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

JUL 17 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#5F3234/FAP#5H5464 [RCB #'s 943 and 944]. Sethoxydim (Poast®) on Sunflowers and Peanuts. Evaluation of Analytical Methods and Residue Data (Accession Number 073424).

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and

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THRU: Charles L. Trichilo, Ph.D., Chief
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BASF Wyandotte Corporation proposes that 40 CFR 180.412 be amended by establishing tolerances for the combined residues of the herbicide 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one (Poast®, sethoxydim, BASF 9052H) and its metabolites containing the 2-cyclohexen-1-one moiety, calculated as the parent compound, in or on the following raw agricultural commodities (rac's):

peanuts	25.0 ppm
peanut, hulls	5.0 ppm
sunflower, seeds	7.0 ppm

In addition, the petitioner also proposes that 21 CFR 561.430 be amended by establishing feed additive tolerances for combined residues of sethoxydim and its metabolites containing the 2-cyclohexen-1-one moiety (calculated as parent compound) in or on the following animal feed items:

peanut soapstock	75.0 ppm
sunflower meal	20.0 ppm

Tolerances for residues of sethoxydim (parent plus metabolites) in/on peanuts and sunflowers were originally proposed in conjunction with PP#3F2950/FAP#3H5413, but were withdrawn in an April 17, 1984, amendment (see K. Arne memo of June 2, 1984). The petitioner states that this new petition "is supported almost entirely by data already reviewed by RCB as part of PP#3F2950 ..."

Sethoxydim tolerances are currently established for residues (parent plus metabolites) in/on cotton, soybeans, sugar beets, and animal commodities at levels ranging from 0.05 to 15 parts per million.

RCB has previously recommended for issuances of Section 18 exemptions for the use of Poast® on peanuts in Oklahoma, Texas, and Virginia, and on sunflowers in North Dakota.

Sethoxydim has not yet been the subject of a Registration Standard.

Conclusions

1. Since the proposed label contains restrictions against feeding treated peanut and sunflower forage or hay to livestock, tolerances will not be required on these commodities.

2. The nature of the residue in oilseed crops is considered adequately understood. The residues of concern consist of sethoxydim and its metabolites containing the 2-cyclohexen-1-one moiety.

3a. The nature of the residue in ruminants will be considered adequately understood provided the petitioner submits reproductions of the TLC chromatograms used to identify metabolites in liver and kidney. If these do not support the petitioner's identification of metabolites, further studies may be needed (see K. Arne memo of June 26, 1985 re: PP#3F2904).

3b. Reiterating the conclusion reached in RCB's review of PP#3F2904 regarding the metabolism of sethoxydim in poultry (see K. Arne memo of June 26, 1985):

> The nature of the residue in poultry is not well understood. Of edible tissues, characterization was attempted only for liver, resulting in identificaition of 41% of this activity. In addition, available methodology is capable of determining only 44% of the liver activity, 43% of the fat activity, and 64% of the muscle activity.

RCB requires that additional attempts be made to characterize activity in poultry fat, muscle, and liver. The extracted activity from fat and muscle should be subjected to TLC, and the methanol soluble liver activity should be subjected to hydrolysis to release any polar conjugates. Any released activity should be characterized. The nature of the residue in eggs is adequately understood.

4a. Adequate analytical methodology is available to enforce the proposed sethoxydim tolerances for plant commodities.

4b. RCB can reach no final conclusions concerning the adequacy of the analytical methodology for enforcement of sethoxydim tolerances for animal commodities until questions concerning the nature of the residue in animals have been resolved (see Conclusions 3a and 3b). Additional analytical methods may be required for animal commodities depending on the outcome of the additional requested metabolism work.

5a. The petitioner should clarify the mode of application for all residue field trial data submitted with PP#3F2950/FAP#3H5413. If the residue data do not reflect aerial application, either additional such data should be submitted or a label (Section B) restriction against aerial application will be required. Should any additional residue data be generated, Conclusions 5b and 5c may require revision.

5b. The proposed sethoxydim tolerances for residues (parent plus metabolites) in/on peanuts, peanut hulls, and sunflower seeds at 25, 5, and 7 ppm, respectively, are adequately supported by the available residue data, pending resolution of Conclusion 5a.

5c. The proposed sethoxydim feed additive tolerances for residues (parent plus metabolites) in peanut soapstock at 75 ppm and sunflower meal at 20 ppm are adequately supported by the available residue data, pending resolution of Conclusion 5a.

6. Until questions concerning animal metabolism of sethoxydim are resolved (see Conclusions 3a and 3b), RCB can reach no conclusions concerning the level of secondary residues in meat, fat, milk, poultry, and eggs resulting from the proposed use on peanuts and sunflowers.

