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

EXPEDITE

JUN 13 1990

Memorandum:

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP#9F3763. Nicosulfuron. Herbicide use in corn. (DEB#'s 6630, 6631, and 6632, no MRID#'s) Amendment dated 5/1/90.

FROM: Jerry B. Stokes, Chemist
Dietary Exposure Branch
Health Effects Division (H7509C)

THRU: Philip V. Errico, Section Head
Dietary Exposure Branch
Health Effects Division (H7509C)

TO: Robert Taylor, PM-25
Fungicide-Herbicide Branch
Registration Division (H7505C)

and

Toxicology Branch
Health Effects Division (H7509C)

The petitioner, DuPont Agricultural Products, has now submitted a cover letter dated 5/1/90, a revised CSF for ACCENT™ technical, a revised Section B, and product and residue data in reply to the outstanding deficiencies cited in the 4/23/90 review of PP#9F3763 (memo of J. Stokes).

Summary of DEB Comments/Conclusions:

All deficiencies for PP#9F3763 are now resolved. However, as stated in conclusion 5e, DEB still reserves the right to require ruminant and poultry feeding studies if real residues of DPX-V9360 occur in future proposed uses on livestock feed items.

DEB also suggests that the PM make EFGWB aware of the revised proposed rotational plantback schedule dated 5/1/90. Their review of 6/1/90 (S. Termes) did not address this revised Section B pertaining to rotational crops.

Recommendation:

TOX considerations permitting, DEB can recommend for the establishment of tolerances for the residues of nicosulfuron

(ACCENT™, DPX-V9360 technical, 3-pyridinecarboxamide, 2-((((4,6-dimethoxypyrimidin-2-yl)aminocarbonyl)aminosulfonyl) -N,N-dimethyl for the proposed herbicide use in/on raw agricultural commodities of corn grain (0.1 ppm), corn forage (0.1 ppm), corn fodder (0.1 ppm), and corn silage (0.1 ppm). No tolerances are proposed or needed at this time for milk, meat, fat, or meat by-products (including liver and kidney) of cattle, goats, hogs, horses, and sheep or, the meat, fat, and meat by-products (including liver and kidney) of poultry, or eggs.

Note to PM:

The petitioner has submitted a revised Section B in which the proposed crop rotational plantback directions have been changed. Therefore, DEB requests that EFGWB reevalute their commments (memo of 6/1/90) in reference to these revised crop rotational plantback directions dated 5/1/90. Their earlier comments (memo of 6/1/90) do not address the revised rotational plant schedule.

Detailed Considerations:

Deficiency #1a, memo of 4/23/90, J. Stokes:

"Petitioner must provide the Chemical Abstracts chemical reference nos. (CAS#'s), if and/or when available, for all impurities listed in the TGAI."

Petitioner's Response, dated 5/1/90:

The revised CSF contains the CAS numbers for all DPX-V9360 impurities currently available. The CAS numbers for the two outstanding compounds will be submitted when available. (See Confidential Appendix).

DEB's Comments/Conclusions:

Deficiency #1a is now resolved.

Deficiency #1b, memo of 4/23/90, J. Stokes:

"Petitioner must report data for one more batch of TGAI. Only the analyses for 4 batches are reported."

Petitioner's Response, dated 5/1/90:

The petitioner has submitted analysis data for an additional batch of DPX-V9360. (See Confidential Appendix).

DEB's Comments/Conclusions:

Deficiency #1b is now resolved.

Note: In the previous 4 batches, the % weight of the a.i. was less than the certified upper limit. This batch slightly exceeds the upper limit. If future batches in the production of this chemical exceed the upper limit, then the petitioner must submit a revised CSF.

Deficiency #1c, memo of 4/23/90, J. Stokes:

"Solubilities are listed for DPX-V9360 in benzene and tetrahydrofuran as 2.7 and 2.6, respectively, in MRID#409545-01, but as 1.7 and 26, respectively, in MRID#409242-03. The petitioner must clarify the correct solubilities."

Petitioner's Response, dated 5/1/90:

The correct values for benzene and tetrahydrofuran are 1.7 g/l and 26 g/l, respectively, as listed in MRID#409242-03.

DEB's Comments/Conclusions:

Deficiency #1c is now resolved.

Deficiency #1d, memo of 4/23/90, J. Stokes:

"Petitioner must submit a revised CSF for ACCENT™ Technical (352-LGL). The certified limit of one impurity is stated incorrectly. (See Confidential Appendix for more details.)"

