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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Subject: EPA Reg. No. 352-538. Harmony Extra Herbicide (50% DPX-M6316, 25% DPX-L5300) on Wheat and Barley. Request for supplemental labeling to extend application timing. DEB No. 7693. MRID Nos. 417512-01 through -09. DP Barcode No. D161719.

From: Clyde T. Stanton, Chemist
Christine L. Olinger, Chemist
Special Review Section 1
Chemistry Branch II - Reregistration Support
Health Effects Division (H7509C)

Thru: Andrew Rathman, Section Head
Special Registration Section 1
Chemistry Branch II - Reregistration Support
Health Effects Division (H7509C)

To: Mary Ermusele-Matzer, PM-23
Fungicide-Herbicide Branch
Registration Division (H7505C)

E. I. du Pont de Nemours & Co., Inc. has requested a registration amendment for Harmony® Extra Herbicide [50% DPX-M6316 (methyl 3-((((4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino)carbonyl)amino) sulfonyl)2-thiophene carboxylate); 25% DPX-L5300 (methyl 2-((((N-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)methyl-amino)carbonyl) amino)sulfonyl)benzoate) (EPA Reg. No. 352-538)] to extend the application timing of the product. The proposed change could reduce the PHI under typical weather conditions from about 60 to about 45 days; under drought-like conditions, the PHI for spring wheat could be reduced to a 25-30 day range. Several new studies have been submitted in support of this amended registration.

The active ingredients each have established permanent tolerances of 0.05 ppm and 0.1 ppm on wheat and barley grain and straw, respectively (40 CFR 180.439, PP#6F3431; 40 CFR 180.451, PP#7F3540). DPX-M6316 and DPX-L5300 are registered for use on

barley and wheat for control of certain broadleaf weeds; in addition, DPX-M6316 is registered for use on soybeans. Both herbicides have application timings restricting their use to between the two-leaf stage and prior to the first node appearing for spring wheat and barley and between the two-leaf stage and third node appearance for winter wheat.

The proposed label amendment would expand the timing application from the two-leaf stage to before the flag leaf is visible. The amended label carries a prohibition on harvesting prior to 45 days following the final application.

Conclusions

1. The new analytical methods used in most of the studies submitted in support of this registration action are sufficient for data collection only. CBRS recommends that if these methods are used in future studies that the conditions be adjusted so that the retention times of standards and extracted samples are equivalent.

2. The stability of extracts cannot be determined for the residue data presented in support of this action.

3. Extraction, analysis, and concurrent fortification data cannot be confirmed for MRID No. 417512-03 (Du Pont No. AMR-1114-88).

4. Provided the questions in Conclusions 2 and 3 above can be satisfactorily addressed, residues of DPX-M6316 and DPX-L5300 are not likely to exceed the established tolerances for wheat grain and straw and barley grain and straw.

Recommendation

CBRS recommends against the proposed label amendment for the reasons stated in Conclusions 2 and 3 above. In order to obtain a favorable recommendation the registrant must clarify when extractions, analyses, and concurrent fortifications were conducted for MRID No. 417512-03 (Du Pont No. AMR-1114-88). CBRS must be able to confirm that sufficient fortifications were conducted and that degradation was not likely to occur during the interval between extraction and analyses. For all studies submitted in support of this action the registrant should report the temperature(s) which all extracts were stored at prior to analysis, and that they were not held for extended periods at room temperature (e.g. in an autosampler). A stability study should be provided for extracts in the final solution at the temperature(s) the extracts were held prior to analysis for up to two months.

## Detailed Considerations

### Analytical Method

Data were collected using a few different methods. A new method, AMR-1242-88 (MRID No. 417512-09), was used with slight modifications for the determination of DPX-L5300. The plant material is extracted with a solution of 0.1 M $K_2HPO_4$ in 30% methanol, with the pH adjusted to 8.5 using phosphoric acid. The homogenized solution is centrifuged and an aliquot of the supernatent is removed for further cleanup. The extract is acidified to pH 2.0 to 3.5 and centrifuged to remove any precipitate. The clear extract is then subjected to clean-up on a phenyl HPLC column with an aqueous eluent of 50% methanol buffered at pH 3.5. The eluent containing the analyte of interest is collected in a volumetric flask held in ice water to prevent degradation. After bringing to volume with water, the solution is analyzed on an HPLC with a Zorbax $R_x$ column with ultraviolet absorbance detection.

