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CONFIDENTIAL

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

APR 26

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: New chemical review of Express[R] [DPX-L5300].

FROM: Charles L. Trichilo, Ph. D., Chief
Residue Chemistry Branch,
Hazard Evaluation Division (TS-769C)

TO: Amy Rispin, Chief
Science Integration Staff
Hazard Evaluation Division (TS-769C)

and

R. Mountfort, PM 23
Herbicide/Fungicide Branch
Registration Division (TS-767C)

Attached is the Product Chemistry and Residue Chemistry review package for Express[R] [DPX-L5300] written in RCB.

These reviews include data received by RCB through Jan 1, 1988.

The RCB due date for these reviews is April 28, 1988. The HED due date for these reviews is May 19, 1988.

This is a first time, food-use permanent tolerance request for Express[R] [PP7F3540]. The reviews of the Product Chemistry and Residue Chemistry data have been formatted to serve as a DPX-L5300 Registration Standard.

RCB's Product Chemistry review of DPX-L5300 is for DPX-L5300 Technical only. As required by the Registration Standard Policy group, the product chemistry data for end-use products are not included in this review. Also, as requested by Mr. Herb Harrison of RD, RCB no longer addresses the physical/chemical properties of manufacturing-use products.

In accordance with instructions from Henry Jacoby, SIPS/HED, Table A's (Generic Data Requirements) for Product Chemistry (Express[R] Technical) and Residue Chemistry are not being

provided at this time. These tables will be generated by RCB when all the data deficiencies listed in these reviews have been filled.

Attachment #4 to this memorandum contains material claimed as Confidential Business Information (CBI). The cc distribution of the copies containing material claimed as CBI is indicated below.

ATTACHMENTS TO THIS MEMORANDUM:

Attachment #1:	New Chemical Residue Chemistry Review, Express[R] [DPX-L5300]	[40 pages]
Attachment #2:	International Residue Limit (Codex) Status Sheet	[1 page]
Attachment #3:	New Chemical Product Chemistry Review, DPX-L5300 (Technical)	[7 pages]
Attachment #4:	CONFIDENTIAL APPENDIXES A thru E to the New Chemical Product Chemistry Review, Express[R] (Technical).	

cc (Cover Memo only):
A. Barton/HED, J. Heckman/HED, H. Jamerson/IR-4

cc (Cover Memo plus the non-CBI Attachments, #1, 2, and 3):
Reading File, Circulation, R. Cook/RCB, H. Jacoby/HED.

cc (Cover Memo plus ALL Attachments):
PP7F3540, DPX-L5300 Registration Standard File, TOX (R. Gardner), ISB/PMSD (E. Eldredge).

TS-769C:RCB:Reviewer:RWCook:rwc:4/21/88:Rm810H:CM2:5577324.
RDI:Section Head:RSQuick:4/15/88:RDSchmitt:4/20/88.
RevPackRDI: Section Head: RSQuick:4/15/88: RDSchmitt: 4/20/88.

ATTACHMENT 1

APR 26 1988

MEMORANDUM

SUBJECT: PP7F3540. DPX-L5300 on Wheat and Barley.
MRID No. 402455-05, 402455-01, 402455-09, 402455-07, 402455-08, 402455-03, 402455-31 (1 of 2), 402455-31 (2 of 2), 402455-29, 402455-30. RCB # 2516, 2517.
Evaluation of Analytical Method and Residue Data.

FROM: R. W. Cook, Chemist
Tolerance Petition Section I
Residue Chemistry Branch,
Hazard Evaluation Division (TS-769C)

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

TO: R. Mountfort, PM 23
Herbicide/Fungicide Branch
Registration Division (TS-767C)

and

Toxicology Branch,
Hazard Evaluation Division (TS-769C)

Background

The petitioner, E. I. du Pont de Nemours & Company, Inc. proposes the establishment of permanent tolerances for residues of the herbicidal chemical methyl-2-[[[[N-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-methylamino]carbonyl]amino]sulfonyl]benzoate in or on wheat grain and barley grain at 0.05 ppm and in or on wheat straw and barley straw at 0.1 ppm, resulting from postemergence application to wheat and barley. The company designations for this chemical are DPX-L5300, IN-L5300, and L5300. There are no known ANSI or ISO names for this chemical. This chemical is also known as benzoic acid, 2-[[[[N-4-methoxy-6-methyl-1,3,5-triazin-2-yl)-N-methylamino]carbonyl]amino]sulfonyl], methyl ester. The chemical is the active ingredient in the formulated pesticide product designated as Express^{R} Herbicide Dry Flowable, containing 75% active ingredient. RCB has previously recommended for temporary tolerances for DPX-L5300 on subject commodities (see memo of 10-18-85, PP5G3296, J. M. Worthington).

DPX-L5300 is structurally related to another sulfonyl urea herbicide, metsulfuron methyl, (40 CFR 180.428), differing by a methyl group.

Since DPX-L5300 and metsulfuron methyl are both used on barley and wheat and have a common moiety, a paragraph in 40 CFR 180.3 specifying that residues resulting from application of both herbicides may not exceed the higher of the two established tolerances will be needed.

SUMMARY OF DEFICIENCIES

Proposed Tolerances

We withhold judgement on the adequacy of the proposed tolerances pending completion of method validations by COB/BUD chemists and receipt/review by RCB of the report from COB on the results of these validations, and further, pending submission of adequate residue data for DPX-L5300 in wheat and barley grain and straw (See **Magnitude of the Residue** below).

Residue Analytical Methods.

We withhold judgement on the adequacy of these analytical methods for residue data gathering and/or enforcement purpose pending completion of method validations by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of these validations.

Recovery data by the modified analytical method are needed.

FDA Multiresidue Protocols.

FDA multiresidue information via protocols I through IV must be submitted for DPX-L5300. Testing through these four protocols may be required for any additional metabolites of toxicological concern.

Nature of the Residue

Plants:

The petitioner should verify the accuracy of the reported value, 0.90 ppm of unknown phenyl ^{14}C in straw [Table 8, MRID 402455-03]. If this value is correct, additional plant metabolism studies will be required to identify these unknowns.

We defer to TOX Branch the question whether plant metabolites are of toxicological concern and whether they should be included in the tolerance expression. Further, we believe that metsulfuron methyl, a herbicide in its own right and a metabolite of Londax^{R}, should be included in the tolerance expression.

Animals:

In order to determine the need for a tolerance and the appropriate tolerance levels in animal tissues, animal metabolism and animal feeding studies are required. Apparent real detectable residues of DPX-L5300 are found in the animal feed item straw (from exaggerated application rates and at PHI greater than 40 day PHI proposed).

If Toxicology Branch concludes that there are additional compounds of toxicological concern, additional animal metabolism and animal feeding studies of such additional metabolites may be required.

Magnitude of the Residue:

We conclude that the submitted residue data for DPX-L5300 in wheat grain and straw and barley grain and straw are not sufficient to conclude that residues of DPX-L5300 will not exceed the proposed tolerances at the proposed 40 day PHI. Additional residue data reflecting the use as proposed, i. e. 40 day PHI and adequate geographic representation are needed. Data should be from the same states as the existing data.

Magnitude of the Residue in Processed Commodities:

A processing study using samples treated with the "highest practical exaggeration rate" should be conducted and the results submitted for review. Residue data should be submitted for wheat bran, flour, middlings, and shorts, and for barley hulls, bran, flour, and pearl barley. Appropriate food/feed additive tolerances should be proposed for wheat milling fractions, and barley milling fractions, if needed.

Storage Stability Data:

If additional metabolites of toxicological concern are regulated, storage stability data will be required.

Meat, Milk, Poultry and Eggs:

Since apparent real residues of DPX-L5300 have been found in straw (albeit, from exaggerated application rates and longer PHI than currently proposed) residue data for meat, milk, poultry and eggs are required

TOPICAL SUMMARIES FOR RESIDUE CHEMISTRY:

A. Background

This is the first request for permanent tolerances for the herbicide DPX-L5300. Currently, temporary tolerances established under PP5G3296 are in effect for residues of DPX-L5300 in or on wheat and barley grain.

B. Proposed Tolerances

We withhold judgement on the proposed tolerances pending completion of method validations by COB/BUD chemists, and receipt/ review by RCB of the report from COB on the results of these validations. See SUMMARY OF DEFICIENCIES above

If and when tolerances are established under this petition, 40 CFR 180.3 will need to be amended to specify maximum tolerance levels for residues of DPX-L5300 and metsulfuron-methyl, which have common metabolites.

C. Chemical Identity

The chemical identity of the active ingredient DPX-L5300 in Express^{R} Herbicide is discussed in the New Chemical Product Chemistry Review, which see.

D. Directions for Use

Express^{R} Herbicide is recommend for selective postemergence control of broadleaf weeds in wheat and barley at rates of 1/6 to 1/3 ounce of Express^{R} per acre.

E. Nature of the Residue

1. Plants

In wheat forage and straw, the terminal residue appears to be sulfonamide urea and saccharin, hydroxylated saccharin, and glucose conjugated saccharin.

In wheat grain, the terminal residue of the phenyl ^{14}C label appears to be sulfonamide urea. Since the amount of triazine ^{14}C label was too low, the terminal residue of the triazine ^{14}C label was not identified in this study.

