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

SEP 10 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6E3411, Sethoxydim in or on Flax - Evaluation of Analytical Methods and Residue Data (Accession No. 262767; RCB No. 937)

FROM: V.F. Boyd, Ph.D., Chemist
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TO: Hoyt Jamerson, PM 43
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and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
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Interregional Research Project No. 4 (IR-4), on behalf of the IR-4 National Director, Dr. R.H. Rupelian and the Agricultural Experiment Station of North Dakota requests the establishment of a tolerance for the combined residues of the herbicide 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio) propyl]-3-hydroxy-2-cyclohexen-1-one and its metabolites containing the 2-cyclohexen-1-one moiety (calculated as the herbicide) in or on the raw agricultural commodity (RAC) flaxseed at 5.0 ppm and flax straw at 2.0 ppm.

Permanent tolerances have been established on cottonseed at 5 ppm, soybeans at 7 ppm, and on sugar beets and animal commodities at levels of 0.05 to 0.5 ppm (40 CFR 180.412). A feed additive tolerance was also established for cottonseed soapstock at 15 ppm (21 CFR 561.430).

Permanent tolerances are pending for residues of sethoxydim on sunflowers and peanuts (PP#5F3234, M. Firestone, July 17, 1985), tomatoes and tomato products (PP#5F3284, C. Deyrup, October 9, 1985), soybean and alfalfa hay and forage (PP#3F2904, S. Malak, June 23, 1986), and strawberries and raspberries (PP#6F3383, F. Boyd, July 16, 1986).

Conclusions

1a. The petitioner will need to specify the method of application used in his field trials. If the residue data do not reflect the proposed use of application by both air and ground equipment, then the petitioner will have the option of submitting the appropriate data or revising the Section B labeling to comply with that method of application used in his field trials.

1b. A label statement concerning the maximum total herbicide (pt/A) application per season is required (see the "Proposed Use" section of this review for further details).

2. Residue Chemistry Branch (RCB) concludes that the nature of the residue in flax is adequately understood. The residues of concern are sethoxydim and its metabolites containing the 2-cyclohexen-1-one moiety.

2b. The residues of concern are adequately delineated for ruminants and poultry. The metabolites contain the 2-cyclohexen-1-one moiety and are identified as MSO, MSO_2, nor-MSO and nor-MSO_2 in ruminants and as MSO, MSO_2, and M_1SO in poultry.

3. Adequate analytical methodology is available for enforcement purposes.

4a. Storage stability of sethoxydim in soybeans under freezer conditions, exhibited no determinable loss of the parent or metabolites over a 2-year period. These data adequately support the storage and handling of field samples (PP#2F2670, M.J. Nelson, April 22, 1983).

4b. The residue data presented are reflective of the proposed use and are considered sufficient for establishing a tolerance residue level of 5.0 ppm for flaxseed and 2.0 ppm for flax straw.

However, the proposed use is expressed in lb ai/A and the established labeling for Poast® is in pt/A. The field trial data do not include information on rate of application correlating pints and lb ai/A. It will be necessary to supply a proposed use in a revised Section B expressed as pt/A. Accordingly, application rates used for each residue field trial must be submitted.

4c. Processed flaxseed resulted in a 23 percent increase in residue level in the extracted presscake. A revised Section F including a higher tolerance for flaxseed meal as a feed additive (probably at 7.0 ppm) will be necessary.

5. The present established tolerances for residues of sethoxydim in/on the meat, milk, poultry, and eggs will not be exceeded as a result of the proposed use.

6. An International Residue Limit Status sheet is included in this review. No Codex, Mexican, or Canadian tolerances are established for sethoxydim on flax.

Recommendations

RCB recommends against establishing the proposed tolerances for sethoxydim and its metabolites in/on flaxseed and flax forage until the deficiencies described above in conclusions 1a, 1b, 4b, and 4c are resolved.

Detailed Considerations

Manufacture and Formulation

The manufacturing process of sethoxydim was discussed in RCB's review of PP#0G2396 (memorandum of E. Zager, December 4, 1980). The technical product is > 94.9 percent pure. The impurities are not expected to present any residue problems.

The formulation to be used on flax, Poast, an emulsifiable concentrate, contains 20.0 percent by weight active ingredient. The inerts have been cleared under 40 CFR 180.1001.

Proposed Use

"For broad spectrum control of grasses, apply a postemergence spray at the rate of 0.5 lb ai/A. If an additional grass control is needed, apply a postemergence spray at the rate of 0.3 lb ai/A 14 to 21 days after first application. Always add 2 pints of oil concentrate per acre.

