois</td>
<td>Ground</td>
<td>14</td>
<td>0.47 (1.0)</td>
<td>0.15</td>
<td>0.62 (2.0)</td>
</tr>
<tr>
<td>Bread</td>
<td>Illinois</td>
<td>Ground</td>
<td>14</td>
<td>0.06 (-)</td>
<td>ND</td>
<td>0.06 (-)</td>
</tr>
</tbody>
</table>

( ) Parenthetical numbers are proposed tolerance.

These data show that the proposed tolerances for grain and straw will be exceeded.

Furthermore, we do not believe that the eight studies for grain and straw and the five studies for forage are an adequate basis upon which to establish tolerances for such an important crop as wheat.

Additional residue data are needed from the major wheat growing areas and from eastern states for wheat grain, forage and straw.

The milling study is an adequate basis upon which to establish tolerances for milling fractions. The data show a 3-fold concentration of residues in milling fractions (except flour) processed from treated wheat. When the petitioner has obtained the additional wheat data as requested above, he should also propose a food additive tolerance for wheat milling fractions (except flour) at a level 3x that of the grain tolerance level. Food additive tolerances should be established under 21 CFR 193 and 21 CFR 561.
Meat, Milk, Poultry and Eggs

Wheat grain, forage, straw and milling fractions are livestock feed items. The grain and milling fractions are poultry feed items.

Tolerances have been established for meat, milk, poultry and eggs to cover secondary residues resulting from residues on other feed items with already established tolerances.

Feeding studies have been submitted for cattle at feeding levels up to 100 ppm, swine at levels up to 10 ppm and chickens at levels up to 10 ppm.

Because we cannot draw a conclusion as to appropriate tolerance levels for wheat grain, forage, straw and milling fractions, we are not making a conclusion on the adequacy of the already established tolerances for meat, milk, poultry and eggs to cover secondary residues in these commodities as a result of feeding the treated crop.

A revised set of tolerances for meat, milk, poultry and eggs using combined residues and chlorpyrifos separately expressed has been proposed (Arne, 9/9/83 PP#3FP2864)

Other Considerations

An International Residue Limit Status Sheet is attached. There are no international or Codex tolerances established for wheat.
### INTERNATIONAL RESIDUE LIMIT STATUS

**CHEMICAL:** Chlorpyrifos  

**CCPR NO.:** 17

**Codex Status:**

- No Codex Proposal  
- Step 6 or above

**Residue (if Step 9):** Chlorpyrifos only

**Crop(s)** | **Limit (mg/kg)**  
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none (on wheat)

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### PETITION No. 3F2947  
5H5411 Boyd 11/3/83

**Proposed U. S. Tolerances**

**Residue:** Chlorpyrifos and its metabolite TCP

**Crop(s)** | **Tol. (ppm)**  
--- | ---  
Wheat Grain | 0.6 (< 0.3 ppm chlorpyrifos)  
Wheat Straw | 6.0 (< 4 ppm chlorpyrifos)  
Wheat Forage | 3.0 (< 2.5 ppm chlorpyrifos)

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### CANADIAN LIMIT

**Residue:**

**Crop** | **Limit (ppm)**  
--- | ---  
none (on wheat)

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### MEXICAN TOLERANCIA

**Residue:**

**Crop** | **Tolerancias (ppm)**  
--- | ---  
none (on wheat)

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