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

SEP 25 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6F3405, Sethoxydim in or on Sugarbeet Tops. Evaluation of Analytical Methods and Residue Data for Increasing the Existing Tolerance. (Accession No.262495; RCB No. 996).

FROM: V. F. Boyd, Ph.D., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

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

TO: Robert Taylor, PM#25
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation (TS-769)

BASF Corporation Chemicals Division, Agricultural Chemicals Group, request the establishment of a new tolerance for combined residues of sethoxydim, 2-[1-(ethoxyimino)butyl]-5[2-(ethylthio) propyl]-3-hydroxy-2-cyclohexen -1-one, and its 2-cyclohexen -1-one-containing metabolites (calculated as the herbicide) in or on the raw agricultural commodity sugar beet tops at 2.0 ppm.

Sethoxydim tolerances are established for sugar beet roots at 0.1 ppm and sugar beet tops at 0.2 ppm (40 CFR 180.412), and a food additive tolerance is established for sugar beet molasses at 0.5 ppm (21 CFR 561-430). These tolerances were recommended for approval by RCB under PP#3F2950, memos of Karl Arne, 2/2/84, 4/5/84 and 6/29/84.

On April 12, 1985 the Petitioner BASF submitted a supplemental amended labelling that restricted against the feeding of sugar beet tops since new residue data generated from trials in California resulted in residue levels as high as 0.71 ppm following application by air and 1.75 ppm following application by ground. The label restriction was recommended under Accession No. 259030 (see review of L. Propst, (9/12/85) until additional residue data could be collected for ascertaining an adequate tolerance level.

In a letter of January 24, 1986 the Petitioner indicated that a feeding restriction for sugar beet tops caused an inconvenience to the California Sugar Beet Growers and the Petitioner requested a re-review of the previously submitted (4/12/85) residue data. RCB's re-review of that residue data still showed that residue levels of sethoxydim on sugar beet tops may exceed the tolerance of 0.2 ppm. The RCB recommendation was that the registrant could continue to restrict feeding of tops or may choose to submit a petition requesting a tolerance of 2.0 ppm. The statement was made, "The registrant should be advised that no amount of additional residue data will negate the valid data previously submitted showing over tolerance residues of Poast® on sugar beet tops occurring as a result of the currently registered uses." (Acc. No. 261077, memo of L. Propst, 3/24/86).

In this petition the Petitioner has chosen to request an increase of tolerance to 2.0 ppm sethoxydim and its metabolites in sugar beet tops. Additional data have not been submitted.

Permanent tolerances have been established on cottonseed at 5 ppm, soybeans at 7 ppm, and on milk, meat, poultry and eggs at levels of 0.05 to 0.5 ppm (40 CFR 180.412).

Conclusions

(1a) The restriction against feeding of sugar beet tops should not be removed from the present label until the danger of overtolerance residue levels does not exist.

(1b) A specific statement of Preharvest Interval (PHI) in number of days needs to be included in the Section B label for the purpose of controlling maximium sethoxydim residues in sugar beet tops.

(2) Residue Chemistry Branch (RCB) concludes that the residues in sugar beet tops and in animals is adequately understood for the purpose of the petition. The residues of concern are the parent compound sethoxydim and its metabolites containing the 2-cyclohexen-1-one moiety.

(3) Adequate analytical methodology is available in Vol. 2 of the FDA Pesticide Analytical Manual for enforcement purposes.

(4a) Adequate storage stability data have been reviewed.

(4b) Submitted Residue data indicate that overtolerance residue levels could be expected in sugar beet tops from the present labeled use.

(4c) The residue data on hand are not adequate to support the proposed tolerance of 2 ppm sethoxydim residues in sugar beet tops. Therefore, additional residue data (to be generated in CA or AZ, ID, MI, and ND or MN) reflective of maximum proposed rate and a minimum proposed PHI, are necessary to establish a residue level for tolerance purposes.

NOTE TO PM: Petitioner should be copied on the detailed discussion of Residue Data in this review, especially the recommendation regarding additional residue field trials for data gathering.

(5) Since sugar beet tops are fed to livestock, an assessment of potential secondary residues in meat and milk will be required when a supportable residue tolerance is proposed.

(6) An International Residue Limit Status sheet is attached. Codex has not established a sethoxydim tolerance on sugar beet tops. Therefore, there will not be a compatibility problem.