Data are presented in the method which demonstrate degradation of the analyte in acidic solutions (pH between 2.0 and 3.5) at various temperatures. Degradation is less than 10% over a 24 hour period when held at -20°C, but is rapid once the temperature is above freezing.

The analytical laboratory conducting the studies reviewed herein made minor changes to the method including differences in sample size and concentrations of solutions used in the HPLC analyses. A very similar method (AMR-1801-90) was used for analysis of DPX-M6316 and is included as an appendix to one report (MRID No. 417512-02). The only major differences are slightly different concentrations of elution solvents used in the HPLC clean-up and analysis. Retention times of standards cannot be directly compared to those in extracted samples. The pH of the final solution is different than those of the standards, which causes about a 0.5 min difference in retention time. The registrant states that the presence/absence of DPX-M6316 in the treated samples may be determined from the retention time of DPX-M6316 in the fortified controls. This is not typically acceptable in analytical methods, particularly enforcement methods. The registrant has not addressed potential interferences with other sulfonylurea herbicides. The method will be considered acceptable for this registration action only, since adequate concurrent fortifications were obtained. CBRS suggests modifying the method for future studies so the retention times of standards and samples are the same.

The new method is very different from the enforcement method for DPX-L5300 (AMR-337-85, Rev. A; MRID No. 403036-01). The plant material is extracted three times with acetonitrile. After centrifuging, the supernatent is evaporated to dryness. The

extract is subjected to a column chromatography clean-up on an Adsorbosil-LC column. Analysis is by HPLC using a Porasil column with photoconductivity detection.

A second method was used for the analysis of DPX-M6316, AMR-646-86, which is the enforcement method. The plant material is extracted twice with ethyl acetate and centrifuged. The supernatent is partitioned three times with sodium bicarbonate and the aqueous phase is adjusted to pH 3.5 with HCl. The acidic extract is partitioned three times with dichloromethane and brought to dryness. The reconstituted extract is analyzed using normal phase HPLC with photoconductivity detection. Good recoveries were obtained for this method in these studies.

Although the new methods have not been previously submitted or been subjected to a radiovalidation, the methods appear to be appropriate for data collection. Good recoveries were obtained for both DPX-L5300 and DPX-M6316 for the matrices discussed herein. Recoveries of DPX-M6316 from grain ranged from 83-111% and 67-113% for straw. For DPX-L5300 recoveries from grain ranged from 59-103% and 63-109% for straw. There is some question about the stability of the extracts for some studies, which is discussed under the individual studies below.

Storage Stability

In the Harmony® New Chemical Registration Standard of 2/12/87 C. Deyrup (RCB No. 1236) concluded that residues of DPX-M6316 are stable under frozen storage for 18 months. In the update to the registration standard (C. Deyrup 2/24/87, RCB No. 2825) the data were extended to a period of 36 months. Residues are stable in/on wheat straw for a period up to 24 months.

Residues of DPX-L5300 are stable up to 21 months, according to the New Chemical Review of 4/26/88 by R. Cook (DEB Nos. 2516 and 2517).

Residue Data

New data from field tests applying Harmony (75% DPX-M6316), Express (75% DPX-L5300) and Harmony Extra (50% DPX-M6316, 25% DPX-L5300) Herbicides were submitted in support of this amended registration. Each study is discussed below.

**MRID No. 417512-03 (Du Pont No. AMR-1114-88)**

Harmony Extra® herbicide (DPX-M6316 and DPX-L5300) was applied to wheat at two test sites (WY and ND) at application rates of 0 and 0.6 oz ai/A DPX-M6316 and 0.3 oz ai/A DPX-L5300. The report states this is a 2X rate but is actually a 1.2X rate. Pre-harvest intervals were 39 and 54 days. No residues were detected in/on the grain at a level of 0.01 ppm or the straw at 0.020 ppm. Samples were analyzed using method AMR-1801-90 for DPX-M6316 and method

AMR-1242-88 for DPX-L5300. Samples were stored up to 14 mos. prior to extraction. Only a range of dates was reported for extraction and analysis so it cannot be determined if sufficient concurrent fortifications were conducted for each chemical/matrix or if the extracts were analyzed within an acceptable period of extraction.

