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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#3F2904. Poast® (sethoxydim) on Alfalfa and Soybeans. Evaluation of Amendment Dated December 6, 1985. Accession #260543. RCB # 306.

FROM : Sami Malak, Ph.D., Chemist
Tolerance Petition Section III
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

TO : Robert J. Taylor/Vickie K. Walters, PM #25
Fungicide-Herbicide Branch
Registration Division (TS-767)

And

Toxicology Branch
Hazard Evaluation Division (TS-769)

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

BASF Wyandotte Corporation (BWC) submits this amendment in response to several data deficiencies cited in the Residue Chemistry Branch (RCB) review of the subject petition (PP#3F2904, K. Arne, June 26, 1985).

BWC had previously requested in connection with PP#3F2904 (J. Onley, 1/12/84) that 40CFR180§412 be amended to establish tolerances for the combined residues of the herbicide, sethoxydim, 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one and its metabolites containing the 2-cyclohexene-1-one moiety (calculated as herbicide)in or on the following raw agricultural commodities:

Soybeans, hay and forage ..... 20 ppm
Alfalfa, hay and forage ..... 20 ppm

The petitioner has since submitted an amendment (Accession # 073398, dated 3/12/85) including a revised Section F proposing establishment of tolerances for the combined residues of the herbicide, sethoxydim, and its metabolites as follows:

Soybean hay	10 ppm
Alfalfa, hay and forage	40 ppm
Milk	0.05 ppm

Permanent tolerances currently established under 40CFR180§412 for the combined residues of the herbicide 2-[1-(ethoxyimino) butyl]-5-[2-cyclohexene-1-one and its metabolites containing the 2-cyclohexene-1-one moiety are: 0.05 ppm for milk; 0.2 ppm for the fat, meat and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep; 5 ppm for cottonseed; 0.5 ppm for eggs; and 10 ppm for soybeans.

The following tolerances for residues of sethoxydim are currently pending: 25 ppm for peanuts, 5 ppm for peanut hulls, 75 ppm for peanut soapstock, 7 ppm for sunflower, and 20 ppm for sunflower meal (all are in conjunction with PP#5F3234, M. Firestone, 7/17/85). Other pending tolerances are: 8 ppm for tomato puree, 24 ppm for tomato paste, and 12 ppm for dried tomato pomace (all are in conjunction with PP#5F3284/FAP#5H5475, C. Deyrup, 10/9/85).

The changes in the requested tolerances were in response to certain deficiencies listed in RCB's memo of 1/12/84 (J. Onley). BWC had since responded to these deficiencies (Accession #073398, dated 3/12/85). RCB found that the requested 10 ppm tolerance for residues of sethoxydim in/on soybean hay is supported by the submitted residue data. No tolerance is proposed for soybean forage because the proposed label prohibits grazing treated soybean fields and feeding treated soybean forage or ensilage to livestock The grazing restriction should include the term "green succulent" to read "Do not graze treated soybean fields and do not feed treated soybean forage (green succulent) or ensilage to livestock. Treated soybean hay may be fed." The petitioner is advised to submit a revised Section B to this effect.

No conclusion was reached concerning the requested 40 ppm for residues of sethoxydim in/on alfalfa forage and hay pending resolution of four major deficiencies including clarification of the mode of application to alfalfa and soybeans (K. Arne, ibid., 6/26/85). These deficiencies are stated below followed by the petitioner's response and RCB's comments.

First, however, we will give a brief description of the analytical methods needed for the review process of additional residue data submitted in this amendment:

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Analytical Methods

The analytical methods used to generate residue data in plant and animal commodities are:

Method BWC 30- This is the original method discussed in connection with PP#2F2670 (M. Nelson, 4/22/83) which is also outlined in PAM II as Method I. In this method, residues of poast and its metabolites are extracted from samples with water/methanol, methanol, or acetonitrile, depending on the sample matrix. After the sample extracts are cleaned up by alkaline precipitation and acidic back extraction, the parent compound and the metabolites are oxidized to 3-[2-(ethoxysulfonyl)propyl]pentanedioic acid and 3-[2-(ethoxysulfonyl) propyl]-3-hydroxypentanedioic acid and then derivatized to the corresponding dimethyl esters, referred to as DME and DME-OH. The derivatives are partitioned into methylene chloride and cleaned up by silica gel column chromtography. Some samples require an additional HPLC cleanup step. The parent compound and the combined metabolites are determined as the pentanedioic acid dimethyl esters by GLC with flame photometric detection. The total residue found is expressed in sethoxydim equivalents.

