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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP #4G3138. DPX-M6316 on barley and wheat. Comments on the analytical method and residue data. Accession Numbers 072845 and 072846.

FROM: for John M. Worthington, Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

TO: Robert Taylor, PM. No. 25
Registration Division (TS-767)
and
Toxicology Branch
Hazard Evaluation Division (TS-769)

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

E.I. du Pont de Nemours and Company proposes the establishment of temporary tolerances for residues of the herbicide, Methyl 3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]-sulfonyl]-2-thiophenecarboxylate, Trade name DPX-M6316 in or on wheat and barley grains at 0.05 ppm and 0.1 ppm in wheat and barley straws.

No tolerances have been previously established or proposed for DPX-M6316. The proposed three year experimental program involves the application of approximately 130 lbs. a.i. to 2600 acres of wheat and barley in the first year, and about 250 lbs. a.i. to 5000 acres in both the second year and third years.

## Conclusions

1. The fate of DPX-M6316 in plants has been adequately delineated for the purpose of the proposed temporary tolerance. DPX-M6316 is considered the primary residue of concern.

2. Adequate methodology is available to enforce the proposed temporary tolerances.

3a. The available residue data are adequate to demonstrate that residues in wheat and barley grain and straw from the proposed use will not exceed the proposed temporary tolerances.

3b. A label restriction against the feeding or grazing of treated forage has been imposed.

3c. Only extremely low residue levels (if any) are expected in wheat and barley grains; and therefore, no milling fraction data are being required for the proposed temporary tolerances.

4. For the purpose of the proposed temporary tolerances only, we can conclude that the proposed use falls under Category 3 of Section 180.6(a).

5. No storage stability data demonstrating that residues are stable under the conditions of storage have been submitted.

## Recommendations

1. Toxicological considerations permitting, Residue Chemistry Branch recommends that the proposed temporary tolerance be granted.

2. For a future permanent tolerance the following will be required:

   a) Completion of the current metabolism studies. If any metabolites are determined to be of concern for the purpose of a future permanent tolerance, the development of appropriate analytical methodology and validation data for the determination of the additional metabolites will also be required.

   b) Storage stability data demonstrating that residues are stable under the conditions of storage.

   c) Additional residue data reflecting residue levels resulting in wheat and barley grains and straw from the proposed use or exaggerated treatment rates.

   d) If the additional studies indicate the presence of residues (including significant metabolites) in treated wheat or barley (grain or straw), appropriate animal feeding studies and possibly tolerance proposals for residues in milk, meat, poultry and eggs will be needed.

e) A grain processing study will be required if real residues are detected in the grains of either wheat and barley.

## Detailed Considerations

### Formulation

DPX-M6316 is formulated as a 75% active ingredient dry flowable powder which is made to be mixed with water. The inert ingredients of the proposed formulation are cleared under Section 180.1001(c) or (d). See the attached Confidential Appendix for a list of the ingredients.

The DPX-M6316 manufacturing process is described in the attached Confidential Appendix. Technical DPX-M6316 is at least 95% pure. We do not anticipate any specific residue problems with the technical impurities resulting from the proposed use.

### Proposed Use

DPX-M6316 is proposed for use to control broadleaf weeds in wheat and barley at rates ranging up to 28.4 g. (1 oz.) active ingredient per acre. Applications are to be made between the 2-leaf and boot stages. No specific preharvest interval has been required; however, the use as proposed provides a minimum interval of about 36 days between treatment and harvest.

Tank mixes with other herbicides are recommended, provided the label instructions for the additional herbicides are also followed.

A restriction against the feeding or grazing of hay from treated areas has been imposed. A 30 day (120 day if tank mixed with Ally™) crop rotation restriction is also imposed.

### Nature of the Residue

Plant Metabolism: An interim report describing a wheat and barley radiotracer metabolism study has been submitted. Wheat and barley plants grown in 1 cubic foot containers were treated at the four-leaf stage with $^{14}C$ thiophene ring labeled DPX-M6316 at a rate equivalent to 1 oz. act./acre and analyzed at 0, 6, 14, 21 and 111 (maturity) days after treatment.

After rinsing, Samples were extracted with an 80/20 acetone/water solution. The mature foliage and grain sample were freeze dried before extraction. Aliquots of both the extracts and the remaining solids were taken to determine the levels of total activity in each fraction.

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The acetone/water extracts were concentrated, acidified and partitioned against methylene chloride and butanol solutions. When further cleanup was needed samples were made alkaline with ammonium carbonate and partitioned against hexane.
The extracts and washes were analyzed by thin layer chromatography or by high performance liquid chromatography. The developed plates were exposed to X-ray film and the activity of the areas with detectable activity determined by LSC. Non labeled standards were co-chromatographed and detected by fluorescence quenching. The 111 day samples were analyzed by programed reverse phase HPLC.

Portions of the acetone/water extracts were adjusted to pH5 and subjected to enzymatic hydrolysis and the hydrolysates partitioned against methylene chloride.