No data on the metabolism of DPX-L5300 in barley plants are presented. It is concluded that the metabolic pathways of DPX-L5300 in barley would be similar to the metabolic pathways in wheat. No additional metabolism data are required for barley.

We defer to TOX Branch the question whether plant metabolites are of toxicological concern and whether they should be included in the tolerance expression. Further, we believe that metsulfuron methyl, a herbicide in its own right and a metabolite of Londax^{R}, should be included in the tolerance expression.

2. Animals

No information is provided on the metabolism of the active ingredient in animals.

In order to determine the need for a tolerance and the appropriate tolerance levels in animal tissues, an animal metabolism study is required pursuant to 40 CFR 158.125(a).

Apparent real detectable residues of DPX-L5300 are found in the animal feed item straw (from exaggerated application rates and at PHI greater than 40 day PHI proposed), and therefore, animal metabolism and animal feeding data are required. If Toxicology Branch concludes that there are additional compounds of toxicological concern, additional animal metabolism and animal feeding studies of such additional metabolites may be required.

F. Residue Analytical Methods

We withhold judgement on the adequacy of these residue analytical methods for residue data gathering and/or enforcement purpose pending completion of method validations by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of these validations.

Recovery data by the modified analytical method are needed.

FDA multiresidue information via protocols I through IV must be submitted for DPX-L5300.

In the event that additional metabolites of toxicological concern must be regulated, adequate analytical methods for the detection and quantitation of such metabolites must be submitted. Testing through the four FDA protocols may be required for any additional metabolites of toxicological concern.

G. Storage Stability Data

We withhold judgement on the adequacy of these data on the storage stability of DPX-L5300 residues in wheat and barley grain and straw pending completion of method validations by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of these validations.

If additional metabolites of toxicological concern are regulated, additional storage stability data for such metabolites will be required.

H. Magnitude of the Residue

We withhold judgement on the adequacy of these residue data pending completion of method validations by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of these validations.

Apparent real residues of DPX-L5300 have been found in the livestock feed item straw (from exaggerated rates but longer PHI than the proposed PHI) and therefore animal metabolism and animal feeding studies will be required. Residue data

for meat and milk are required; we withhold judgement regarding the need for residue data from poultry and eggs, pending a determination of the adequacy of the analytical method for DPX-L5300 in grain (See **Residue Analytical Methods** above).

Additional residue data are needed on wheat grain and straw and barley grain and straw reflecting the proposed 40 day PHI.

I. Tolerance Assessment

If/when the permanent tolerances for this present petition are favorably recommended for, a request for an updated TAS assessment will be initiated by this Branch. Any TAS review which is then performed will issue as a separate memo, directed to the Product Manager (R. Mountfort, PM 23, Herbicide/Fungicide Branch.

J. International Harmonization

There are no Canadian or Mexican IRLs established for Express^{R}, and no Codex proposals for Express^{R} at Step 6 or above. The question of compatibility or harmonization of the tolerance expression and/or residue levels does not arise in connection with the review of this petition.

K. Other Considerations

No **"OTHER CONSIDERATIONS"** apply in the review of this petition.

DETAILED CONSIDERATIONS:

Manufacturing Process and Formulation:

Summary:

The chemical identity of the active ingredient DPX-L5300 in Express^{R} Herbicide is discussed in the New Chemical Product Chemistry Review, an attachment to this review, which see.

Discussion:

The manufacturing process for DPX-L5300 is discussed in the confidential appendix to J. M. Worthington review dated 10-18-85 in regard to PP5G3296, which see.

The product Express^{R} Herbicide is formulated to contain 75% active ingredient in a dry flowable powder intended to be mixed

with water. See the above mentioned Confidential Appendix to PP5G3296.

The chemical identity of the active ingredient DPX-L5300 in Express[R] Herbicide is discussed in the New Chemical Product Chemistry Review, which see.

Proposed Use:

Summary:

Express[R] Herbicide is recommend for selective postemergence control of broadleaf weeds in wheat and barley at rates of 1/6 to 1/3 ounce of Express[R] per acre.

Discussion:

Express[R] Herbicide is recommend for selective postemergence control of broadleaf weeds in wheat and barley.

Apply 1/6 to 1/3 oz. "Express"[R] per acre to wheat or barley for control and/or partial control.

Apply 1/4 to 1/3 oz. "Express"[R] when weed infestation is heavy or application timing and environmental conditions are marginal.

"For best control use 1/3 oz. 'Express'[R] per acre."

"Apply uniformly using properly calibrated air or ground equipment. Use at least 3 gallons of spray volume per acre by air or 5 gallons per acre by ground."

"Pest stage: Annual broadleaf weeds should be past the cotyledon stage, actively growing and less than 4 inches tall or across."

"Crop Stage: Apply after the crop is in the 2-leaf stage but before the boot-stage (Zadoks 12-39). Do not apply 'Express'[R] within 40 days of harvest."

"Do not apply 'Express'[R] through any type of irrigation system."

"Do not graze or feed forage or hay from treated areas to livestock."

"Do not apply to wheat or barley crops underseeded with another crop."

"Express^{R} may be tank mixed with suitable registered herbicides to control weeds other than those listed."

"DO NOT tank mix with 'Hoelon' 3EC [1] as grass weed control may be reduced."

NATURE OF THE RESIDUE:

Summary.

In wheat forage and straw, the terminal residue of the phenyl ^{14}C label appears to be sulfonamide urea and saccharin, hydroxylated saccharin, and glucose conjugated saccharin.

In wheat grain, the terminal residue of the phenyl ^{14}C label appears to be sulfonamide urea. Since the amount of triazine ^{14}C label was too low, the terminal residue of the triazine ^{14}C label was not identified in MRID 402455-30.

Previous studies with excised wheat plants showed ^{14}C-triazine metabolites include metsulfuron-methyl, O-demethyl-triazine amine and N-demethyl triazine amine.

No data on the metabolism of DPX-L5300 in barley plants are presented. It is concluded that the metabolic pathways of DPX-L5300 in barley would be similar to the metabolic pathways in wheat. No additional metabolism data are required for barley.

The petitioner should verify the accuracy of the reported value, 0.90 ppm of unknown ^{14}C in straw. If this value is correct, additional plant metabolism studies will be required to identify these unknowns.

Discussion.

Plants

The short-term metabolism of either phenyl or triazine ^{14}C-DPX-L5300 in excised wheat seedlings has been discussed (J. M. Worthington, PP5G3296, Oct. 18, 1985). That study, an interim report, was considered adequate for the purposes of establishing temporary tolerances, but for establishing permanent tolerances, ^{14}C-studies of metabolism under field conditions would be required.

Previous studies with excised wheat plants showed that ^{14}C-triazine metabolites include:

DPX-L5300 (6%)

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[1] Trademark of Hoechst-Roussel Agri-Vet Company.

4-methylamino-6-methyl-1,3,5-triazin-2-ol (27%)
[O-demethyl triazine amine];
4-methyloxy-6-methyl-1,3,5-triazin-2-amine (17%)
[N-demethyl triazine amine];
metsulfuron-methyl (4%)
hydroxylated DPX-L5300 (5%) [tentative identification].

These same studies with excised wheat plants showed one ^{14}C-phenyl metabolite:

methyl 2-(aminosulfonyl) benzoate (24%)
[also reported as a metabolite of metsulfuron methyl].

Remaining ^{14}C-phenyl metabolites were minor, unidentified amounts of ^{14}C.

In the study titled "The Metabolism of [Phenyl(U)-^{14}C] and Triazine-2-^{14}C] DPX-L5300 in Field Grown Wheat" by D. L Ryan, and J. J. Dulka, (MRID 402455-30) DPX-L5300 was applied foliarly to winter wheat (variety Arthur 71 variety) in the tiller stage at about 1 ounce a.i./A. The active ingredient was radiolabeled uniformly in the phenyl ring or the 2-position of triazine moiety. The radiolabeled active ingredient was dissolved in water: acetone: surfactant WK (193:7:0.26 v/v/v). Samples were taken at 0 days (after application spray dried) and at 4, 8, 14, 21, 28, and 63 days (maturity) after application by cutting 30-40 plants at the soil line with scissors. Samples were frozen until analysis. Appropriate sample aliquots were taken at various intervals for combustion and LSC of total radioactivity. Immature foliage (forage), grain, and straw were analyzed separately. Phenyl-^{14}C treated wheat grain was extracted with (4:1 v/v) acetone:0.1 M ammonium carbonate; triazine-^{14}C treated wheat grain was extracted with (3:1 v/v) methanol:2.0 M ammonium carbonate. Up to 93%, 70%, and 67% of the phenyl-^{14}C was extracted from immature foliage (forage), mature grain, and straw respectively. For triazine-^{14}C, up to 93%, 61%, and 60% was extracted from immature foliage (forage), mature grain, and straw respectively. The remaining amounts were considered unextractable. However, further extraction of the mature straw released the indicated additional percentage of ^{14}C (from phenyl-^{14}C and triazine-^{14}C, respectively): sonication @ 50^{o} C with ammonium carbonate 7.8% and 7.6%; cellulase incubation 2.8% and 4.6%; protease incubation 2.6% and 5.3%; HCl reflux 9.9% and 8.1%; and bound residue 9.8% and 14.4%; a total of additional extraction 33% and 40%.