**MRID No. 417512-06 (Du Pont No. AMR-1158-88)**

Harmony® herbicide (DPX-M6316) was applied to wheat at six test sites [MT, SD, WY (two sites), TX, and CA] at application rates of 0, 0.5, and/or 0.9 oz ai/A. Pre-harvest intervals ranged from 25 to 40 days. Applications were made at stages later than typically permitted on the label in order to obtain the shorter PHIs. All grain samples were analyzed for residues of DPX-M6316; however the straw sample from the high rate WY site was the only straw sample analyzed. No residues were detected in/on the grain at a level of 0.01 ppm or the straw at 0.020 ppm. Samples were analyzed using the enforcement method and the new method (AMR-1801-90). Concurrent fortifications ranged from 73 to 111% for wheat grain using the enforcement method; for the other method the single concurrent fortification for the grain was 96% and for the straw, 67%. Samples were stored up to 10 mos. prior to extraction. Extracts were analyzed within an acceptable period of extraction.

**MRID No. 417512-02 (Du Pont No. AMR-1437-89)**

Harmony® herbicide (DPX-M6316) was applied to barley at two test sites (MT and ND) at application rates of 0 and 0.5 oz ai/A. Pre-harvest intervals were 40 and 41 days. Applications were made at stages somewhat later than typically permitted on the label in order to obtain the shorter PHIs. No residues were detected in/on the grain at a level of 0.02 ppm. Residues in the treated straw from the MT site were 0.026 ppm and the ND site, 0.048 ppm. All samples are below the 0.1 ppm tolerance. Samples were analyzed using the new method (AMR-1801-90). Concurrent fortifications ranged from 83 to 100% for barley grain; the single straw fortification showed a recovery of 113%. Samples were stored up to 11 mos. prior to extraction. Extracts were analyzed within an acceptable period of extraction.

**MRID No. 417512-01 (Du Pont No. AMR-1156-88)**

Express® herbicide (DPX-L5300) was applied to wheat at five test sites (MT, WY, TX, CA and SD) at application rates of 0 and 0.25 oz ai/A. Pre-harvest intervals ranged from 25 to 40 days. Applications were made at stages somewhat later than typically permitted on the label in order to obtain the shorter PHIs. Method AMR-1242-88 was used to collect residue data. No residues were detected in/on any grain or straw sample at a level of 0.02 ppm for grain and 0.03 ppm for straw. Concurrent fortifications ranged from 73 to 100% for wheat grain and 70 to 109% for straw. Samples were stored up to 24 mos. prior to extraction. Extracts were analyzed within an acceptable period of extraction.

**MRID No. 417512-07 (Du Pont No. AMR-1157-88)**

Express® herbicide (DPX-L5300) was applied to barley at three test sites (ID, CA and SD) at application rates of 0 and 0.25 oz ai/A. Pre-harvest intervals ranged from 24 to 43 days. Applications were made at stages somewhat later than typically permitted on the label in order to obtain the shorter PHIs. Method AMR-1242-88 was used to collect residue data. No residues above the limit of quantitation (0.02 ppm) were detected in/on any grain sample. Only the treated straw sample from CA showed residues, at approximately 0.03 ppm, which is below the quantitation limit of 0.04 ppm. Concurrent fortifications ranged from 59 to 91% for barley grain and the single fortification for straw showed 71% recovery. Samples were stored up to 21 mos. prior to extraction. Extracts were stored up to nine days after extraction prior to analysis.