"Do not apply Poast to flax within 75 days of harvest. Do not graze or feed treated flax forage to livestock."

There is no specific limitation on the total amount of Poast to be applied during one season, although a maximum of 0.8 lb ai/A is implied. A definite statement of the maximum amount to be applied per growing season is needed.

The labeling indicates that applications may be made through air or ground equipment. The petitioner will need to specify the method of application used in his field trials. If the residue data do not reflect the proposed use of application by both air and ground equipment, then the petitioner will have the option of submitting the appropriate data or revising the Section B labeling to comply with that method of application used in his field trials.

Nature of the Residue

Plants

No metabolism data were submitted with this petition. C^{14}-sethoxydim has been successfully studied in tomatoes (PP#5F3284, C. Deyrup, October 9, 1985); in soybeans and alfalfa (PP#3F2904, K. Arne, June 26, 1985); and in sugar beets (PP#3F2950, K. Arne, February 2, 1984). Metabolism of sethoxydim yields a myriad of products of which six were identifiable in tomatoes and alfalfa, nine were identifiable in soybeans, and four were identifiable in sugar beets. In each of these dissimilar crops the identifiable metabolites were common to each plant or identifiable as being derived by a common pathway of degradation. All metabolites contained the 2-cyclohexen-1-one moiety.

RCB concludes that the nature of the residue in flax is adequately understood for the purposes of this proposed use. The residues of concern are sethoxydim and its metabolites containing the 2-cyclohexen-1-one moiety.

Animals

In animals, C^{14}-sethoxydim studies were performed in goats and laying hens (PP#3F2904, K. Arne, June 25, 1985). From metabolism data submitted, it was concluded that residues of sethoxydim in ruminants were the parent and its metabolites MSO, MSO_2, nor-MSO, and nor-MSO_2. In poultry, the residues were parent plus its metabolites MSO, MSO_2, and M_1SO. These conclusions are stated in the S. Malak evaluation of PP#3F2904, dated June 23, 1986.

RCB concludes that the nature of the residue in ruminants and poultry from sethoxydim use is adequately delineated. The residue of concern is the parent compound and its 2-cyclohexen-1-one moiety containing metabolites.

Analytical Methodology

The analytical methods used to determine residues of sethoxydim in flaxseed and flax straw are designated as BWC Method No. 30 or 30H. BWC-30 is used to monitor residues in meat, milk, poultry and eggs, soybeans, and flaxseed. In PAM II this method is Method I for sethoxydim residues. A variation of this method, BWC-30H, is available to monitor alfalfa and soybean hay and flax straw. In brief, the method consists of extracting the sample with methanol, precipitating protein with $Ca(OH)_2$, partitioning the acidified filtrate with methylene chloride, concentration of the organic layer and oxidation of the residue with H_2O_2 in the presence of $Ba(OH)_2$ to give the substituted pentanedioic acids, and formation of the corresponding methyl esters (DME and DME-OH) with methanolic hydrogen chloride. The esters are cleaned up on a silica gel column and quantitated with GC/FPD in the sulfur mode. Some samples require an additional HPLC cleanup prior to GLC.

The sensitivity of the method is reported as 0.05 ppm for flaxseed and 0.5 ppm for flax straw.

Recoveries of parent and two major metabolites are as follows:

Sample Material	Fortification Compound	Fortification Range (ppm)	Average Recovery(%)
Flaxseed	Sethoxydim	0.05-10.0	95
"	MSO	0.05-20.0	96
"	5-OH	0.05-20.0	84
Flaxstraw	Sethoxydim	0.5-10.0	98
"	MSO	0.5-10.0	98
"	5-OH	0.5-10.0	85
Processed Seed:			
Presscake	Sethoxydim	0.5	92
"	MSO	0.05-5.0	100
"	5-OH	0.05-5.0	85

Sample Material	Fortification Compound	Fortification Range (ppm)	Average Recovery(%)
Presscake (extracted)	Sethoxydim	0.5	94
"	MSO	0.05-5.0	96
"	5-OH	0.05-5.0	82
Crude oil (expeller)	Sethoxydim	0.5	92
"	MSO	0.05-5.0	96
"	5-OH	0.05-5.0	85
Crude oil (solvent)	Sethoxydim	0.5	88
"	MSO	0.05-5.0	97
"	5-OH	0.05-5.0	84

RCB concludes that adequate methodology is available for regulatory purposes.