The foliage extracts were concentrated by removal of acetone through rotary evaporation, leaving aqueous ammonium carbonate extracts. These aqueous extracts were partitioned with methylene chloride (twice the aqueous volume) for 3 to 7 times to remove plant pigments. The methylene chloride extracts were concentrated by rotary evaporation.

The methylene chloride extracts were analyzed by thin-layer chromatography (TLC) and high-performance liquid chromatography (HPLC). The thin-layer chromatography mobile phase was methylene chloride:methanol:1 M ammonium hydroxide (185:12:3 v/v/v). Reference compounds were located by fluorescence quenching while ^{14}C was located by autoradiography. Zones of ^{14}C were scraped from the thin-layer chromatography plate. For high-performance liquid chromatography (HPLC), aliquots of methylene chloride extracts were diluted with acetonitrile and then concentrated to appropriate volume. The phenyl-^{14}C was analyzed using gradient program 1 while the triazine-^{14}C was analyzed by gradient program 2. Both gradient programs are available in the submission. High-performance liquid chromatography (HPLC) fractions were collected at the retention times of reference standards (times verified daily) and ^{14}C analyzed by LSC.

The aqueous extracts were analyzed by TLC and HPLC. For thin-layer chromatography, the extract was diluted to known volume, the pH adjusted to 3.5-4.0 with 1.0 M phosphoric acid, and extracted three times with methylene chloride. The methylene chloride volume was reduce and samples developed on TLC plate with a mobile phase of toluene:acetone:methanol:ammonium hydroxide 50:50:25:1 v/v/v/v. For high-performance liquid chromatography (HPLC) the sample was adjusted to pH 2.6-2.8 with 1.0 M phosphoric acid and frozen immediately in dry ice:acetone mixture. After freeze-drying to remove water, the resulting residue was taken up in starting mobile phase, centrifuged, and analyzed by the appropriate gradient program for phenyl-^{14}C or triazine-^{14}C.

The concentration of ^{14}C in wheat forage was 5.5 ppm phenyl-^{14}C and 4.2 ppm triazine-^{14}C at day 0 (in tillering stage) and 0.75 and 0.5 ppm respectively at 28 days after treatment. Mature straw contained 0.55 ppm and 0.37 ppm of phenyl-^{14}C and triazine-^{14}C respectively, and grain 0.05 ppm and 0.01 ppm of phenyl-^{14}C and triazine-^{14}C respectively.

CONCENTRATION OF TOTAL ^{14}C IN WHEAT TISSUES. (PPM)

Time (Days)	Sample Type	[Phenyl-^{14}C]	[Triazine-^{14}C]
0	Forage	5.49	4.23
4	Forage	2.84	1.48
8	Forage	1.85	1.53
14	forage	1.11	0.70
28	Forage	0.75	0.51
63	Straw	0.55	0.37
63	Grain	0.05	0.01

Table 2: MRID 402455-03

RESIDUE LEVELS OF DPX-L5300 AND PHENYL-^{14}C METABOLITES IN WHEAT FORAGE AND STRAW (PPM)

	Days						
Metabolite	0	4	8	14	28	63	
DPX-L5300	3.55	0.19	0.07	0.03	0.01	0.01	
Saccharin	0.51	0.16	0.07	0.04	0.03	0.01	
Glu-Con-metsulfuron methyl	0.03	0.42	0.29	0.17	0.10	0.03	
Glu-Con-saccharin	0.02	0.11	0.12	0.12	0.12	0.04	
Hydroxylated-saccharin	0.01	0.20	0.17	0.10	0.05	0.04	
Hydroxyl.-metsulfuron methyl	0.06	0.04	0.03	0.01	0.01	0.01	
Sulfonamide	0.06	0.13	0.07	0.03	0.02	0.01	
Hydroxylated sulfonamide	0.10	0.14	0.06	0.04	0.03	----	
Sulfonamide urea	0.02	0.06	0.07	0.03	0.02	0.03	
DPX-L5300 acid	0.04	0.02	0.01	0.01	a	a	
Metsulfuron methyl	0.10	0.02	0.01	0.01	a	a	
Unknown P4	0.03	0.01	0.10	0.06	0.05	0.02	
Unknown P5	a	0.16	0.12	0.07	0.07	0.02	
All other unknowns	0.37	0.51	0.30	0.19	0.14	0.90	**

a = <0.01

Table 8: MRID 402455-03

** This value appears incorrect. The petitioner should verify the accuracy of this value. If this reported value, 0.90 ppm of unknown ^{14}C in straw is correct, additional plant metabolism studies will be required to identify these unknowns.

RESIDUE LEVELS OF DPX-L5300 AND TRIAZINE ^{14}C METABOLITES IN WHEAT FORAGE AND STRAW (PPM)

	Days					
Metabolite	0	4	8	14	28	63
DPX-L5300	3.45	0.06	0.02	a	a	a
Triazine amine	0.20	0.03	0.01	a	a	a
-Hydroxyl.triazine amine	0.01	0.09	0.09	0.04	0.03	0.01
O-Demethyl triazine amine	0.02	0.11	0.13	0.06	0.04	0.01
N-Demethyl triazine amine	a	0.03	0.04	0.01	0.01	0.01
Glu-Con-metsulfuron methyl	0.01	0.32	0.36	0.17	0.10	0.03
Hydroxyl. metsulfuron methyl	0.01	0.02	0.01	0.01	a	0.01
O-Dem.-N-Dem.Triazine amine	a	0.01	0.02	0.01	0.01	0.01
DPX-L5300 acid	0.01	a	a	a	a	a
Metsulfuron methyl	0.02	0.01	a	a	a	a
Unknown T7	0.01	0.07	0.11	0.06	0.05	0.01
Unknown T10	a	0.03	0.05	0.03	0.03	0.02
Unknown T11	0.01	0.06	0.08	0.04	0.03	0.03
All other unknowns	0.12	0.21	0.18	0.08	0.05	0.04

a = <0.01

Table 9: MRID 402455-03

RESIDUE LEVELS OF DPX-L5300 AND PHENYL-^{14}C METABOLITES IN WHEAT GRAIN

Metabolite	% Total Radioactivity	PPM
Saccharin	44.6	0.02
Glu-Con-saccharin	1.9	a
Hydroxylated-saccharin	11.3	a
Sulfonamide	3.5	a
Sulfonamide urea	1.7	a
All other unknowns	5.2	a

a = <0.01

Table 10: MRID 402455-03

The actual concentration of unextractable ^{14}C in forage was <0.1 ppm (both 14C labels, through 28 days), while in mature straw <0.2 ppm was unextractable (both ^{14}C labels, at 63 days).

Forage and straw: In mature straw, the extractability of ^{14}C ranged 52% to 68% (from both radiolabels). When exhaustive extraction procedures were applied to unextractable ^{14}C in mature straw, additional amounts of ^{14}C were released, leaving only 10%-15% (phenyl-^{14}C and triazine-^{14}C respectively) of the total ^{14}C unextractable.

DPX-L5300 ^{14}C-phenyl metabolites in wheat green forage included saccharin, glucose conjugate of metsulfuron methyl, glucose conjugate of saccharin, hydroxylated saccharin, hydroxylated sulfonamide, sulfonamide, and sulfonamide urea. DPX-L5300 ^{14}C-phenyl metabolites in wheat straw were glucose conjugate of metsulfuron methyl, glucose conjugate of saccharin, hydroxylated saccharin, and sulfonamide urea.

DPX-L5300 ^{14}C-triazine metabolites in wheat green forage included glucose conjugate of metsulfuron methyl, O-demethyl triazine amine, and -hydroxylated triazine amine. In wheat straw the major metabolite was glucose conjugate of metsulfuron methyl.

Grain: The triazine-^{14}C in grain was <0.01 ppm, too small to analyze by high-performance liquid cochromatography.

When phenyl-^{14}C treated grain containing 0.05 ppm was analyzed, no DPX-L5300 was found. The primary phenyl-^{14}C grain metabolite was isolated and partially purified by solid sorbant

extraction on C-18 Bond Elut columns prior to thin-layer chromatography analysis. Small portions of the partially purified grain metabolites were hydrolyzed (both acidic and alkaline conditions) and compared by high-performance liquid chromatography (HPLC) to the hydrolyzed reference chemical sulfonamide urea. Under alkaline conditions, both the extract material and reference material were shown to decompose to acid sulfonamide urea.

Sulfonamide urea comprised 45% of the total radioactivity in grain. Metabolites detected in smaller amounts include saccharin 11.3%; hydroxylated saccharin 3.5%, sulfonamide 1.9%, glucose conjugate of saccharin 1.7%, and unknowns 5.2%. Thus, in phenyl-^{14}C treated wheat grain, about 65% of the ^{14}C residue is identified, and about 35% is unextractable or unidentified extractable.

We defer to TOX Branch the question whether plant metabolites are of toxicological concern and whether they should be included in the tolerance expression. Further, we believe that metsulfuron methyl, a herbicide in its own right, should be included in the tolerance expression.

Animals:

Summary.

No information is provided on the metabolism of the active ingredient in animals.