Petitioner's Response, dated 5/1/90:

A revised CSF dated 5/1/90 has been submitted to correct the stated limit of one impurity. (See CSF for 352-LGL dated 5/1/90).

DEB's Comments/Conclusions:

Deficiency #1d is now resolved.

Deficiency #3a, memo of 4/23/90, J. Stokes:

"The nature of the residue in the corn plant is adequately understood for the proposed use, i.e., the primary residue of regulatory concern is the parent, DPX-V9360. The need to include metabolite pyridine sulfonamide will be determined after the requested residue data (See Conclusion 5b) have been reviewed."

Petitioner's Response, dated 5/1/90:

"It is felt that the data presented for the magnitude of the residue analysis of the metabolite pyridine sulfonamide as a response to Conclusion 5b obviates the need for it to be included as 'residue of regulatory concern' (Conclusion 3a) because concentration of this metabolite was below the quantitation limits (0.05 ppm) for corn samples treated at the proposed maximum application rate (70 g a.i./ha or 1 oz a.i./acre) or twice the maximum application rate at 8 different sites. Therefore, we believe that the following concerns/requests should not be required: a poultry metabolism

study (Conclusion 3d); analytical enforcement methods for cattle, horses, swine, and sheep meat, fat, and meat byproducts, including liver and kidney (Conclusion 4c); analytical enforcement methods for poultry meat, fat, and meat byproducts, including liver and kidney (Conclusion 4d); evaluation of FDA Protocol IV for pyridine sulfonamide (Conclusion 4e); determination for secondary residues in meat, milk, poultry and eggs according to 40 CFR 180.6(a) (Conclusion 5c); need for tolerances for meat, fat, and meat byproducts, including liver and kidney (Conclusion 5d); a ruminant study (Conclusion 5e); and a poultry feeding study (Conclusion 5f)."

The deficiencies mentioned in the petitioner's response in the above paragraph are as follows:

"3d. The nature of the residue in poultry may not be adequately understood. The need for a poultry metabolism study will be determined after the requested residue data (See conclusion 5b) have been reviewed.

4c. Analytical enforcement methods may be needed for cattle, horses, swine, and sheep meat, fat, and meat byproducts (including liver and kidney). The requested residue data (See conclusion 5b) must be reviewed before this need can be determined.

4d. Analytical enforcement methods may be needed for poultry meat, fat, and meat byproducts (including liver and kidney). The requested additional residue data (See conclusion 5b) must be reviewed before this need can be determined.

4e. DPX-V9360 was analyzed by the FDA Protocol IV. The parent did not give a detectable response on the HPLC/fluorescence detector system. No metabolites were analyzed. Protocols I, II, or III were not run because DPX-V9360 is thermally labile and not suitable for GLC analysis. If metabolite pyridine sulfonamide is added to the tolerance expression, then this residue must be evaluated with the FDA multiresidue protocols.

5c. DEB must first review the additional residue data (See conclusion 5b) before a determination can be made with respect to 40 CFR 180.6(a) for the secondary residues in meat, milk, poultry, and eggs.

5d. The need for tolerances for meat, fat, meat byproducts (including liver and kidney), or eggs of poultry can not be determined until the additional residue data (See conclusion 5b) have been reviewed.

5e. No ruminant feeding studies were submitted. The goat metabolism study adequately represented an exaggerated feeding level. DEB, at this time, will not require a ruminant feeding study. However, when real residues

of DPX-V9360 occur in livestock feed items, a ruminant feeding study may be required. Also, if the metabolite pyridine sulfonamide is determined to be of regulatory concern, then a ruminant feeding study may be needed.

5f. A poultry feeding study may be required, and is dependent upon the results of the requested additional residue data (See conclusion 5b)."

DEB's Comments/Conclusions:

Samples from 8 sites, selected from the magnitude of residue study of DPX-V9360 on corn, were analyzed for pyridine sulfonamide. No quantifiable residues (<0.05 ppm) of pyridine sulfonamide were detected in samples taken at or after the proposed 30-day PHI. Samples were analyzed from crops treated at either the 1X or 2X application rates. Samples analyzed included forage, middough (silage), stover (fodder), and grain.