Recommendation

RCB cannot recommend for establishing a tolerance of 2ppm sethoxydim residues in sugar beet tops until deficiencies listed in conclusions 1b, 4b, 4C, and 5 have been resolved. At this time, RCB recommends against removal of the label statement restricting against feeding of Poast treated sugar beet tops.

Detailed Considerations

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 sugar beets is Poast® herbicide (EPA Registration No. 7969-58) which contains 20 percent ai by weight. All inerts are cleared under 400 CFR 180.1001.

Proposed Use

The only change in proposed use is the request for removal of the statement, "Do not feed treated sugar beet tops to livestock". Otherwise the labeled use is as presented previously (PP#32950, K. Arne, 2/2/84):

"For control of grasses in states other than California, Arizona, and New Mexico, Poast is to be applied at rates of 1-2 pints (0.2-0.4 lb. a.i.)/A. In California, Arizona, and New Mexico rates of up to 2 1/2 pts (0.5 lbs. a.i./A) may be needed. No more than 5 pints/A are to be applied per growing season. There is no PHI stipulated for sugarbeets, but the general directions advise one application 15-30 days after planting and a second application, if needed, a few weeks later; since sugarbeets have a long growing season the practical minimum PHI would be about 100 days."

The proposed use would indicate that the residue level from two applications of 0.5 lbs /ai/A and a PHI of about 100days would probably result in a high residue level in sugarbeet tops. Applications are made by air or ground.

RCB thus concludes the following:

(a) The restriction against feeding of sugarbeet tops should not be removed from the present label until the danger of overtolerance residue levels does not exist.

(b) A specific statement of Preharvest Interval in number of days needs to be included in the Section B label for the purpose of controlling maximum sethoxydim residues in sugarbeet tops.

Nature of the Residue

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 identified metabolities 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 sugar beets 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.

In animals, C^{14}sethoxydim studies were performed in goats and laying hens (PP#3F2904, K. Arne, 6/25/85). From amended data it was concluded that concerned residues of sethoxydim in ruminants were the parent and its metabolites MSO, MSO_2 nor-MSO, and nor-MSO_2 In poultry, residues of concern 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 concluded 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 containing metabolities.

Analytical Methodology

The analytical methods used to determine residues of sethoxydim in sugar beet tops are designated as BWC Method No. 30 or 30H. BWC-30 is used to monitor residues in meat, milk, poultry and eggs, soybeans and sugar beet roots. In PAM II this method is Method I for sethoxydim residues. A variation of this method, BWC-30H is available to monitor alfalfa, soybean hay, and sugar beet tops. 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.

Recovery values and check data show adequate sensitivity (0.05 ppm) and proficiency of the method (PP#3F2950, K. Arne, 2/2/84).

Residue Data

The efficiency of the Method 30B (see PAM II) for extraction of sethoxydim residues and storage stability data for sugar beets were presented and reviewed in PP#3F2950. Adequate storage stability data have been reviewed.

Table I Sugar beet Top Residues of Sethoxydim

Location and Trial No.	Rate (lb.ai/A)	PHI (days)	Total Residues (ppm)	Treatment Dates
CO #217	0.5 0.5	122 91	<0.05 0.07	6/11/82 7/12/82
MN #219	0.5 0.5	101 81	<0.05 0.10	6/11/82 7/01/82
ND #220	0.5 0.5	118 98	<0.05 0.10	6/25/82 7/15/82
MI #221	0.5 0.5	118 110	<0.05 <0.05	5/26/82 6/03/82
CA #222	0.5+0.5	224	<0.05	3/10/82 3/18/92
CA #223	0.5+0.5	298	<0.05	6/02/82 6/10/82
CA #224	0.5+0.5	220	<0.05	2/18/82 3/04/82
CA #225	1.0	112	NR	7/01/82
ND #226	1.0	155	NR	6/21/82
CA #4115	0.5+0.5(A)	121	0.11	5/03/84 5/23/84
	0.5+0.5(G)	104	1.44	5/01/84 5/24/84
CA #4116	0.5+0.5(A)	101	0.71&0.69	5/23/84 6/12/84
	0.5+0.5(G)	104	1.75&1.48	5/24/84 6/09/84
CA #4117	0.5+0.5(A)	76	0.14	5/11/84 6/12/84
	0.5+0.5(G)	76	0.11	5/11/84 6/12/84

NR=no residue

All residue data on sugar beet tops, presented to date, are summarized in Table I below. The nine field trials numbered from #217 to #226 were originally presented in PP#3F2950 as data to support the 0.2 ppm tolerance for sethoxydim in sugar beets. The final three studies were submitted under the petitioner's letter against feeding sugar beet tops, due to overtolerance residue data. All data in Table I were re-reviewed by RCB upon the January 24, 1986 letter request of the petitioner.