Apparent real detectable residues of DPX-L5300 are found in the animal feed item straw (from exaggerated application rates and at PHI greater than 40 day PHI proposed), and therefore, animal metabolism and animal feeding data are required. If Toxicology Branch concludes that there are additional compounds of toxicological concern, additional animal metabolism and animal feeding studies of such additional metabolites may be required. In order to determine the need for a tolerance and the appropriate tolerance levels in animal tissues, an animal metabolism study is required pursuant to 40 CFR 158.125(a).

Discussion.

No information is provided on the metabolism of the active ingredient in animals.

However, since apparent real detectable residues of DPX-L5300 are found in the animal feed item straw (from exaggerated application rates and at PHI greater than 40 day PHI proposed), animal metabolism and animal feeding data are required. If

Toxicology Branch concludes that there are additional compounds of toxicological concern, additional animal metabolism and animal feeding studies of such additional metabolites may be required.

RESIDUE ANALYTICAL METHOD:

Summary.

We withhold judgement on the adequacy of these analytical methods for residue data gathering and/or enforcement purpose pending completion of method validations by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of these validations.

Recovery data by the modified method should be submitted.

In the event additional metabolites of toxicological concern must be regulated, adequate analytical methods for the detection and quantitation of such metabolites must be submitted.

FDA multiresidue information via protocols I through IV must be submitted for DPX-L5300. Testing through these four protocols may be required for any additional metabolites of toxicological concern.

Discussion.

The proposed analytical method is DuPont Study No. AMR-337-85, Revision A "Determination of Residue of DPX-L5300 in Crops by Liquid Chromatography" by L. W. Hershberger and N. S. Heckendorn, dated January 30, 1986 (MRID 403036-01). The method is a modification of AMR-337-85 which was considered in PP5G3296 (J. M. Worthington, 10-18-85). The modifications include the substitution of a micro-Porasil^{R} column for Zorbax^{R}-SIL column in the liquid chromatograph and the use of cyclohexane, 2-propanol, methanol mixture as mobile phase instead of cyclohexane, 2-propanol, acetonitrile.

In brief, the method uses an acetonitrile extraction of 10 grams of wheat grain or wheat green forage, or 5 grams of wheat straw with 120 ml of solvent. The samples were homogenized with a Tissumiser^{R} and then centrifuged at 2500 rpm for 5 minutes. Samples were extracted twice more with 100 ml. of acetonitrile and combined with the first extract. The extract was evaporated on a rotary evaporator until only 1 ml of acetonitrile remained, and the final drying was done with nitrogen.

Adsorbosil^{R}-LC silica cleanup columns were prepared by slurrying the silica with 2-propanol and pouring the slurry into 75 ml. Bond Elute^{R} column equipped with 20 m frit. Silica was also covered with frit. The columns were washed with 75 ml. of

chloroform, but the elution was stopped to avoid pulling air into the washed silica. Samples were transferred to the silica columns with 3 x 5 washes with chloroform and the interior of the column rinsed with another 10 ml. chloroform. The column was then eluted with 60 ml of a solution of cyclohexane [925 ml] : 2-propanol [50 ml] : methanol [35] : glacial acetic acid [5 ml] : deionized water [50 l]. The chloroform and the above solvent mixture washes were discarded. The DPX-L5300 was eluted from the column with an additional 50 ml of the above solvent mixture. The eluant was carefully taken to dryness on the N-VAP^{R} evaporator. Prior to HPLC analysis, the dried samples were stored at 4 C.

High-performance liquid chromatography (HPLC) was performed on a micro-Porasil^{R} column in a Waters liquid chromatograph equipped with Tracor Model 695 photo-conductivity detector. The detector was modified by removing ion exchange resin tube and pump, and by using a metering valve to balance flow through reference and analytical conductivity cells. The mobile phase solution and the sample solvent solution consisted of cyclohexane [780 ml] : 2-propanol [110 ml] : methanol [110]. The mobile phase solution (but not sample solvent solution) also contained glacial acetic acid [1 ml] : deionized water [100 l]. The column conditioning solvent of 2-propanol [400 ml] : methanol [400] : glacial acetic acid [200 ml] : deionized water [40 ml] were used to condition new silica column and to recondition older contaminated columns. Analysis included injection volume of 25 l, flow rate 0.5 ml/min, oven temperature of 35 C and detector attenuation of 1 x 2.

Results were calculated according to the equation:

$$C = \frac{(P)\ \ (V)}{(S_a)\ \ (W)}$$

where C = sample concentration, P is sample peak height, V is the final sample volume in ml., S_a is the average sensitivity of the standard, and W is the weight of sample in grams.

An EPA method validation/method trial in our Beltsville laboratories has been requested (see memo of R. W. Cook, 9/14/87).

The proposed method is reported to be sensitive to 0.01 ppm DPX-L5300 in grain and 0.02 ppm in straw, although Section G (PP7F3540) reports the proposed grain tolerance 0.05 ppm is 2.5 times the quantitation limit of the method. Final conclusions on the adequacy of the proposed analytical method awaits successful completion of the requested method validation in our laboratories.

Recovery data presented in PP5G3296, Determination of Residues of DPX-L5300 in Crops by Liquid Chromatography, by L. W. Hershberger and N. S. Heckendorn, Report AMR-337-85, Tab 27, Section D, Vol. I of V, marked "Trade Secret" (MRID 073785) are shown in the table below:

Recovery of DPX-L5300

Crop	Samples	Fortific.	Recovery %	Average %
Barley grain	2	0.01 - 0.02	85 - 109	97
Barley Straw	4	0.02 - 0.04	73 - 118	89
Wheat Grain	11	0.01 - 0.02	70 - 108	90
Wheat Straw	9	0.02 - 0.04	70 - 110	88
Wheat Green Forage	3	0.01 - 0.10	75 - 85	81

Additional recovery data (and including the above presented recovery data) are presented in PP7F3540, Determination of Residues of DPX-L5300 in Crops by Liquid Chromatography, by L. W. Hershberger and N. S. Heckendorn, Report AMR-337-85, Revision A, dated 1/30/86 (MRID 403036-01) are shown in the table below:

Recovery of DPX-L5300

Crop	Samples	Fortific.	Recovery %	Average %
Barley Grain	10	0.01 - 0.02	79 - 112	97
Barley Straw	12	0.02 - 0.04	68 - 118	84
Wheat Grain	15	0.01 - 0.02	70 - 108	91
Wheat Straw	14	0.02 - 0.04	65 - 110	83
Wheat Green Forage	3	0.01 - 0.10	75 - 85	81

Further residue recovery data are presented in MAGNITUDE OF THE RESIDUES ON GRAIN AND STRAW FROM WHEAT AND BARLEY AFTER TREATMENT WITH EXPRESS® HERBICIDE by Richard A. Guinivan, Report No. AMR-841-87, dated 4/20/87 (MRID 402455-29). These data reflect recovery values in several laboratories:

Recovery of DPX-L5300

Crop & Lab No.	Samples	Fortific.	Recovery %	Average %
Barley Grain 1	6	0.01 - 0.02	85 - 110	101
Barley Straw 1	8	0.02 - 0.04	70 - 118	85
Wheat Grain 1	12	0.01 - 0.02	70 - 110	92
Wheat Straw 1	10	0.02 - 0.04	70 - 110	83
Barley Grain 2	8	0.02 - 0.04	76 - 97	85
Barley Straw 2	6	0.05 - 0.1	73 - 100	82
Wheat Grain 2	8	0.01 - 0.02	75 - 100	89
Wheat Straw 2	2	0.05 - 0.075	79 - 82	81
Barley Grain 3	1	0.02	105	105
Barley Straw 3	1	0.04	85	85

Wheat Grain	3	3	0.01 - 0.04	55 - 95	80
Wheat Straw	3	1	0.04	95	95
Barley Grain	4	12	0.01	86 - 117	99 *
Barley Straw	4	10	0.02	71 - 115	91 *
Wheat Grain	4	20	0.01	81 - 112	98 *
Wheat Straw	4	22	0.02 - 0.2	74 - 120	95 *

* Recoveries corrected for background.

The above listed recovery data are derived from the unmodified residue analytical method. The petitioner asserts that the modifications will have no effect on recovery data which were obtained by the method without modification. While it appears that the unmodified method (i.e., Report AMR-337-85) provides adequate recovery, we have no evidence that the modified method provides adequate recovery. We conclude recovery data by the modified method are required.

We withhold judgement on the adequacy of these analytical methods for residue data gathering and/or enforcement purpose pending completion of method validations by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of these validations.

The petitioner questions the need for FDA multiresidue information by Protocols I through IV, stating that they have a lack of clarity on exactly what is being asked for by the EPA. They do report that the molecular structure of DPX-L5300 will not survive GC injection temperatures, will not derivatize under Protocol IV and does not have significant natural fluorescence. (MRID 402455-31). We conclude that FDA multiresidue information via protocols I through IV must be submitted for DPX-L5300. Testing through these four protocols may be required for any additional metabolites of toxicological concern.

In the event additional metabolites of toxicological concern must be regulated, adequate analytical methods for the detection and quantitation of such metabolites must be submitted.

STORAGE STABILITY

Summary. Frozen storage of wheat grain and wheat straw samples does not adversely affect the residue levels of DPX-L5300.