Method detectibility is reported at 0.05 ppm.

In a method tryout, EPA obtained recoveries of Poast and metabolites MSO_2, $M2SO_2$, and 5-OH-MSO_2 that ranged from 73 to 85% for duplicate soybean samples fortified with each compound at 0.1 ppm level. Recoveries of Poast and $M2SO_2$, each added to duplicate beef liver samples at the 0.2 ppm level, ranged from 92 to 95%. Recoveries of MSO_2 and 5-OH-MSO_2, each added to duplicate milk samples at the 0.05 ppm level, ranged from 72 to 90%. See figure 2 below for structures and chemical names/on the aboave abbreviations.

Methods 30H, 30G, and Direct Oxidation (D.O.)

These methods contain slight modifications and variations to method BWC 30 aimed at increasing accountability from the various matrices. These modified methods are discussed by Dr. K. Arne (ibid., 6/26/85). The methods were found comparable to method BWC 30.

Method 30G determines sethoxydim and metabolites in/on alfalfa and soybean forage. Method 30H determines sethoxydim residues in/on alfalfa and soybean hay. The most important modifcation in both methods is the deletion of the dichloromethane partitioning step that, in method BWC 30, occurs just before the oxidtion step. Sensitivity of both methods is reported at 0.05 ppm of sethoxydim equivalents from DME and DME-OH (0.10 ppm total).

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Method D.O. is more suitable for the determination of sethoxydim residues in/on chicken tissues. The original method, BWC 30, is valid for analysis of residues in milk, eggs, and ruminant tissues. In both methods sethoxydim metabolites are derivatized to their corresponding dimethyl ester, 3[2-(ethoxysulfonyl)propyl]pentanedioic acid dimethyl ester, referred to as DME; hydroxy dimethyl ester, 3-[2-(ethylsulfonyl)propyl]-3-hydroxypentanedioic acid dimethyl ester, referred to as OH-DME; and the DME less CH_2 group, 3-[2-(methylsulfonyl)propyl]pentanedioic acid methyl ester, referred to as nor-DME. The nor-series differ from their corresponding metabolites by having CH_3-group instead of an ethyl group attached to the S-atom. The direct oxidation method (DO) was validated against method BWC-30 using goat tissues and milk as well as chicken tissues and eggs, all carrying radioactive residues. The DO method differs from the BWC-30 method in that in the DO the sample is oxidized directly without prior dichloromethane partitioning, and it has slightly higher accountability, reported in this amendment in the range of 51.5-78.7%, relative to the partition method with reported recovery in the range of 57.5-75.1%. The total residue found is expressed in sethoxydim equivalents. Both methods are capable of detecting the nor-series of sethoxydim and metabolites (Telecommunicatiion with Dr. Ed Tanke of BASF on 5/29/86). In the 6/26/85 amendment Dr. K. Arne stated that the direct oxidation method recovered a greater percentage of the activity, however, the difference between the two methods is not great.

The enforcement method has not undergone a MTO for the nor-metabolites, however, the PAM II enforcement method has been validated by the petitioner by fortifying beef tissue, liver kidney and milk using MSO, OH-MSO_2 and nor-MSO at levels from 0.01-0.5 ppm. Recoveries were reported in the range of 86-113%, 83-110%, and 86-96%; averaging 93%, 97%, and 89% for MSO, MSO_2, and nor-MSO_2, respectively.