Depending on the outcome of the further requested work and data concerning the metabolism of sethoxydim in livestock, additional feeding studies may be required.

7. An International Residue Limit Status sheet is attached to this review. Since no Codex, Canadian, or Mexican limits/tolerances are established for sethoxydim residues in/on sunflowers and peanuts, there are no compatibility problems.

Recommendation

At this time, RCB recommends against the proposed sethoxydim tolerances on peanut and sunflower commodities for the reasons cited under Conclusions 3a, 3b, 4b, 5a, and 6. Pending resolution of Conclusion 5a, Conclusions 5b and 5c are considered tentative.

Manufacture and Formulation

The manufacturing process for technical sethoxydim is discussed in RCB's review of PP#0G2396 (see E. Zager memo of December 4, 1980). The technical material is greater than 94.9 percent pure. RCB does not expect impurities in the technical material to present a residue problem.

The formulation proposed for use on peanuts and sunflowers is Poast® herbicide (EPA Registration No. 7969-58) which contains 20 percent ai by weight. All inerts are cleared under 40 CFR 180.1001.

Proposed Uses on Peanuts and Sunflowers

a. Peanuts

For control of postemergent annual and perennial grasses, Poast® is to be applied once at a rate of 1 to 2 pints (0.2 to 0.4 lb ai)/A, or twice at rates of 1 to 1.5 pints (0.2 to 0.3 lb ai)/A for the first application and 1 pint (0.2 lb ai)/A for the second application.

All applications must include the use of an EPA-approved oil concentrate at a rate of 2 pints/A. Application can be made by ground equipment using a volume of 5 to 20 gal of spray solution per acre, or by aerial equipment using a volume of 5 to 10 gal of spray solution per acre.

The proposed use for peanuts includes the following restrictions:

i. Do not apply Poast® to peanuts within 70 days of harvest (i.e., PHI = 70 days).

ii. Do not apply more than 2.5 pints of Poast® (0.5 lb ai)/A/season.

iii. Do not feed treated peanut forage or hay to livestock.

The maximum amount of Poast® to be applied per season (2.5 pints) to peanuts is now half of that proposed in conjunction with PP#3F2950/FAP#3H5413. Also, the tolerance for peanut hay proposed in conjunction with PP#3F2950/FAP#3H5413 has been replaced in the subject petition with a livestock feeding restriction.

b. Sunflowers

For control of postemergent annual and perennial grasses, apply Poast® to sunflowers once at a rate of 0.5 to 2.5 pints (0.1 to 0.5 lb ai)/A, or twice at rates of 1 to 1.5 pints (0.2 to 0.3 lb ai)/A for the first treatment and 1 pint (0.2 lb ai)/A for the second treatment.

The use of EPA-approved oil concentrates and the directions for ground and aerial application are the same as that proposed for peanuts.

The proposed use for sunflowers includes the following restrictions:

i. Do not apply Poast® to sunflowers within 70 days of harvest.

ii. Do not apply more than a maximum of 2.5 pints of Poast® (0.5 lb ai)/A/season.

iii. Do not feed treated sunflower forage to livestock.

The use proposed in conjunction with the subject petition for sunflowers is the same as that previously proposed in conjunction with PP#3F2950/FAP#3H5413.

Nature of the Residue

a. Plants

No new plant metabolism studies were submitted in conjunction with the subject petition.

The metabolism of ^{14}C-labeled sethoxydim in sugarbeets and soybeans/alfalfa has been extensively discussed in RCB's reviews of PP#3F2950/FAP#3H5413 (see K. Arne memo of February 2, 1984), and PP#3F2904 (see K. Arne memo of June 26, 1985), respectively.

The metabolism of sethoxydim in these plants is very complex, although the majority of the terminal residue consists of compounds containing the 2-cyclohexen-1-one moiety, which can be detected by the available analytical methodology (see Analytical Methodology section of this review).

Thus, the nature of the residue in peanuts and sunflowers is considered adequately understood. The residues of concern in these crops consist of parent plus metabolites containing the 2-cyclohexen-1-one moiety.

b. Animals

No new livestock metabolism studies were submitted in conjunction with the subject petition.

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The metabolism of ^{14}C-sethoxydim in lactating goats and laying hens has been extensively discussed in RCB's review of PP#3F2904 (see K. Arne memo of June 26, 1985).

In goats, metabolism of sethoxydim involves oxidation of the sulfur atom to the sulfoxide and sulfone, demethylation to form a "nor" series of metabolites, hydroxylation of the ring in the 5-position, de-ethoxylation of the imino group, and formation of an oxazole via Beckman rearrangement. Metabolites formed by these processes are determined by the proposed analytical methodology (i.e., the petitioner has demonstrated that the proposed methodology will determine a majority of the total radioactive residue in milk and tissue resulting from ingestion of ^{14}C-sethoxydim.