Residue levels of DPX-L5300 decrease in wheat and barley grain and straw stored under ambient conditions.

Storage stability data are needed for any additional metabolites of toxicological concern.

Discussion.

Frozen Storage

(MRID 402455-29):

Untreated samples of wheat grain and wheat straw were fortified with solutions of DPX-L5300 at 0.1 ppm concentration and sample containers were removed at various intervals and analyzed according to method AMR-337-85, Revision A (1/30/86). In frozen storage for intervals up to 21 months, DPX-L5300 was recovered from wheat grain and straw at levels greater than 86%. The petitioner concludes that freezer storage of wheat grain and wheat straw samples does not adversely affect the residue levels of DPX-L5300. We concur with the petitioner's conclusions in this respect. Although barley grain and barley straw samples were not subject to the frozen storage stability tests herein, we consider the wheat studies to be adequate to cover the storage stability of DPX-L5300 in barley grain and straw.

If additional metabolites of toxicological concern are regulated, storage stability data will be required.

Ambient Storage

(MRID 402455-29):

Untreated samples of wheat grain, wheat straw, barley grain and barley straw were fortified with solutions of DPX-L5300 at 0.1 ppm (grain) and 0.2 ppm (straw) concentration and sealed in glass containers. Sample containers were removed at various intervals and analyzed according to method AMR-337-85, Revision A (1/30/86). Each analysis included duplicate stored samples, one stored control, and a new fortification of a stored control.

Recovery of DPX-L5300 from wheat and barley samples at 0 days ranged from 74% to 98%. However, after 5-6 days of ambient storage, residue levels of DPX-L5300 were <20% in barley grain, barley straw, wheat grain, and wheat straw. When corrected for percent recovery in the new fortification (i.e., when the data are normalized to current recovery data), residue levels of DPX-L5300 were about 40% of initial fortification level. These data indicate rapid decrease in residue levels in wheat and barley grain and straw stored under ambient conditions, as likely would be the case under normal cultural practices.

If additional metabolites of toxicological concern are regulated, storage stability data will be required.

MAGNITUDE OF THE RESIDUE:

Summary. Field trials of DPX-L5300 (most trials with 75% dry flowable, several trials with 75% wettable powder) in Express^{R} (and Matrix^{R}) formulations on wheat are reported in 14 states and Canada; and on barley in 9 states. Eight wheat trials used proposed dosage rate of 0.25 oz. a.i./A; most trials were conducted at 0.5 to 2.0 oz. a.i./A (2X to 8X application). No residue trials were conducted on either wheat or barley at the proposed 40 day PHI. The shortest PHI was 42 days (wheat) and 45 days (barley).

No detectable residues of DPX-L5300 (per se) were found in wheat grain at any interval or application rate (1X - 8X) when analyzed by a method with detection levels of 0.01 ppm (one contractor laboratory analyzed at 0.02 ppm detection level). The proposed tolerance level is 0.05 ppm of the parent compound, DPX-L5300.

Detectable residues of DPX-L5300 (0.03 to 0.076 ppm) were found in wheat straw at 56-74 days treated at 2X to 8X normal application rates. The lower exaggerated rate (2X) showed highest residue levels (0.076 ppm).

No detectable residues of DPX-L5300 (per se) were found in barley grain at any interval or application rate (1X - 8X) when analyzed by a method with detection levels of 0.01 ppm (one contractor laboratory analyzed at 0.02 ppm detection level).

A detectable residue of DPX-L5300 (0.050 ppm, Powell, WY) was found in one sample of barley straw (with no ambient storage) at 69 days after treatment at 8X normal application rates.

The submitted residue data for DPX-L5300 in wheat grain and straw and barley grain and straw are not sufficient to conclude that residues of DPX-L5300 will not exceed the proposed tolerances at the proposed 40 day PHI. Additional residue data reflecting the use as proposed, i. e. 40 day PHI are needed; geographic representation should be considered in light of the needed residue data. Data should be from the same states as the existing residue data. If additional metabolites of toxicological concern are regulated, additional field residue data for such metabolites will be required. We withhold judgement on the adequacy of these residue data pending completion of method trials by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of these trials.

Discussion:

Field trials of DPX-L5300 in Express^{R} (and Matrix^{R}) formulations are reported in 14 states; additional residue data are available from studies in Canada (MRID 402455-29). Matrix^{R} is a mixture of DPX-L5300 and DPX-M6316 [DuPont "Harmony"] intended for application to wheat and barley. Wheat samples taken at harvest were either stored at ambient temperature or frozen immediately. Therefore, the petitioner reports storage stability studies for both frozen storage and ambient conditions.

Wheat:

Residue trials on wheat were conducted with Express^{R} Herbicide in CA (4), CO (2), FL, ID (3), IN, MN (2), NE, NC, ND (6), OH (2), OK, OR (4), SD (2), WA. Treatment was with 75% dry flowable formulation, except several trials were conducted with 75% wettable powder formulation. Two wheat studies in Canada used Matrix^{R} Herbicide (mixture of DPX-L5300 and DPX-M6316 [DuPont "Harmony^{R}"]) at lower dosage rates. Only 8 of the trials were conducted at the proposed dosage rate of 0.25 oz. a.i./A; the majority of the trials were conducted at 0.5 to 2.0 oz. a.i./A (2X to 8X application). Some residue data are reported from the application of Matrix^{R} formulation at lower dosage rates.

The preharvest interval proposed on the Express^{R} label is 40 days; there are no residue trials conducted on either wheat or barley at the proposed 40 day PHI and no data at intervals shorter than 40 days. The shortest preharvest interval for wheat is one trial in Fargo, ND, at 42 days after application. Other trials were conducted at intervals up to 140 days. The utility of residue data at 140 days in support of the proposed 40 day PHI is open to question.

No detectable residues of DPX-L5300 (per se) were found in wheat grain at any interval or application rate (1X - 8X) when analyzed by a method with detection levels of 0.01 ppm (one contractor laboratory analyzed at 0.02 ppm detection level). The proposed tolerance level is 0.05 ppm of the parent compound, DPX-L5300.

Wheat Straw

Detectable residues of DPX-L5300 (0.03 to 0.076 ppm) were found in wheat straw at 56-74 days treated at 2X to 8X normal application rates. The lower exaggerated rate (2X) showed highest residue levels (0.076 ppm). Of these wheat straw samples, one had ambient storage while the other two had immediate frozen storage after field sampling.

Based upon this data the petitioner concludes:

The highest residues resulted from samples with the shortest preharvest interval and residues decrease as preharvest intervals increase.

While the data demonstrate that the shortest preharvest intervals show the highest residues, we disagree with the petitioner's second conclusion since there are no residue decline data demonstrating that residues decrease. Residue levels are lower at longer intervals than shorter intervals, but that does not in fact imply decrease in the residue itself. The petitioner should submit residue decline data, i.e. multiple sampling of the same field over time, to show a decrease in residues.

The presence of detectable residues of DPX-L5300 in wheat straw at 56-74 days after treatment at the 2X application rate indicates that at 40 days PHI (proposed), detectable residues of DPX-L5300 may occur in the animal feedstuff wheat straw. In order to help determine appropriate tolerance levels in animal tissues, animal metabolism and feeding studies are required pursuant to 40 CFR 158.125(a), Guidelines Reference No. 171-4.

It must be noted that the method of analysis is for the parent compound only. The ^{14}C wheat metabolism study (see Nature of the Residue discussion above) only about 65% of the residue is identified (none as DPX-L5300) as sulfonamide urea (45%), saccharin 11.3%; hydroxylated saccharin 3.5%, sulfonamide 1.9%, glucose conjugate of saccharin 1.7%, and unknowns 5.2%. About 35% is unextractable or unidentified extractable. If Toxicology Branch is concerned with any of these metabolites, residue analytical methods for such metabolites and additional field residue data may be necessary.

Barley:

Residue trials on barley were conducted with Express^{R} Herbicide in CA (2), CO, ID (6), MN (3), MT, ND (2), OR (4),WA (6), WY. Treatment was with 75% dry flowable formulation, except several trials were conducted with 75% wettable powder formulation. Only 2 of the trials were conducted at the proposed dosage rate of 0.25 oz. a.i./A; the majority of the trials were conducted at 0.5 to 2.0 oz. a.i./A (2X to 8X application). Several trials were conducted on barley using Matrix^{R} formulation at dosage rates of 0.125 to 0.25 oz. a.i./A.

The preharvest interval proposed on the Express^{R} label is 40 days; there are no residue trials conducted on barley at the proposed 40 day PHI and no data at intervals shorter than 40 days. The shortest preharvest interval for barley is one trial in Sterling ND at 45 days after application. Other trials were conducted at intervals up to 113 days. The utility of residue

data at 113 days in support of the proposed 40 day PHI is open to question.

No detectable residues of DPX-L5300 (per se) were found in barley grain at any interval or application rate (1X - 8X) when analyzed by a method with detection levels of 0.01 ppm (one contractor laboratory analyzed at 0.02 ppm detection level).

Barley Straw

A detectable residue of DPX-L5300 (0.050 ppm, Powell, WY) was found in one sample of **barley straw** (with no ambient storage) at 69 days after treatment at 8X normal application rates.