The initial acetone washes removed approximately 20-25% of the total recovered activity. The majority of the activity (approximately 50-85%) was recovered in the acetone/water extract. Non-extractable activity levels in treated foliage ranged from 5-55% and averaged 22%. At 111 days after treatment, between 15 and 33% of the total plant activity was detected in mature grain. The absolute levels of activity declined from approximately 2 ppm at day 0 to about 0.20 ppm in foliage and 0.01 ppm in grain at 111 days.

The parent compound accounted for 75 to 83% (1.4 ppm) of the total residue in foliage at day 0 and declined to 10-15% (0.01 ppm) on day 28. No detectable levels of the DPX-M6316 were in the straw or mature grain samples. The portion of activity remaining in the aqueous phase after the methylene chloride and butanol partitioning steps increased steadily with time, indicating increasingly more polar degradation products.

The major metabolite, methyl 3-(aminosulfonyl)-2-thiophenecarboxylate, accounted for 2 to 17% of the total activity in plants. 3-(Aminosulfonyl)-2-thiophenecarboxyllic acid was also detected. The preliminary report indicates that remainder of the recovered activity was more polar than the parent compound. The hydrolysis experiment indicates that glucose conjugation is not a significant metabolic pathway. Additional investigations into the nature of the metabolites are continuing, including a field radiolabeled metabolism study.

Considering the low levels of activity expected at harvest and the fact that all the unidentified material has been shown to be more polar than the parent compound, the fate of DPX-M6316 is considered adequately understood for the purpose of the proposed temporary tolerance. DPX-M6316, per se, is the primary residue of concern.

No animal metabolism data are presented in support of the subject petition. However, considering the very low levels expected in feed items derived from treated wheat and barley and the label

restriction against the grazing or feeding of treated hay to livestock, RCB can consider the fate of DPX-M6316 adequately delineated for the purpose of the proposed temporary tolerance.

For a future permanent tolerance a completion of the continuing metabolism studies will be required. If any metabolites are determined to be of concern for the purpose of a future permanent tolerance, the development of appropriate analytical methodology and validation data for the determination of the additional metabolites will also be required.

Analytical Method

The proposed analytical method for DPX-M6316 residues in wheat and barley involves an ethyl acetate and acetic acid extraction. After centrifugation the extract is partitioned against an aqueous sodium bicarbonate solution and the aqueous layer is acidified and partitioned against methylene chloride. The methylene chloride layer is carefully evaporated to dryness. The sample is redissolved in 3:1 solution of cyclohexane and isopropanol and filtered through a millipore® filter for analysis by HPLC using a photo-conductivity detector.

The proposed procedure is reportedly sensitive to 0.02 ppm DPX-M6316 in wheat and barley grain and sensitive to 0.05 ppm in wheat and barley straw. Recoveries of DPX-M6316 from wheat and barley grains and straws fortified at levels ranging from 0.02 to 0.1 ppm ranged from 59 to 100% averaged 79.6%. All grain and straw control values were reported as <0.02 ppm and <0.05 ppm, respectively.

We consider the proposed procedure adequate to enforce the proposed temporary tolerance.

Residue Data

Residue data have been submitted from 14 experiments conducted in 9 different states. Wheat and barley grains and straw were analyzed for residues of DPX-M6316 after treatments at up to two times the maximum proposed rate. The reported preharvest intervals ranged from 48 to 118 days. None of these samples showed any detectable (<0.02 ppm in grain and <0.05 ppm in straw) residues.

Since only extremely low residue levels (if any) are expected in wheat and barley grains, no milling fraction data are required for the proposed temporary tolerance.

In lieu of tolerance proposals for residues in forage, a label restriction against the grazing or feeding of treated forage has been imposed.

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The available residue data are adequate to demonstrate that residues will not exceed the proposed temporary tolerances.

No storage stability data demonstrating that residues are stable under the conditions of storage have been submitted. Such data will be required for a future permanent tolerance.

Additional residue data reflecting residue levels resulting in wheat and barley grains and straw from the proposed use or exaggerated treatment rates will be be required for a future permanent tolerance. If residues are detected in the grains of barley or wheat a process study will be required.

Meat, Milk, Poultry, and Eggs

Considering the very low levels of residues expected in treated wheat and barley grains and straw, RCB can conclude that for the purpose of the proposed temporary tolerances the proposed use falls under Category 3 of Section 180.6(a).

If the additional data required for the future permanent tolerance indicate the presence of of residues (including significant metabolites) in treated wheat or barley (grain or straw), appropriate animal feeding studies and possibly tolerance proposals for residues in milk, meat, poultry and eggs will be needed.

cc(w/CBI att): PP# No. 4G3138, PM-25, TOX, J. Worthington
cc : Reading file, Circu, FDA, EEB, EAB, R. Thompson (RTP)

TS-769:Reviewer:JMWORTHINGTON:Date:10/21/84
RDI:Section Head:ARR:Date:10/30/84:RDS:Date:10/30/84

Harmony Reviews

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Pages 7 through 8 are not included in this copy.

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X Identity of product inert ingredients

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