In RCB's June 29, 1985, review of PP#3F2904, it was concluded that the nature of the residue in ruminants is considered adequately understood, provided the petitioner submits reproductions of the TLC chromatograms used to identify metabolites in liver and kidney. If these do not support the petitioner's identification of metabolites, further work may be needed.

The laying hen metabolism study submitted with PP#3F2904 was considered inadequate for determining the nature of the residue in poultry because of all edible tissues, characterization was attempted only for liver, and since the proposed methodology is capable of determining only 44 percent of the liver ^{14}C-activity, 43 percent of the fat ^{14}C-activity, and 64 percent of the muscle ^{14}C-activity. In RCB's review of this study (see K. Arne memo of June 28, 1985), it was concluded that although the nature of the residue in eggs is adequately understood, additional attempts should be made to characterize ^{14}C-activity in poultry fat, muscle, and liver. The extracted ^{14}C-activity should be subjected to TLC, and the methanol soluble liver ^{14}C-activity should be subjected to hydrolysis (acid, base and enzyme) to release any polar conjugates. Any released ^{14}C-activity should be characterized.

Analytical Methodology

The analytical method used to determine residues of sethoxydim (parent plus metabolites containing the 2-cyclohexen-1-one moiety) in/on peanuts, peanut hulls, and sunflower seeds and meal is designated BWC Agricultural Chemicals Method No. 30. A similar method of analysis for peanut and sunflower soapstock is designated Method No. 30F. In conjunction with PP#3F2670, Method 30 was successfully tried out on soybeans, milk, and liver (see M. Nelson memo of April 22, 1983).

In brief, these methods involve residue extraction (the extraction depends on the substrate), oxidation with hydrogen peroxide to the substituted pentanedioic acids which are then converted to the corresponding dimethyl esters. These residues are cleaned up by solvent partitioning and column chromatography before being determined via GLC using a flame photometric detector in the sulfur mode.

Control and fortification/recovery data presented in RCB's review of PP#3F2950/FAP#3H5413 (see K. Arne memo of February 2, 1984), are repeated below:

Commodity	Control (ppm)	Fortification (ppm)	Recovery % Range	(Average)
peanuts				
nuts	< 0.10-5.4*	0.05-20	66-106	86
hulls	0.06-0.1	0.05-5	67-118	91
process fractions		0.05-60	53-94	82
sunflowers				
seeds	0.08-0.15	0.05-5	72-120	100
process fractions	0.01	0.04-5	60-115	74

* this value is considered anomalous

In RCB's review of PP#3F2950/FAP#3H5413 (see K. Arne memo of February 2, 1984), it was stated that the above control and recovery values are adequate, but no conclusion can be reached as to the adequacy of the analytical methodology until plant metabolism questions are resolved and until it is demonstrated that the method will determine weathered residues.

Since the nature of the residue is now considered adequately resolved in oilseed crops (soybeans, peanuts, sunflowers), and since the Method No. 30 extraction step can recover 91 percent of the total radioactivity in soybean seeds from plants treated with ^{14}C-sethoxydim (see K. Arne memo of June 26, 1985, re: PP#3F2904), RCB now concludes that adequate methodology is available for the enforcement of proposed sethoxydim tolerances for residues (parent plus metabolites) in/on peanuts and sunflowers.

However, because questions remain concerning the nature of the residue in ruminants and poultry, RCB can reach no final conclusion concerning the adequacy of enforcement methods with regard to the analysis of animal commodities. Additional analytical methodology may be required for poultry depending on the outcome of the additional requested metabolism work.

Residue Data

No new residue data were submitted in the subject petition. The petitioner refers to residue data submitted in conjunction with PP#3F2950/FAP#3H5413.

Since the mode of application is not clear for these previous studies, the petitioner should submit this information in a future amendment. If the residue data do not reflect aerial application,

either additional such data should be generated or aerial application should be restricted in a revised Section B. Should additional data be generated, the tentative conclusions reached below may require revision.

a. Peanuts

Field trials were conducted in the states of Texas, Oklahoma, Alabama, Georgia, North Carolina, and Virginia. As a result of one application at a rate of 0.5 lb ai/A and PHI's ranging from 45 to 118 days (note: maximum proposed use allows up to 0.5 lb ai/A/season with a 70-day PHI), total sethoxydim residues (parent plus metabolites) ranged from 0.09 to 17.1 ppm in/on peanut nut meat and 0.09 to 3.2 ppm in/on peanut hulls (note: these values are apparently uncorrected for method recovery).