We conclude that the submitted residue data for DPX-L5300 in wheat grain and straw and barley grain and straw are not sufficient to conclude that residues of DPX-L5300 will not exceed the proposed tolerances at the proposed 40 day PHI. The residue data at intervals greater than about 70 days PHI probably do not support the 40 day PHI. For wheat, only 27 of 66 samples are less than 70 days. For barley, 21 of 40 samples had PHI of 70-days or less. For wheat and barley treated with Matrix^{R} Herbicide, 13 of 19 samples reflect <70 day PHI.

Additional residue data reflecting the use as proposed, i. e. 40 day PHI are needed; geographic representation should also be considered in light of the needed residue data. If additional metabolites of toxicological concern are regulated, additional field residue data for such metabolites will be required.

Residues of DPX-L5300 in Wheat Grain and Straw
Samples in Frozen Storage from Harvest.
Formulation: Express^{R}

Location	Days PHI	Oz/AI Rate	PPM Grain	PPM Straw
Fargo, ND	42	0.50	<0.01	<0.01
American Falls, ID	56	0.50	<0.01	0.076
American Falls, ID	56	1	<0.01	0.066
Sabin, MN	60	0.50	<0.01	<0.02
Elgin, OH	60	1.0	<0.01	<0.02
Argusville, ND	69	0.5	<0.01	<0.05
Argusville, ND	69	1.0	<0.01	<0.05
Argusville, ND	69	0.5	<0.01	<0.05
Argusville, ND	69	1.0	<0.01	<0.05
Gooding, ID	89	0.5	<0.01	<0.02
Gooding, ID	89	1.0	<0.01	<0.02
Stockton, CA	91	0.5	<0.01	*
Stockton, CA	91	1.0	<0.01	*
Garfield, WA	103	0.50	<0.01	<0.02
Nez Perce, ID	106	0.50	<0.01	<0.02
Nez Perce, ID	106	1.0	<0.01	<0.02

Zamora, CA	111	0.5	<0.01	*
Zamora, CA	111	1.0	<0.01	*
Canby, OR	119	0.25	<0.01	<0.02
Canby, OR	119	0.50	<0.01	<0.02
Dufer, OR	120	1.0	<0.01	<0.02
Hanley, Saskatchewan	68	0.64	<0.01	<0.02
Hanley, Saskatchewan	76	0.86	<0.01	*
Hanley, Saskatchewan	83	0.86	<0.01	*

Residues of DPX-L5300 in Wheat Grain and Straw Samples in Ambient and Frozen Storage from Harvest.
Formulation: Express®

	Days	Ambient	Oz/AI	PPM	
Location	PHI	Storage	Rate	Grain	Straw
Butler, IN	46	9	1.0	<0.01	*
Butler, IN	46	9	2.0	<0.01	*
Obetz, OH	49	61	1.0	<0.01	*
McKenzie, ND	55	20	0.5	<0.01	<0.02
McKenzie, ND	55	20	1.0	<0.01	<0.02
Harrold, SD	55	1	0.25	<0.01	<0.02
Harrold, SD	55	1	0.5	<0.01	<0.02
Harold, SD	55	1	1.0	<0.01	<0.02
Regan, ND	62	2	0.75	<0.01	*
Indianola, NE	63	29	1.0	<0.01	<0.02
Indianola, NE	63	29	1.0	<0.01	<0.02
Indianola, NE	63	29	2.0	<0.01	<0.02
Indianola, NE	63	29	2.0	<0.01	<0.02
Sabin, MN	67	3	0.25	<0.01	*
Eureka, SD	71	18	0.5	<0.01	<0.02
Eureka, SD	71	18	1.0	<0.01	<0.02[1]
Fayetteville, NC	74	14	1.0	<0.01	<0.02
Fayetteville, NC	74	14	1.0	<0.01	<0.02
Fayetteville, NC	74	14	2.0	<0.01	<0.02
Fayetteville, NC	74	14	2.0	<0.01	0.03
Bradenton, FL	76	22	1.0	<0.01	<0.02
Bradenton, FL	76	22	1.0	<0.01	<0.02
Bradenton, FL	76	22	2.0	<0.01	<0.02
Bradenton, FL	76	22	2.0	<0.01	<0.02
McKenzie, ND	55	8	0.25	<0.01	*
McKenzie, ND	55	8	1.0	<0.01	*
Roggen, CO	79	5	1.0	<0.01	*
Roggen, CO	79	5	1.0	<0.01	*
Roggen, CO	79	5	1.0	<0.01	*
Elgin, OR	83	4	1.0	<0.01	*
Monte Vista, CO	97	2	1.0	<0.01	*
Wamkoms, OK	100	31	0.5	<0.01	<0.02
Wamkoms, OK	100	31	1.0	<0.01	<0.02
The Dalles, OR	115	43	1.0	<0.01	<0.02
The Dalles, OR	115	43	2.0	<0.01	<0.02
The Dalles, OR	115	43	2.0	<0.01	<0.02
Woodland, CA	120	5	1.0	<0.01	<0.02

Woodland, CA	120	5	2.0	<0.01	<0.02
Tranquility, CA	140	6	0.5	<0.01	<0.02
Tranquility, CA	140	6	1.0	<0.01	<0.02
Tranquility, CA	140	6	2.0	<0.01	<0.02

[1] Corrected from Table 6, Appendix 2B, Section 2

Residues of DPX-L5300 in Barley Grain and Straw Samples in Ambient and Frozen Storage from Harvest
Formulation: Express[R]

Location	Days PHI	Ambient Storage	Oz/AI Rate	PPM Grain	PPM Straw
Sterling, ND	45	10	0.5	<0.01	<0.02
Sterling, ND	45	10	1.0	<0.01	<0.02
Sabin, MN	67	3	1.0	<0.01	<0.02
Moses Lake, WA	69	4	1.0	<0.01	<0.02
Spokane, WA	75	21	0.5	<0.01	<0.02
Spokane, WA	75	21	1.0	<0.01	<0.02
Garfield, WA	75	26	0.5	<0.01	<0.02
Garfield, WA	75	26	1.0	<0.01	<0.02
Mead, CO	89	21	1.0	<0.01	<0.02
Mead, CO	89	21	1.0	<0.01	<0.02
Mead, CO	89	21	1.0	<0.01	<0.02
Pixley, CA	113	8	0.5	<0.01	<0.02
Pixley, CA	113	8	1.0	<0.01	<0.02

Residues of DPX-L5300 in Barley Grain and Straw Samples in Frozen Storage from Harvest.
Formulation: Express[R]

Location	Days PHI	Oz/AI Rate	PPM Grain	PPM Straw
Crookster, MN	50	0.5	<0.01	*
Crookster, MN	50	1.0	<0.01	*
Crookster, MN	50	0.5	<0.01	<0.02
Burley, ID	60	0.5	<0.01	<0.02
Burley, ID	60	1.0	<0.01	<0.02
Burley, ID	60	2.0	<0.01	<0.02
American Falls, ID	61	0.5	<0.01	<0.02
American Falls, ID	61	1.0	<0.01	<0.02
Castleford, ID	62	0.5	<0.01	<0.02
Castleford, ID	62	1.0	<0.01	<0.02
Powell, WY	69	1.0	<0.01	<0.02
Powell, WY	69	2.0	<0.01	0.05
Pomeroy, WA	69	0.375	<0.01	<0.02
Pomeroy, WA	69	1.0	<0.01	<0.02
Swan Valley, ID	70	0.5	<0.01	<0.02
Swan Valley, ID	70	1.0	<0.01	<0.02
Nampa, ID	77	1.0	<0.01	<0.02
Nampa, ID	77	1.0	<0.01	<0.02
Nampa, ID	77	2.0	<0.01	<0.02

Nampa, ID	77	2.0	<0.01	<0.02
Corvallis, OR	87	0.5	<0.01	*
Corvallis, OR	87	1.0	<0.01	*
Corvallis, OR	87	0.5	<0.01	*
Corvallis, OR	87	1.0	<0.01	*
Knights Landing, CA	108	0.25	<0.01	*
Knights Landing, CA	108	0.50	<0.01	<0.02
Knights Landing, CA	108	1.0	<0.01	<0.02
Bentley, Alberta	76	0.86	<0.01	<0.02

Residues of DPX-L5300 in Wheat Grain and Straw Samples in Frozen Storage from Harvest.
Formulation: Matrix^{R}

	Days	Oz/AI	PPM	
Location	PHI	Rate	Grain	Straw
American Falls, ID	56	0.17	<0.01	*
American Falls, ID	56	0.33	<0.01	*
Argusville,ND	69	0.17	<0.01	*
American Falls, ID	69	0.33	<0.01	*

Residues of DPX-L53 00 in Barley Grain and Straw Samples in Frozen Storage from Harvest
Formulation: Matrix^{R}

	Days	Oz/AI	PPM	
Location	PHI	Rate	Grain	Straw
Thompson, ND	61	0.17	<0.01	<0.05
Thompson, ND	61	0.33	<0.02	<0.05
Amsterdam, MT	62	0.125	<0.02	<0.05
Amsterdam, MT	62	0.125	<0.02	<0.05
Amsterdam, MT	62	0.5	<0.02	<0.05
Amsterdam, MT	62	0.5	<0.02	<0.05
Parma, ID	64	0.125	<0.02	<0.05
Parma, ID	64	0.5	<0.02	<0.05
Corvallis, OR	87	0.25	<0.02	<0.05
Corvallis, OR	87	0.33	<0.02	<0.05
Corvallis, OR	87	0.25	<0.02	<0.05
Corvallis, OR	87	0.33	<0.02	<0.05
Mead, WA	92	0.17	<0.02	*
Mead, WA	92	0.33	<0.02	*
Pomeroy, WA	99	0.187	<0.02	*
Pomeroy, WA	99	0.375	<0.02	*

Grain Processing Studies:

Summary:

No grain processing or milling fraction data are submitted.