Residue Data

Storage Stability

No storage stability was performed for flax since storage stability in soybeans and soybean forage samples was previously reported (PP#3F2904, J.H. Onley, January 12, 1984). Soybean forage samples spiked at 1.0 ppm with sethoxydim and the MSO metabolite gave recovery ranges of 81 to 118 percent and 75 to 112 percent, respectively, after 27 months storage at -15 °C. Soybean seed samples fortified with 1 ppm sethoxydim or 0.5 ppm MSO or 5-OH-MSO_2 and stored at -15 °C for 24 months when analyzed gave 85 to 114 percent recovery for sethoxydim; 92 to 107 percent recovery for MSO; and 70 to 94 percent recovery for 5-OH-MSO_2.

It is concluded from these studies that the storage stability in soybean forage is adequate for 27 months and in soybean seed for 24 months and these data are acceptable for flax straw and seed storage stability.

Flax Seed

A total of nine studies were carried out at four locations using two different quantities of Poast (0.5 lb ai/A and 0.5 + 0.3 lb ai/A) at each of the four locations and a third quantity

(0.5 + 0.5 lb ai/A) in a single study for processing purposes. The total residues of sethoxydim were found to be:

Location	Rate (lb ai/A)	PHI (days)	Total Residue (ppm)
Minot, ND	0.5	67	0.33
	0.5 + 0.3	31	1.23
Fargo, ND	0.5	99	0.24
	0.5 + 0.3	77	1.32
Grand Forks, MN	0.5	75	0.85
	0.5 + 0.3	61	3.30
Brookings, SD	0.5	63	0.17
	0.5 + 0.3	50	0.89
Minot, ND	0.5 + 0.5	52	3.4

At the maximum rate of 0.5 + 0.3 lb ai/A the total residues of sethoxydim ranged from 0.89 ppm to 3.30 ppm with PHI's of 31 to 77 days.

The data from flaxseed are similar to cottonseed data (PP#2F2748, J.H. Onley, December 15, 1982) where applications of 0.5 + 0.3 lb ai/A resulted in residues of < 0.05 to 4.0 ppm, at PHI's of 39 to 159 days in cottonseed. A tolerance of 5 ppm is established for cottonseed.

The Agricultural Statistics Publication for 1984 lists only three states--Minnesota, North Dakota, and South Dakota--as major production areas. The above tabulated data of sethoxydim residues in flaxseed were generated on flax grown in three States--North Dakota, South Dakota, and Minnesota. These data indicate that a tolerance of 5.0 ppm would not be exceeded by application of 0.5 + 0.3 lb ai/A, with a 75-day PHI. However, there are several inconsistencies between the Section B labeling and the use parameters recorded as a part of the residue field trials:

1. Labeling in Section B indicates application by air or ground can be made, but residue field data do not spell out the methods of application. The petitioner needs to address this issue.

2. The proposed use includes the rate as 0.5 + 0.3 lb ai/A, but the established Poast printed label presents rates in terms of pt/A of the EC (1.5 lb/gal of sethoxydim). Thus, for consistency the Poast application rate for use on flax should be presented in terms of pt/A in a revised Section B.

3. The proposed use indicates an application rate of 0.5 + 0.3 lb ai/A of sethoxydim, but does not specify a maximum application per season. A maximum amount (pints)/season should be spelled out on the proposed label.

Flaxseed Products

Flaxseed was processed from a single trial in Minot, ND following application of Poast at 0.5 + 0.5 lb ai/A, and harvesting seed at a 52-day PHI:

Commodity	Total Residues (ppm)
Flaxseed	3.4
Presscake	4.0
Presscake (solvent extracted)	4.4
Crude oil (expeller)	1.5
Crude oil (solvent extracted)	1.4

Sethoxydim residues concentrate slightly (23 to 25%) or 1.25:1.0 in the presscake or meal. Since meal (including hulls) is the single feed item of flax processing, a tolerance of 5.0 ppm in flaxseed could result in a theoretical residue of 6.25 ppm in flax meal. A new Section F requesting a feed additive amendment of 7.0 ppm, sethoxydim residues in flaxseed meal for 21 CFR 561.430 is considered necessary.