Based upon the submitted data in response to deficiiency 5b, deficiencies #'s 3a, 3d, 4c, 4d, 4e, 5c, 5d, 5e, and 5f are now resolved. TOX considerations permitting, the tolerance will consist of the parent compound. However, as stated in Conclusion 5e, DEB still reserves the right to require ruminant and poultry feeding studies if real DPX-V9360 residues occur in future proposed uses on livestock feed items.

Deficiency #3b, memo of 4/23/90, J. Stokes:

"The pH of the soil used in the plant metabolism study must be submitted.

Petitioner's Response, dated 5/1/90:

The pH of the soil was determined in duplicate. The values are 6.9 and 7.1 as stated in Table I of the plant metabolism study report (MRID#410826-26).

DEB's Comments/Conclusions:

Deficiency #3b is now resolved.

Deficiency #4a, memo of 4/23/90, J. Stokes:

"An analytical enforcement method has been submitted for the parent only. The methodology is adequate for enforcement purposes for the residues of DPX-V9360 in corn forage and grain. Before we determine the adequacy of the proposed enforcement method on corn fodder, the petitioner should submit the characteristics of the corn fodder supplied to the Agency laboratory for the PMV, e.g., maturity at harvest, moisture content, with or without ears, etc. After reviewing this information the proposed enforcement method may require rewriting or modification for this commodity. The petitioner should also specify in the clarification/rewrite of the method that the pH levels of all mobile phases must be

closely monitored and maintained accurately according to instructions. The petitioner must properly define the Zorbax"Rx column. Is it a C8 or C18 bonded phase? No methods were submitted for any plant metabolites. If pyridine sulfonamide is added to the tolerance expression, then enforcement methodology and a method validation by the Agency laboratory will be needed."

Petitioner's Response, dated 5/1/90:

The petitioner has supplied the requested data for the corn fodder samples and has identified the Zorbax"R_X column. The petitioner has also submitted a rewrite of the analytical methodology (DuPont Study No. AMR-1260-88, Revision No. 1, dated 4/25/90) to emphasize the importance of accurate pH in the method, to address the potential for interference of the method by other pesticides also used on corn, to discuss the importance of the centrifugation in the method, and to discuss the necessary modification of the solvent volume and/or sample size for the analysis of extremely dry corn fodder samples.

DEB's Comments/Conclusions:

Adequate data has been submitted for the corn fodder samples. The rewritten analytical methodology adequately satisfies DEB's concerns in regards to control of pH of the mobile HPLC phase, and analysis of extremely dry corn fodder samples. Based upon the residue data submitted in response to Conclusion 5b, analytical methodology will not be needed for pyridine sulfonamide.

Deficiency #4a is now resolved.

Deficiency #4b, memo of 4/23/90, J. Stokes:

"Additional data, i.e., sample HPLC charts to adequately support the procedure outlined (i.e., pH alteration of HPLC solvent) for the analysis for DPX-V9360 residues in the presence of other interferring pesticides, should be submitted to DEB for review."

Petitioner's Response, dated 5/1/90:

The petitioner has submitted data in which 14 herbicides and insecticides, commonly used on corn, were tested for interference with the proposed analytical methodology. No interferences were detected. In addition, two Dupont sulfonylurea corn herbicide candidates, DPX-M6316 and DPX-E9636, were analyzed by the proposed method; both elute outside the effluent collection window and will not interfer with the analysis of DPX-V9360 residues.

DEB's Comments/Conclusions:

Deficiency #4b is now resolved.

Deficiency #5a, memo of 4/23/90, J. Stokes:

"The residue data adequately support the proposed 0.1 ppm tolerances for DPX-V9360 in/on corn forage, corn fodder, corn silage, and corn grain. However, based upon the submitted residue data these tolerances could possibly be decreased to 0.05 ppm. Before making a final conclusion on the appropriate tolerance levels in corn, additional residue data are required for parent DPX-V9360 in all corn r.a.c.'s from the states listed in the Group B and C on the proposed label. Also another PMV may have to be performed if our final recommendation is the 0.05 ppm level for the parent DPX-V9360.