**MRID No. 417512-04 (Du Pont No. AMR-1073-88)**

Two different formulations of Express® herbicide (DPX-L5300) were applied to barley at two test sites (MN and CA) at application rates of 0, 0.25, and 0.5 oz ai/A. Pre-harvest intervals were 57 and 62 days. Method AMR-1242-88 was used to collect residue data. Residues in/on grain were detected only in the high rate sample from CA, but were still below the established tolerance. No residues were detected in the straw samples from MN. The 1X (0.25) straw sample from CA showed an average residue of 0.087 ppm for the new formulation and 0.066 for the current formulation, and average residues of 0.23 ppm were found in/on the 2X sample for the new formulation and 0.28 ppm for the current formulation. These values for the 2X rate are above the established tolerance of 0.1 ppm. Concurrent fortifications ranged from 88 to 89% for barley grain and 80 to 83% for straw. Samples were stored up to 15 mos. prior to extraction. Extracts were stored up to nine days after extraction prior to analysis.

**MRID No. 417512-05 (Du Pont No. AMR-1074-88)**

Two different formulations of Express® herbicide (DPX-L5300) were applied to wheat barley at seven test sites (MT, SC, IN, OH, ND, OK, and TX) at application rates of 0, 0.25, and 0.5 oz ai/A. Pre-harvest intervals ranged from 41 to 60 days. Method AMR-1242-88 was used to collect residue data. No residues were detected in any grain sample using either formulation at a detection limit of 0.01 ppm or in any straw sample at the 1X rate at the same detection limit. Residues up to 0.02 ppm were detected in a few of the 2X fate samples from treatment with either formulation. Concurrent fortifications ranged from 70 to 103% for barley grain and 63 to 90% for straw. Extracts were stored up to 2 mos. prior to extraction, which is much longer than typically acceptable, particularly since the analyte tends to degrade in acidic solutions. In order for these data to be considered valid, stability data over a 2 month period must be presented.

**MRID No. 417512-08 (Du Pont No. AMR-1196-88)**

Express® herbicide (DPX-L5300) was applied to barley and wheat at two test sites (CA and SD) for barley and a single site (CA) for wheat at application rates of 0, 0.25, and 0.5 oz ai/A. Pre-harvest intervals ranged from 36 to 38 days. Applications were made at stages somewhat later than typically permitted on the label in order to obtain the shorter PHIs. Method AMR-1242-88 was used to collect residue data. No residues were detected above the limit of quantitation (0.03 ppm) in any grain sample; one sample showed residues between the limit of detection and limit of quantitation. The wheat and straw sample from the CA site showed residues slightly below the limit of quantitation (0.06 ppm) at the 1X (0.25) rate; straw samples from the 2X plots range from non-detectable (SD) to 0.11 ppm for the wheat straw sample, which is slightly higher than the established tolerance of 0.1 ppm. Concurrent fortifications were 100% for both barley and wheat grain and ranged from 86 to 89% for barley straw. No fortifications were conducted for wheat straw. Samples were stored up to 18 mos. prior to extraction. Extracts were analyzed within an acceptable period of extraction.

Discussion

The data presented apparently support the registrant's claim that residues exceeding the established tolerances are not likely to occur as a result of extending the application timing. A few questions remain before CBRS can recommend for this registration action. Most samples were extracted within an acceptable interval after sampling. In the few cases where the samples exceeded the storage stability interval, they were analyzed soon after that such that significant degradation was not likely to occur. CBRS is concerned about degradation of the sample extracts prior to analysis since data have been presented showing rapid degradation of the active ingredients in acidic solution at room temperature. The registrant must clarify when extractions, analyses, and concurrent fortifications were conducted for MRID No. 417512-03 (Du Pont No. AMR-1114-88). CBRS must be able to confirm that sufficient fortifications were conducted and that degradation was not likely to occur during the interval between extraction and analyses. For all studies submitted in support of this action the registrant should report the temperature(s) which all extracts were stored at prior to analysis, and that they were not held for extended periods at room temperature (e.g. in an autosampler). A stability study should be provided for extracts in the final solution at the temperature(s) the extracts were held prior to analysis for up to two months. Once these concerns are addressed satisfactorily CBRS could recommend for the proposed amended registration.

cc: CLOlinger (CBRS), Circulate, RF, SF (2), Amended Reg. File (2), RDSchmitt, C. Furlow (PIB/FOD)
H7509C:CBRS:CLOlinger:clo:CM#2:Rm 803C:557-1406: 6/12/91
RDI: ARRathman: 6/12/91 EZager: 6/12/91