> The results of a processing study using samples treated with the "highest practical exaggeration" should be submitted for review. Residue data should be submitted for wheat bran, flour, middlings, and shorts, and for barley hulls, bran, flour, and pearl barley and appropriate food additive tolerances proposed if necessary.

Discussion:

The petitioner has not submitted any wheat or barley grain fractionation (processing) data. We note that while the field residue data indicate no detectable residues in wheat or barley grain at longer intervals, we have little data showing no detectable residues at the proposed 40 day PHI. Further, it must be noted that we are unable to draw final conclusions on the adequacy of the residue data until a successful method trial is reported in our laboratories. Further, if Tox Branch is concerned with the 35% of the phenyl-^{14}C which is unextractable or unidentified in wheat grain, additional field residue data for the additional metabolites may be necessary.

The petitioner should be advised to conduct a processing study using samples treated with the "highest practical exaggeration" and the results submitted for review. Residue data should be submitted for wheat bran, flour, middlings, and shorts, and for barley hulls, bran, flour, and pearl barley and appropriate food additive tolerances proposed if necessary.

The following information should be considered:

> When using exaggerated rate data for consideration of food additive tolerances, the petitioner should be careful not to propose a food additive tolerance based on data not reflective of real world use. The petitioner should also be careful not to propose a food additive tolerance if there is no reasonable chance that the processed product will carry residues higher that the RAC. Occasionally use of exaggerated rate data will result in no clear indication of whether a food additive tolerance is needed or if it is needed, what level it should be. In these situations considerable judgment, based on all pertinent data, will be required. ...This will include, at a minimum, the metabolism studies and the chromatogram (or other raw analytical data) for the RAC samples. In some cases it may be possible to estimate residue levels for chromatograms where the response is below the limit of reliable quantitation but indicative of a "true" residue.

Meat, Milk, Poultry and Eggs

Summary.

No information is submitted concerning residues of DPX-L5300 in meat, milk, poultry or eggs. In the absence of animal metabolism and animal feeding data, we are unable to draw any conclusions regarding the presence of DPX-L5300 (or any metabolites of toxicological concern) in meat, milk, poultry and eggs.

Dietary burdens on cattle include wheat and barley grain (to 80%) and straw (to 10%). Apparent real residues of DPX-L5300 have been found in straw from exaggerated application rates but longer PHI than proposed. Based upon this information, tolerances may be required for meat and milk.

Poultry and egg tolerances may not be required, if there are no detectable residues in wheat grain and barley grain (from exaggerated application rates) and no detectable residues in grain milling fractions of DPX-L5300 (including any metabolites of toxicological concern), when analyzed by a validated and adequate analytical method.

Discussion:

No information is submitted concerning residues of DPX-L5300 in meat, milk, poultry or eggs. In the absence of animal metabolism and animal feeding data, we are unable to draw any conclusions regarding the presence of DPX-L5300 (or any metabolites of toxicological concern) in meat, milk, poultry and eggs.

Wheat and barley straw are used up to 10% in the diets of both beef and dairy cattle; straw is not used for poultry feed. Wheat grain, wheat milling fractions, and barley grain are used to the following extent in the diets of various livestock:

DIETARY BURDEN OF LIVESTOCK

Animal	% Wheat	% Milling Fractions	% Barley
Beef cattle	50	25	80
Dairy cattle	50	25	50
Broilers	70	10	50
Layer Hens	50	5	50
Boars & Sows	80	10	80
Finishing Animals	90	5	40

Since apparent real residues of DPX-L5300 have been found in animal feed items such as straw, residue data from animal feeding studies are required. These studies should include any

additional plant metabolites of toxicological concern. Tolerances may be required for meat and milk.

If there are no detectable residues in wheat grain and barley grain (from exaggerated application rates) and no detectable residues in grain milling fractions of DPX-L5300 (including any metabolites of toxicological concern), when analyzed by a validated and adequate analytical method (i.e., pending completion by EPA laboratory), poultry and egg tolerances may not be required.

TOLERANCE ASSESSMENT

> **Summary**. If/when the permanent tolerances for this present petition are favorably recommended for, a request for an updated TAS assessment will be initiated by this Branch. Any TAS review which is then performed will issue as a separate memo, directed to the Product Manager (R. Mountfort, PM 23, Herbicide/-Fungicide Branch.

Discussion.

A Tolerance Assessment System (TAS) analysis has not been performed on DPX-L5300 (Express^{R} Herbicide) in conjunction with the establishment of temporary tolerances.

If/when the permanent tolerances for this present petition are favorably recommended for, a request for an TAS assessment will be initiated by this Branch.

Any TAS review which is then performed will issue as a separate memo, directed to the Product Manager (R. Mountfort, PM 23, Herbicide/Fungicide Branch.

No TAS analysis will be conducted as part of this present review document; TAS considerations are the purview of the TAS Program Staff of RCB.

INTERNATIONAL HARMONIZATION

> **Summary**. There are no Canadian or Mexican IRLs established for Express^{R}, and no Codex proposals for Express^{R} at Step 6 or above. The question of compatibility or harmonization of the tolerance expression and or residue levels does not arise in connection with the review of this petition.

Discussion. There are no Canadian or Mexican international residue limits (IRLs) established for Express^{R}; neither is there any codex proposals for Express^{R} at Step 6 or above. (See

International Residue Limit Status sheet, appended to this review as an Attachment.)

Since there are no established IRLs for Express^{R}, the question of compatibility or harmonization of the tolerance expression and or residue levels does not arise in connection with the review of this petition.

OTHER CONSIDERATIONS

Summary. No "OTHER CONSIDERATIONS" apply in the review of this petition.

Discussion. All the relevant issues have been addressed under specific topic headings in the body of this review. No "Other Considerations" apply in the review of this petition.

cc: S.F., R.F., PP7F3540, R.W.Cook, PMSD(ISB),TOX.
TS-769C:RCB:Reviewer:RWCook:rwc:4/25/88:Rm810H:CM2:5577324.
RDI:Section Head:RSQuick:4/15/88:RDSchmitt:4/20/88.

BIBLIOGRAPHY

Technical Report No.	References Used	Accession/ MRID No.
AMR-787-87	The Metabolism of [Phenyl(U)-^{14}C] and [Triazine-2-^{14}C]DPX-L5300 in Field Grown Wheat. D. L. Ryan, J. J. Dulka. E. I. du Pont de Nemours and Company, PP#7F3540, Section D.	402455-30
AMR-841-87	Magnitude of the Residues on Grain and Straw from Wheat and Barley after Treatment with Express^{R} Herbicide R. A Guinivan, E. I. du Pont de Nemours and Company, PP#7F3540, Section D.403036-01	
AMR-337-85	Determination of Residue of DPX-L5300 in Crops by Liquid Chromatography. L. W. Hershberger, N. S. Heckendorn. E. I. du Pont de Nemours and Company. PP#7F3540, Section D.	403036-01
5300/PC-11	Product Identity, Description of Process, Formation of Impurities, and Certification of Limits for DPX-L5300. J.H. Jensen. E. I. du Pont de Nemours and Company, PP#7F3540, Section B	402455-03
5300/PC-12	Characterization of L5300 for Registration. W. L. Champion. E. I. du Pont de Nemours and Company, PP#7F3540, Section B	402455-05
AMR-407-85	Octanol/Water Partition Coefficient of [Phenyl] 14C(U) DPX-L5300. H. Y. Mohammed. E. I. du Pont de Nemours and Company. PP7F3540.	402455-01
5300/PC-13	Vapor Pressure of DPX-L5300. A. C. Barefoot. E. I. du Pont de Nemours and Company, PP7F3540.	402455-09
X130.300(R)	Xylene Isomers Determination of Ethylbenzene and the Isomers of Xylene in Technical and Formulated Samples, Gas Chromatography (GC) Methods. E. I. du Pont de Nemours and Company, PP7F3540, Section A.	402455-07

BIBLIOGRAPHY

Technical Report No.	References Used	Accession/ MRID No.
P348.100(R)	Pesticides and Related Substance, Determination of Anions and Cations, Ion Exchange Liquid Chromatography Method. E. I. du Pont de Nemours and Company. PP#7F3540, Section B.	402455-08
AMR-337-85	Supplement to: Determination of Residues in DPX-L5300 In Crops by Liquid Chromatography. C. L. McIntosh. E. I. du Pont de Nemours and Company. PP7F3540,Section D.	402455-31

INTERNATIONAL RESIDUE LIMIT STATUS

E. Kwes 3/15/88

CHEMICAL DPX-L5300 (DuPont Express)