Flax Straw

As in the flaxseed trials (with exception of the processing study), eight studies were performed at four locations using two different quantities of Poast for postemergence weed control:

Location	Rate (lb ai/A)	PHI (days)	Total Residue (ppm)
Minot, ND	0.5	67	< 1.00
	0.5 + 0.3	31	1.02
Fargo, ND	0.5	99	< 1.00
	0.5 + 0.3	77	< 1.00
Grand Forks, MN	0.5	75	< 1.00
	0.5 + 0.3	61	1.23
Brookings, SD	0.5	63	< 1.00
	0.5 + 0.3	50	< 1.00

The two measurable quantities of residue were for MSO and no detectable hydroxy metabolite was present. Therefore, the maximum quantities of sethoxydim residues in flax straw are 1.02 ppm and 1.23 ppm, or less.

RCB concludes that the above data indicate that a tolerance of 2.0 ppm sethoxydim residues would not be exceeded in flax straw as a result of the proposed use.

In summary, the residue data presented are geographically adequate and present sufficient residue results in RAC and processed commodity to allow for tolerance setting. Providing the proposed use and labeling (Section B) are properly revised as indicated, RCB could recommend for a 5.0 ppm tolerance in the RAC, flaxseed, and a 2.0 ppm tolerance for sethoxydim residues in flax straw. A revised Section F including a feed additive proposal of 7.0 ppm will be necessary for a tolerance in flaxseed meal.

Meat, Milk, Poultry and Eggs

Tolerances are established in meat, meat byproducts, and fat of all livestock and poultry at 0.2 ppm; in milk at 0.05 ppm; and in eggs at 0.5 ppm (40 CFR 180.412). These levels were established by sethoxydim feeding studies in poultry at 25 ppm and in cattle (ruminants) at 50 ppm (PP#3F2904, K. Arne, June 26, 1985).

Flax meal is a feed for dairy and beef cattle, swine, and poultry. Flaxseed is a feed for poultry and swine, while flax straw is fed to cattle. The three feed items are rather unsignificant as potential contributors to secondary residues from sethoxydim when you consider that any livestock must be fed at a level > 50 ppm and poultry must be fed at a level of > 25 ppm in order to exceed the tolerance levels established for meat, milk, poultry, and eggs. As an example of flax residues' contribution in animal diets, the following typical rations are calculated for total sethoxydim residues:

Dairy Cattle

Flax meal 25% x 7 ppm	=	1.75
Flax Straw 10% x 2 ppm	=	0.20
*Alfalfa hay 65% x 20 ppm	=	13.00
		14.95 ppm

Swine

Flax meal - 5% x 7 ppm	= 0.35
Flaxseed - 20% x 5 ppm	= 1.00
Soybeans - 20% x 10 ppm	= 2.00
*Soybean forage - 20% x 20 ppm	= 4.00
(Corn - 35%)	
	7.35 ppm

Poultry

Flax meal - 3% x 7 ppm	= 0.21
Flaxseed - 3% x 5 ppm	= 0.15
Alfalfa seed - 20% x 2 ppm	= 0.40
Cottonseed - 10% x 5 ppm	= 0.50
Soybeans - 50% x 10 ppm	= 5.00
(Corn - 17%)	
	6.26 ppm

*Tolerances not established, but are recommended by RCB.

It is clear from the dietary rations, including flax feed items, that the tolerances established for meat, milk, poultry, and eggs will not be exceeded by secondary residues resulting from the proposed tolerance levels of sethoxydim residues in flax.

Other Considerations

An International Residue Limit Status sheet is attached. No international tolerances for flax are established. Therefore, there is no compatibility problem.

Attachment

RCB:TS-769:F.Boyd:Edited by vg:CM#2:Rm804:X77484:9/10/86
cc: circ, R.F., EAB, PP#6E3411, EEB, TOX, PMSD/ISB, F. Boyd
RDI: J.H. Onley, 8/27/86; R.D. Schmitt, 8/27/86

87814:Boyd:C.Disk:KENCO:8/28/86:sj:lf

ATTACHMENT

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL SETHOXYDIM (POAST®) PETITION NO. 6E3411

CCPR NO. _____

BPP 9/5/86

F. Hue 9/9/86

Codex Status

Proposed U.S. Tolerances

[✓] No Codex Proposal
Step 6 or above

Residue (if Step 9): _____

Residue: SETHOXYDIM AND 2-CYCLOHEXEN-1-ONE CONTAINING METABOLITES

Crop(s) Limit (mg/kg)

Crop(s)	Tol. (ppm)
Flaxseed	5.0
Flax straw	2.0

CANADIAN LIMIT

Residue: parent compound.

Crop	Limit (ppm)
Flax	0.1 1/

MEXICAN TOLERANCIA

Residue: _____

Crop	Tolerancia (ppm)
None.	

NOTES:

1/ Negligible residue type limit