Petitioner's Response, dated 5/1/90:

The most current label does not use the A, B, and C rotational crop grouping. The rotational crop plantback directions are now based on crop and soil pH. Studies from 12 representative test sites (8 states) were conducted with the herbicide DPX-V9360. Data are submitted for the DPX-V9360 application rate of 2.0 oz a.i./A (2X the maximum use rate) in various field corn varieties. Only two forage samples are reported at the proposed maximum use rate of 1.0 oz a.i./A. The soil pH ranged from 5.6 to 7.9. Treated and control samples of forage, silage, fodder, and grain were retrieved according to the following schedules:

Sampling Summary

Site	PHI (days) Forage	Silage	Fodder	Grain
Belleville, IL	30	80	120	120
Bluffs, IL	--	78	116	116
Eldridge, IA	15,29	--	---	---
Farmington, MN	15,29	57	120	120
Greenville, MS	30	83	104	104
Longmont, CO	28	82	117	117
Madera, CA	30	68	120	120
New Castle, IN	28	76	120	120
Palo, IA	29	--	---	---
Phelps, NY	30	89	116	116
Stockton, CA	30	78	110	110
Towanda, IL	32	62	107	107

West Fargo, ND was listed in Table 2, but no data was submitted in the packet for this site.

Residues of DPX-V9360 on Forage, Silage, Fodder, and Grain

Sample	Rate (oz a.i./A)[a]	PHI(days)	Residues (ppm)[b]
forage	1.0	15	<0.05 - 0.09[c]
		29	<0.05
forage	2.0	15	<0.05 - 0.35[d]
		29	<0.05 - 0.09[e]
silage	2.0	45-85	<0.05
fodder	2.0	72-128	<0.05
grain	2.0	72-128	<0.05

[a] 1.0 oz a.i./A and 2.0 oz a.i./A represent 1X and 2X, respectively.

[b] Analytical methodology measures parent, DPX-V9360, only.

[c] 2 samples (Eldridge, IA and Farmington, MN) gave residues ≥ limit of detection (0.05 ppm): 0.07 and 0.09 ppm.

[d] 2 samples (Eldridge, IA and Farmington, MN) gave residues ≥ limit of detection: 0.09 and 0.35 ppm.

[e] 2 samples (Eldridge, IA and Farmington, MN) gave residues ≥ limit of detection: 0.06 and 0.08 ppm.

No detectable residues (<0.05 ppm) were found in almost all of the samples of silage, fodder, or grain at 2X application rates at the proposed 30-day PHI. Only two sites gave DPX-V9360 residues >0.05 ppm (See footnotes in above table), but these levels were almost at the limit of detection (<0.05 ppm) by the proposed PHI of 30 days. Mean percent recoveries of fortified control samples ranged from 88 to 97%; standard relative deviations ranged from 6 to 8%. A total of 24 spiked control samples were run.

DEB's Comments/Conclusions:

Based upon previously and presently submitted residue data, and the corn plant metabolism data, it appears that DPX-V9360 rapidly degrades in corn, and that the concentration of the parent decreases below the 0.05 ppm detection limit within the proposed 30-day PHI at the maximum application rate of 1.0 oz a.i./A. This would adequately support the proposed 0.10 ppm tolerance on corn forage, silage, fodder, and grain when applied postemergence to corn at 1.0 oz a.i./A. DEB had previously questioned if the tolerances could be decreased from 0.1 ppm to 0.05 ppm. Applications at a 2X rate at several locations have yielded low,

but real DPX-V9360 residues in corn forage. With a normal 1X field application row overlap can actually become a 2X application rate. In addition, the submitted data support a 60-day PHI for corn silage, and a 90-day PHI for corn fodder and grain for DPXV9360 residues at a 0.05 ppm level; these PHI's could be included on the proposed label in addition to the 30-day PHI for forage. However, as an alternative, the 0.1 ppm tolerance would adequately cover any DPX-V9360 residues that might be present in silage, fodder, or grain without the requirement of the 60- and 90-day PHI's, respectively.

Therefore, DEB has determined that the proposed 0.1 ppm tolerances are adequate.

Deficiency #5a is now resolved.

Deficiency #5b, memo of 4/23/90, J. Stokes:

"Residue data are also required for the metabolite pyridine sulfonamide from six different US locations (3 samples of forage, 3 samples of fodder, and 3 samples of grain from each location) using samples which have already been analyzed for parent DPX-V9360. Appropriate storage stability data are also needed for the pyridine sulfonamide. The need for tolerances for metabolite pyridine sulfonamide will be determined after review of the requested field residue data."

Petitioner's Response, dated 5/1/90:

Samples from 8 sites, selected from the magnitude of residue study of DPX-V9360 on corn, were analyzed for pyridine sulfonamide. No quantifiable residues (<0.05 ppm) of pyridine sulfonamide were detected in samples taken at or after the proposed 30-day PHI. Samples were analyzed from crops treated at either the 1X or 2X application rates. Samples analyzed included forage, middough (silage), stover (fodder), and grain.

