(3-19-96)

**MEMORANDUM**

SUBJECT: **2,4-D.** (030001) Storage Stability Study on Various Raw and Processed Agricultural Commodities. GDLN 171-4(e)
DP Barcode: D220451; CBRS No. 16425; MRID No.: 438099-01 ; Rereg. Case No. 0073.

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CBRS has been requested to review a storage stability study submitted by the Industry Task Force II on 2,4-D Research Data. The study was conducted to examine the stability of 2,4-D in corn (grain, forage, and fodder); sorghum grain; wheat (grain, forage, and straw); sugarcane cane; rice grain; rangeland grass and hay; soybean seed; corn starch, flour, and oil; wheat flour; sugarcane sugar, molasses, and bagasse; and rice bran and hulls.

The qualitative nature of the residue in plants is adequately understood; per the HED Metabolism Committee, the residue of concern in plant commodities is parent 2,4-D.

Tolerances for plant commodities are currently expressed in terms of 2,4-D *per se* [40 CFR

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§180.142 (a through f, i, j, and k), §185.1450(a), and §186.1450]. Tolerances for animal commodities are expressed in terms of the combined residues of 2,4-D and/or its 2,4-dichlorophenol metabolite [40 CFR §180.142(h)].

Codex MRLs for residues of 2,4-D are expressed in terms of 2,4-D *per se*. The CODEX MRL and the U.S. tolerance expression are compatible for plant commodities only, pending incorporation of the HED Metabolism Committee recommendations into the tolerance expression for animal commodities. Issues regarding harmonization of U.S. tolerances with the Codex MRLs will be addressed when the registration eligibility of 2,4-D is determined.

## CONCLUSIONS

1. The storage stability data show that residues of 2,4-D are stable under frozen storage conditions for a period of at least 12 months in/on the following raw and processed commodities: corn (grain, forage, and fodder); sorghum grain; wheat (grain, forage, and straw); sugarcane cane; rice grain; rangeland grass and hay; soybean seed; corn starch, flour, and oil; wheat flour; sugarcane sugar, molasses, and bagasse; and rice bran and hulls.

2. Given that the registrant has provided adequate data to support the long-term (> ca.2-3 years) storage stability of 2,4-D, CBRS concludes that no storage stability concerns or data requirements remain for 2,4-D for each of the following three crop groupings: (1) oilseeds or nuts; (2) leafy vegetables; and (3) grain crops provided that field trial samples are not stored for appreciably longer than ca. 2-3 years. There are currently no storage stability data to support any past field trials conducted with fruit or fruiting vegetables and/or root crops.

3. CBRS also concludes that sufficient storage stability data has been provided to support the following processed commodities of corn (starch, flour, and oil), wheat flour, sugarcane (sugar, molasses, and bagasse); and rice (bran and hulls) provided that storage intervals for these 171-4(l) studies did not exceed approximately 2-3 years.

## RECOMMENDATIONS

The registrant should be informed that GDLN 171-4(e) storage stability data requirements for any and all previous magnitude of the residue studies have been met for each of the following three crop groupings: (1) oilseeds or nuts; (2) leafy vegetables; (3) grain crops provided that field trial samples have not and/or are not stored for appreciably longer than ca. 2-3 years. The registrant should also be informed that sufficient storage stability data has been provided to support the following processed commodities of corn (starch, flour, and oil), wheat flour, sugarcane (sugar,molasses, and bagasse); and rice (bran and hulls) provided that storage intervals for these 171-4(l) studies did not exceed approximately 2-3 years. There are currently no storage stability data to support any past field trials conducted with fruit or fruiting

vegetables and/or root crops. If the registrant chooses to continue to support any of these latter uses, additional storage stability data will be required.

## DETAILED CONSIDERATIONS

This study was conducted to examine the stability of the 2,4-D parent in various raw and processed agricultural commodities stored frozen at nominal temperatures of -12 to -27 C for up to 12 months.

### Residue Analytical Method

Samples from the storage stability studies were analyzed for residues of the 2,4-D parent using EN-CAS's Method ENC-2/93, a validated GC/ECD method with an LOQ of ca. 0.01 ppm. The registrant included a description of this method in its Appendix I. Briefly, residues are extracted from plant matrices into 0.5 M KOH in ethanol:$H_2O$ (EtOH, 1:1, v/v) and filtered. The resulting extract is refluxed for 1 hour in ~0.2 M HCl. Hydrolyzed residues are then cleaned-up using a $C_{18}$ solid phase extraction column by rinsing with water and hexane, and then eluting with hexane:ethyl acetate (EtOAc, 1:1, v/v). Residues are then partitioned into 0.1 M $Na_2HPO_4$, acidified, and partitioned into diethyl ether ($Et_2O$). Residues are concentrated to dryness and then derivatized to the methyl ester with 14% boron trifluoride in methanol (MeOH). For samples of soybean (seed and forage), sugarcane, and rice straw, the derivatized sample is then oxidized with potassium permanganate. The derivatized residues from each matrix (except wheat forage and grain) are then partitioned into 25% toluene in hexane and cleaned-up using an Alumina column eluted with 25% toluene in hexane. For wheat forage and grain samples, the derivatized residues are extracted into toluene, diluted with hexane (toluene:hexane, 1:2, v/v), and cleaned-up using an Alumina column eluted with 35% toluene in hexane. Methylated residues in all matrices are determined by GC/ECD.