Taking into account method recovery, RCB tentatively considers the proposed 25 ppm and 5 ppm sethoxydim tolerances for peanut nut meat and hulls, respectively, adequate to cover parent plus metabolites residues resulting from the proposed use on peanuts.

b. Peanut Processed Fractions

The following table summarizes the results of a peanut processing study:

Sample	Residue Level (ppm)	Concentration Factor	Maximum Expected Residue (ppm)
peanut nut meat	16.3	-	25.0[a]
screwpress cake (spc)	12.3	0.75	18.9
solvent extracted spc	9.8	0.60	15.0
crude oil	8.5	0.52	13.0
refined oil	2.8	0.44	11.1
soapstock	48.4	2.97	74.2

[a] proposed tolerance

Based on the above results, RCB tentatively considers the proposed 75 ppm tolerance for residues of sethoxydim (parent plus metabolites) in peanut soapstock adequately supported.

c. Sunflowers

Sunflower field trials were conducted in the states of Minnesota, North Dakota, Texas, Kansas and Illinois. As a result of one application at a rate of 0.5 lb ai/A and PHI's of 53 to 118 days (note: maximum proposed use allows up to 0.5 lb ai/A/season with a 70-day PHI), total sethoxydim residues ranged from 0.08 to 5.8 ppm in/on sunflower seeds.

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RCB tentatively considers these data adequate to support the proposed 7.0 ppm tolerance covering residues of sethoxydim in/on sunflowers resulting from the proposed use.

d. Sunflower Seed Processed Fractions

The results of two sunflower seed processing studies are tabularized below:

Sample	Residue Level (ppm)	Concentration Factor	Maximum Expected Residue (ppm)
sunflower seeds	2.9	-	7.0[a]
hulls	1.4	0.48	3.4
meal	3.8	1.31	9.2
crude oil	0.91	0.31	2.2
refined oil	< 0.05	-	-
soapstock	5.1	1.76	12.3
sunflower seeds	2.1	-	7.0[a]
hulls	0.67	0.32	2.2
meal	5.5	2.62	18.3
crude oil	0.72	0.34	2.4
refined oil	0.22	0.10	0.73
soapstock	3.9	1.86	13.0

[a] proposed tolerance

Based on the above results, RCB tentatively considers the proposed 20 ppm tolerance for residues of sethoxydim (parent plus metabolites) in sunflower meal adequately supported. Although residues concentrate in sunflower soapstock, this is not considered an animal feed item, thus, no tolerance is required.

Residue in Meat, Fat, Milk, Poultry, and Eggs

Peanut meal and soapstock, as well as sunflower meal and hulls can be used as livestock feed items.

The results of goat, cattle, and hen feeding studies are discussed in RCB's review of PP#3F2904 (see K. Arne memo of June 26, 1985).

Until animal metabolism questions are resolved (see Nature of the Residue section of this review), RCB cannot reach any conclusions concerning the level of secondary residues in meat, fat, milk, poultry and eggs resulting from the proposed uses.

Depending on the outcome of the requested further studies concerning the metabolism of sethoxydim in poultry, additional feeding studies may be required.

Other Considerations

An International Residue Limit Status sheet is attached to this review. Since no Codex, Mexican, or Canadian tolerances/limits are established for sethoxydim on sunflowers and peanuts, there are no compatibility problems.

cc: R.F., Circu, Reviewer, TOX, EAB, EEB, PP#5F3234/FAP#5H5464
FDA, Robert E. Thompson (RTP), PMSD/ISB
RDI:JHOnley:7/9/85:RDSchmitt:7/9/85
TS-769:Reviewer:MPFirestone:typed by Kendricks: edited by wh
:RM 810:CM#2:7/17/85

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL: sethoxydim (Poast®)

PETITION NO.: 5F3234/5H5464

CCPR NO.:

REVIEWER: Michael P. Firestone

I, ltr 5/22/85

Codex Status

☒ No Codex Proposal Step 6 or above

Residue (if Step 9):

Crop(s) | Limit (mg/kg)

Proposed U.S. Tolerances

Residue: sethoxydim [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).

Crop(s)	Tol. (ppm)
peanuts	25
peanut hulls	5
peanut soapstock	75
sunflower seeds	7
sunflower meal	20

CANADIAN LIMIT

Residue:

Crop(s)	Limit (ppm)
none (on above commodities)	1/

MEXICAN TOLERANCIA

Residue:

Crop(s)	Tolerancia (ppm)
none	

Notes: 1/ There are Canadian 0.1ppm negligible residue type limits on other commodities, including flax & rapeseed.