Pyridine sulfonamide was extracted from the matrix with acetone/water buffered with ammonium carbonate. The extract was centifuged, and the supernate acidified and partitioned with methylene chloride. The methylene chloride solution was adsorbed onto a silica gel Bond Elut™ column and eluted with acetonitrile/methylene chloride (1:1). The organic phase was evaporated and the residue dissolved in the mobile HPLC phase. The analysis was performed using normal phase HPLC equipped with a photoconductivity detector. Mean percent recoveries of pyridine sulfonamide from spiked matrices (0.1 ppm) were: forage 78%, silage, 77%, fodder 76%, and grain 79%. Standard relative deviations ranged from 9 to 13%.

A freezer-stored forage sample which had been treated with [pyridine-2-14C]DPX-V9360 were checked in regards to storage stability of pyridine sulfonamide. At day 0, the sample analyzed for 0.108 ppm pyridine sulfonamide and after 7 months analyzed for 0.107 ppm pyridine sulfonamide.

DEB's Comments/Conclusions:

Based on the submitted data, no quantifiable levels of pyridine sulfonamide should be in the r.a.c. commodities of corn foroge, silage, fodder, or grain. TOX considerations permitting, DEB does not recommend inclusion of this metabolite in the tolerance expression at this time.

Deficiency #5b is now resolved.

Deficiency #5g, memo of 4/23/90, J. Stokes:

"Food/feed additive tolerances may not be needed. No detectable DPX-V9360 residues (<0.05 ppm) were found in corn grain treated at 8.0 oz a.i./A (8X of label rate) or in the resulting processed commodities, corn oil or corn meal, from such grain. Storage stability data are adequate for the proposed herbicide use on field corn. However, these samples (grain, meal, and oil) must be analyzed for metabolite pyridine sulfonamide. Storage stability data should be included for this metabolite. The petitioner must also submit the pH of the soil used in the 8X application rate."

Petitioner's Response, dated 5/1/90:

The pH of the soil was 5.4.

The analysis of the grain from a crop treated with [pyridine-2-14C]DPX-V9360 at 1.0 oz a.i./A (proposed maximum rate) resulted in a total 14C-activity of 0.002 ppm, based on DPX-V9360 equivalents. If the total 14C-residue was comprised only of pyridine sulfonamide, then the concentration would be 0.001 ppm based on pyridine sulfonamide equivalents. Using a concentration factor of 25 for corn oil, in a worst-case scenario the concentration of pyridine sulfonamide would only be 0.025 ppm, one-half the quantitation limit (0.05 ppm).

Results from the analysis of pyridine sulfonamide in grain samples from field-treated corn (8 sites) showed the levels of pyridine sulfonamide to be below the limit of detection (0.05 ppm).

DEB's Comments/Conclusions:

DEB accepts the petitioner's explanation and concludes there is no need for food or feed additive tolerances for the proposed use on corn.

Deficiency #5g is now resolved.

Other Considerations:

In the previous memo of 4/23/90, I requested that EFWGB be made aware of the proposed crop rotational plantback directions.

Comments on the proposed crop rotational directions [See memo of 6/1/90, E. Regelman, EFGWB, (S. Termes, EFGWB reviewer)] have been forwarded to DEB.

However, in an amendment date 5/1/90 the petitioner has submitted a revised Section B in which the proposed crop rotational plantback directions have been changed. EFGWB should be made aware of these revised crop rotational plantback directions dated 5/1/90.

Attachment: Confidential Appendix: CBI (product chemistry for nicosulfuron), 3 pages

cc with Attachment: J. Stokes (DEB); PP#9F3763; Nicosulfuron S.F.; C. Furlow (PIB/FOD)
cc without Attachment: Kariya (DRES/SACB); S. Termes (EFGWB, H7507C); R.F.; Circulation (7)
RDI: PErrico:6/8/90:RLoranger:6/8/90
H7509C:DEB:JStokes:js:Rm 803C:CM#2:557-1478:6/11/90

PRODUCT CHEMISTRY

for

nicosulfuron

(DXP-V9360)

CONFIDENTIAL

Accent residue chemistry review

Page _____ is not included in this copy.

Pages 13 through 14 are not included in this copy.

The material not included contains the following type of information:

X Identity of product inert ingredients

___ Identity of product impurities

X Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

X The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