The registrant included in the submission sample chromatograms and residue data sheets. The average concurrent method recoveries were acceptable, yielding an overall mean and standard deviation of 89% $\pm$ 10% (n=232) for the storage stability analyses performed in this study.

### Storage Stability Data

All sample matrices (except processed fractions) were homogenized by chopping and blending in a Hobart Mixer in the presence of dry ice, fortified with an appropriate quantity of 2,4-D (generally, 0.1 to 2 ppm), and then stored frozen for up to 12 months. For each matrix, a sample set consisted of five samples: two aged samples fortified at Day 0, two samples freshly fortified with 2,4-D for determination of concurrent recoveries, and one control sample.

Following the storage period (which ranged from 0 to 12 months), samples were analyzed for residues of 2,4-D using the above-described EN-CAS ENC 2-93 method. Control samples had nondetectable residues. The recoveries of 2,4-D fortified samples following various intervals of freezer storage are presented in Table 1.

The submitted studies are acceptable and may be used to satisfy 171-4(e) guideline requirements. The storage stability data show that residues of the 2,4-D parent are stable under frozen storage conditions for a period of at least 12 months in/on the following commodities: corn (grain, forage, and fodder); sorghum grain; wheat (grain, forage, and straw); sugarcane cane; rice grain; rangeland grass and hay; soybean seed; corn starch, flour, and oil; wheat flour; sugarcane sugar, molasses, and bagasse; and rice bran and hulls. With the storage stability data provided for the 2,4-D parent compound in the current submission, CBRS concludes that no storage stability concerns or data requirements remain for 2,4-D for each of the four following RAC crop groupings: (1) oilseeds or nuts; (2) leafy vegetables; and (3) grains provided that field trial samples are not stored for appreciably longer than ca. 2-3 years. There are currently no storage stability data to support any past field trials conducted with fruit or fruiting vegetables and/or root crops. CBRS also concludes that sufficient storage stability data has been provided to support the following processed commodities of corn (starch, four, and oil), wheat flour, sugarcane (sugar,molasses, and bagasse); and rice (bran and hulls) provided that storage intervals for these 171-4(k) studies did not exceed approximately 2-3 years.

cc: RF, SF, List A Rereg. F. Circ., DJM
RDI: Pilot Team:3/12/96;RPerfetti3/19/96;EZager:3/19/96.

Table 1. Percent recovery of 2,4-D-fortified samples following freezer storage at -12 to -27 C.

| Commodity | Matrix | Storage Interval | | | | |
|---|---|---|---|---|---|---|
| | | 0-day | 30-day | 90-day | 180-day | 365-day |
| Corn | Grain | 95, 118, 88 | 82, 104 | 101, 108 | 105, 99 | 91, 93 |
| | Forage | 95, 91, 89 | 97, 94 | 90, 94 | 93, 98 | 104, 96 |
| | Fodder | 97, 96, 96 | 96, 95 | 98, 92 | 82, 85 | 74, 98 |
| | Starch | 98, 102, 105 | 106, 112 | 106, 104 | 101, 111 | 98, 103 |
| | Flour | 74, 64, 81 | 90, 89 | 106, 105 | 89, 80 | 91, 100 |
| | Oil | 92, 92, 91 | 100, 88 | 99, 86 | 94, 87 | 90, 93 |
| Sorghum | Grain | 84, 83, 91 | 89, 89 | 92, 91 | 99, 103 | 87, 88 |
| Wheat | Grain | 79, 80, 84, 87 | 105, 105 | 90, 91 | 92, 94 | 98, 98 |
| | Forage | 84, 82 | 102, 102 | 93, 99 | 96, 97 | 91, 92 |
| | Straw | 81, 86, 93, 99 | 103, 102 | 95, 93 | 10, 88 | 100, 105 |
| | Flour | 91, 84, 84 | 95, 94 | 98, 101 | 89, 94 | 82, 100 |
| Sugarcane | Cane | 82, 86, 73 | 94, 90 | 102, 104 | 96, 97 | 93, 101 |
| | Sugar | 94, 86, 81 | 95, 95 | 92, 89 | 91, 83 | 88, 77 |
| | Molasses | 84, 85, 86 | 98, 95 | 95, 98 | 114, 112 | 100, 94 |
| | Bagasse | 73, 68, 75 | 91, 96 | 92, 96 | 90, 87 | 86, 84 |
| Rice | Grain | 110, 107, 109 | 98, 94 | 99, 101 | 87, 95 | 100, 97 |
| | Bran | 84, 92, 91 | 104, 96 | 96, 79 | 100, 102 | 88, 88 |
| | Hulls | 72, 73, 70 | 98, 98 | 103, 105 | 87, 78 | 99, 80 |
| Grass/Hay | Grass | 88, 91, 89, 98 | 96, 91 | 100, 101 | 97, 89 | 83, 86 |
| | Hay | 94, 86, 89 | 99, 86 | 96, 93 | 115, 110 | 90, 86 |
| Soybean | Seed | 86, 93 | 93, 95 | 98, 92 | 90, 71 | 96, 93 |

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