CODEX NO. _____

CODEX STATUS:

☑ No Codex Proposal Step 6 or above

Residue(if Step 8): _____

Crop(s)	Limit (mg/kg)

PROPOSED U.S. TOLERANCES:

Petition No. 7F3540

RCB Reviewer RU Cook

Residue: DPX-L5300 per se

Crop(s)	Limit (mg/kg)
Wheat grain	0.05
Wheat straw	0.10
Barley grain	0.05
Barley straw	0.10

CANADIAN LIMITS:

☑ No Canadian limit

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

☑ No Mexican limit

Residue: _____

Crop(s)	Limit (mg/kg)

DPX-L5300 = methyl-2-[[[[N-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-methylamino]carbonyl]amino]sulfonyl]benzoate

NOTES:

Form revised 1986

ATTACHMENT 3

APR 26 1988

MEMORANDUM

SUBJECT: New Chemical Product Chemistry Review DPX-L5300 (Technical)

REVIEWER: R. W. Cook, Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

PRODUCT MANAGER: R. Mountfort, PM 23
Herbicide/Fungicide Branch
Registration Division (TS-767C)

EPA Reg No:	352-LNO
Petition No.:	7F3540
MRID/Acces. No	073786 402455-05 402455-03 402455-09
RCB No:	2516, 2517.
Common Name	None.
Trade Names	Express^{R} Herbicide
Company Code No:	DPX-L5300, IN-L5300, L5300
Applicant:	E. I. du Pont de Nemours and Company, Wilmington, DE.
Type Product:	Herbicide

SUMMARY OF DEFICIENCIES FOR PRODUCT CHEMISTRY
ExpressR Herbicide

No additional information is required to satisfy data requirements of 40 CFR 158-120 for ExpressR Technical.

DETAILED CONSIDERATIONS:

BACKGROUND

Product Chemistry data requirements for the registration of a pesticide product are listed in 40 CFR 158.120

Each of those data requirements is cross-referenced to the Product Chemistry Guidelines Reference Number in the Pesticide Assessment Guidelines, Subdivision D, Product Chemistry (October 1982; EPA-540/9-82-018), which provide detailed information on the types and minimum amounts of data/information an applicant must submit in support of registration.

The kind of data required by 40 CFR 158.120 for a technical product, and the Product Chemistry Guidelines Reference Numbers are summarized below:

40 CFR 158.120 Data Requirement	Guidelines Refs. No.
Product Identity and Composition	§61-(1-3)
Analysis and Certification of Product Ingredients	§62-(1-3)
Physical and Chemical Characteristics	§63-(2-13)

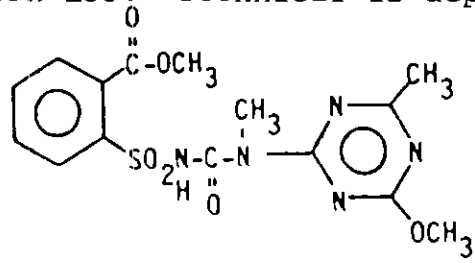
The data/information the applicant has submitted to fulfill these data requirements for registration of the technical grade of the active ingredient DPX-L5300 Technical are the subject of this review. Any existing data gaps are identified and description of the data/information needed to fill the data gaps are provided.

PRODUCT IDENTITY AND COMPOSITION

§61-1 Product Identity and Disclosure of Ingredients

Express^{R} Herbicide is the trade name of a new herbicide for which registration is sought by E. I. du Pont de Nemours and Company, Wilmington, DE.

The structure of DPX-L5300 Technical is depicted below:



The chemical name (CAS) for DPX-L5300 Technical is methyl-2-[[[[N-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-N-methylamino] carbonyl]amino]sulfonyl]benzoate.

The tradename for herbicides formulated from DPX-L5300 Technical is Express^{R} Herbicide.

Code numbers used by E. I. du Pont de Nemours and Company to designate this herbicide include DPX-L5300, IN-L5300, and L5300.

Other identifying characteristics and codes are:

Empirical Formula:	$C_{15}H_{17}N_5O_6S$	(MRID 073786)
Molecular Weight:	395.39	(MRID 073786)
CAS Registry No:	10120-48-0	(MRID 402455-03)

§61-2 Description of Beginning Materials and Manufacturing Process

The data/information the petitioner has submitted in response to this requirement are given in Confidential Appendix A.

RCB concludes (see Confidential Appendix A) no additional information is required to satisfy data requirements of 40 CFR 158.120 - Description of Beginning Materials and Manufacturing Process (Guidelines Ref. No. §61-2) for DPX-L5300 Technical.

§61-3 Discussion of Formation of Impurities

The data/information the petitioner has submitted in response to this requirement are given in Confidential Appendix B.

RCB concludes (see Confidential Appendix B) no additional information is required to satisfy data requirements of 40 CFR 158.120 - Discussion of Formation of Impurities (Guidelines Ref. No. §61-3) for DPX-L5300 Technical.

ANALYSIS AND CERTIFICATION OF PRODUCT INGREDIENTS

§62-1 Preliminary Analysis

The data/information the petitioner has submitted in response to this requirement are given in Confidential Appendix C.

RCB concludes (see Confidential Appendix C) no additional information is required to satisfy data requirements of 40 CFR 158.120 - Preliminary Analysis (Guidelines Ref. No. §62-1) for DPX-L5300 Technical.

§62-2 Certification of Ingredient Limits

The data/information the petitioner has submitted in response to this requirement are given in Confidential Appendix D.

RCB concludes (see Confidential Appendix D) no additional information is required to satisfy data requirements of 40 CFR 158.120 - Certification of Ingredient Limits (Guidelines Ref. No. §62-2) for DPX-L5300 Technical.

§62-3 Analytical Methods to Verify Certified Limits

The data/information the petitioner has submitted in response to this requirement are given in Confidential Appendix E.

RCB concludes (see Confidential Appendix E) no additional information is required to satisfy data requirements of 40 CFR 158.120 - Analytical Methods to Verify Certified Limits (Guidelines Ref. No. §62-3) for DPX-L5300 Technical.

PHYSICAL AND CHEMICAL PROPERTIES

The physical and chemical properties test requirements for the technical grade of active ingredient are detailed in the Pesticide Assessment Guidelines, Subdivision D, Product Chemistry, §63-2 through §63-13, and 40 CFR 158.120.

The applicant has submitted the following information to meet these data requirements for DPX-L5300 Technical:

§63-2 - Color	White	(MRID 073786)
§63-3 - Physical State:	Solid	(MRID 073786)
§63-4 - Odor	None	(MRID 073786)
§63-5 - Melting Point	141°C.	(MRID 073786)
§63-6 - Boiling Point	Not applicable, since the technical grade of the active ingredient is not a liquid at room temperature; 40 CFR 158.120(b)(7).	
§63-7 - Density	1.54 g/cc	(MRID 073786)
§63-8 - Solubility		(MRID 073786)
In Water at 25°C	28 mg/L at pH 4.0 50 mg/L at pH 5.0 280 mg/L at pH 6.0	
In Organic Solvents at 25°C	43.8 g/L Acetone 54.2 g/L Acetonitrile 3.12 g/L Carbon Tetrachloride 17.5 g/L Ethyl Acetate 0.028 g/L Hexane 3.39 g/L Methanol	(MRID 073786)
§63-9 - Vapor Pressure	3.9×10^{-10} at 25°C (Knudsen method) (MRID 402455-09) $<8.3 \times 10^{-7}$ at 70°C (gas saturation) (MRID 402455-09) 2.7×10^{-7} at 25°C (gas saturation) (MRID 402455-09)	
§63-10 - Dissociation Constant	$pK_a = 5.0$	(MRID 073786)
§63-11 - Octanol/Water Partition Coefficient	0.3 at pH 7. 15 at pH 5 (calculated). 0.003 at pH 9 (calculated).	(MRID 073786)
§63-12 - pH	4.27 (slurry in water)	(MRID 073786)

§63-13 - Stability	Relatively unstable in most solvents, especially aqueous solvents. Stable to metals. Decomposes on melting. Relatively stable to sunlight. (MRID 073786)

Information for §63-2 through §63-13 was obtained from MRID No. 402455-09, (PP7F3540, Section A) or MRID 073786 (PP5G3296, Section A, Vol. II of V, Ref. 8) as indicated above.

RCB concludes no additional information is required to satisfy the data requirement of 40 CFR 180.120 (Guidelines Ref. No. §63-2 through 1§63-13 on the Physical and Chemical Characteristics of DPX-L5300 Technical.

BIBLIOGRAPHY

Technical Report No.	References Used	Accession/ MRID No.
N/A	PESTICIDE PETITION FOR TEMPORARY TOLERANCES FOR DPX-L5300 IN OR ON WHEAT AND BARLEY. E. I. du Pont de Nemours and Company. PP#5G3296, Section A, Vol. II of V, Ref. 8.	073786
N/A	PESTICIDE PETITION FOR TOLERANCES OF DPX-L5300 IN OR NO WHEAT AND BARLEY. E. I. du Pont de Nemours and Company, Section A.	402455-03 402455-05 402455-09

Pages 43-103 Claimed confidential by submitter