These data in Table I will now be examined for supporting a proposed tolerance of 2 ppm, sethoxydim residues in sugar beet tops. Since the proposed use recommends rates as low as 0.2 lb. ai/A and as high as 0.5+0.5 lb.ai/A, we must examine the highest rate data for determining maximum potential residues. Since an over-the-top application can be made, according to label, as late as 50 days post-planting, the dissipation of leaf and stem residues should be a function of Pre-Harvest Interval (PHI). Examining the Table I data based on an application rate of 0.5+0.5 lb. ai/A and PHI of approximately 100 days, we conclude:

(1) Of 17 trials only 3 (all done in CA) are valid residue data reflective of the proposed maximum use.

(2) These trials #4115, 4116, and 4117) present a wide disparity of results from 0.11 ppm at a 76 day PHI and and also at a 12/day PHI, to a maximum residue of 1.75 ppm at 104 day PHI.

(3) There are good agreements in the replicated samples of trial #4116; 0.71 and 0.69=0.70 mean, and 1.75 and 1.48= 1.61 mean. Also, there is intertrial agreement for Trial #4115 with 1.44 ppm and Trial #4116 with 1.48 ppm at 104 day PHI.

(4) These residue data are insufficient to determine an adequate tolerance level on sugar beet tops .

Additional residue data are required to determine the maximum sethoxydim residues in sugar beet tops from the maximum proposed use. The petitioner must be reminded that his label permits up to a total of 5 pints (1.0 lb ai/A) of Poast for use in sugar beets (see "Restrictions and Limitations for Sugar Beets" section on the proposed label). Residue data generated in CO, MN, ND, and MI reflect the use of only 2 1/2 pints (0.5 lb ai/A) of Poast per season. Therefore, four additional field trials reflecting

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the maximum rate of application per growing season and a shorter PHI of approximately 100 days are recommended in the following locations; 1 in CA or AZ, 1 in ID, 1 in MI and 1 in ND or MN. All field trials should employ application by ground. The studies in MI and ND or MN should also employ application by air. All field trials should employ harvest for analysis at a PHI approximately 100 days after last application.

The additional residue data requested should allow determination of a residue level which is reflective of the intended rate of application and minimum PHI. The minimum PHI, in days, should then be specified in a revised Section B labeling.

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 0.5 ppm; and in eggs at 0.5 ppm (CFR 40 180.412). These levels were established by sethoxydim feeding studies in poultry at 25 ppm and in cattle (ruminants) at 50 ppm, K. Arne, 6/26/85).

Sugar beet tops are not a poultry feed. Since sugar beet tops are fed to livestock, an assessment of potential secondary residues in meat and milk will be required when a supportable residue tolerance is proposed.

Other Considerations:

An International Residue Limit Status sheet is attached. No international tolerances for sugar beet tops are established and no conflict of the chemical basis of tolerance expression would occur from the proposed use.

RCB:TS-769:F.Boyd:gm:CM#2:Rm804:557-7329/9/23/86
cc: Circu., R.F., PP#3E2889, EEB, TOX, PMSD/ISB, F. Boyd
RDI:JHOnley-8/26/86;R.D.Schmitt-9/11/86

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Sethoxydim

CCPR NO.

PETITION NO. 6F3405

Boyd 9/11.

J. Jones 9/12/86

Codex Status

Proposed U.S. Tolerances

[✓] No Codex Proposal
Step 6 or above

Residue (if Step 9):

Residue: Sethoxydim & 2-cyclohexen-1-one containing metabolites.

Crop(s) Limit (mg/kg)

Crop(s) Tol. (ppm)

Sugar beet tops 2.0

CANADIAN LIMIT

Residue:

Crop Limit (ppm)

sugar beets 0.1 1/

MEXICAN TOLERANCIA

Residue:

Crop Tolerancia (ppm)

none

NOTES:

1/ Negligible residue limit, No information on whether this includes tops.