We will initiate a MTO for the nor-metabolites using the existing enforcement methodology. We will not hold up our concurrence in this tolerance request, if the petitioner agrees to submit the following metabolites to EPA , RTP and COB, Beltsville laboratory: MlSO, nor-MSO, and nor-MSO_2.

Adequate analytical methodologies are available for enforcement of the proposed tolerances. PAM II, Method I, designated as BWC-30, is suitable for enforcement of ruminant tissue and milk tolerances. A variation of BWC-30 method, designated as method 30G, is suitable for enforcement of sethoxydim tolerances in alfalfa forage. A variation in method BWC-30,

designated as method 30H, is suitable for enforcement of sethoxydim tolerances in alfalfa and soybean hay. Finally, a variation of BWC-30 method, designated as the Direct Oxidation method (DO) is suitable for enforcement of the poultry tissue and eggs tolerances. The BWC-30 and DO methods are capable of determining the nor-series of sethoxydim and metabolites.

We recommend that variations in method BWC 30 be included in PAM II as a lettered supplement to Method I for sethoxydim. In the mean time, RCB will initiate a MTO using the existing enforcement methodology for the nor-metabolites of sethoxydim.

Deficiency #1

The petitioner should submit reproduction of TLC's that were used to identify metabolites in liver and kidney of goats. If these are satisfactory, nothing further will be required in conjunction with the goat metabolism study.

Petitioner's Response

The petitioner submitted the requested reproductions of TL chromatograms used to identify sethoxydim metabolites in liver and kidney of the goat reported in Lab Comp. 1069. In these plates, a urine sample from the goat was cochromatographed with liver and kidney methanolic extracts. In essence, the urine sample served as a standard since it contains known metabolites previously identified against 10 known reference compounds (excellent TL Chromatograms are included in HRC Report #415, amendment of 3/12/85). On this basis, known liver and kidney metabolites were scraped off and radioassayed either individually or as pooled samples. Characterization of the metabolites was accomplished on the basis of R_f-value, coupled with the aid of radio-HPLC and chemical behaviors (liquid-liquid partitioning of urine samples at different pH values).

Analysis was accomplished by the use of method BWC-30, referred to as the partition method which is outlined in PAM II as Method I, and variation thereof designated as the direct oxidation method discussed above under Analytical Methods.

Extraction with methanol solubilized 74% of the liver activity and 67% of the kidney activity. Of these 56% and 58% of the total radioactivity were identified in the goat liver and kidney, respectively. For identification, the methanolic extracts were subjected to TLC, developed in dichloromethane/acetone solvent system (1:1). One chromatogram (Figure 9, Acc. # 260543) was spotted with liver and kidney extracts of the goat, and the second (Figure 10, Acc. # 260543) was spotted with kidney, liver and urine extracts. These TLC data, along with HPLC and chemical evidence, support identification of the following metabolites in the goat liver:

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2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 48% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 25% of the total radioactivity; and unidentified materials, accounting for 27% of the total radioactivity. Using the direct oxidation method it was shown that 63% of the total radioactive residues in the liver samples were oxidized to yield 3:1 mixture of DME and OH-DME. For detailed information on the names and structural formulas of the compounds, please refer to Figures #1, 2 and 3 in this review as well as our discussion under deficiency #2.

RCB's Comments

The petitioner complied with RCB's request and submitted the requested TLC used to identify metabolites in liver and kidney of the goat. In addition to the TL chromatograms, identification is supported by the use of radio-HPLC and chemical behaviors on partitioning at different pH values. From the available data, including those in the 6/26/85 amendment and noting that the goat metabolism study was carried out using the sulfoxide metabolite (^{14}C-labeled BAS 9052 H sulfoxide designated as ^{14}C-MSO), the petitioner has demonstrated that in goats the following metabolic routes take place:

1. The sulfur atom is oxidized to the sulfoxide and sulfone.

2. Demethylation to form a "nor" series of metabolites occurs.

3. The ring is hydroxylated in the 5-position.

4. The imino group is de-ethoxylated.

5. An oxazole is formed as a result of Beckman rearrangement.

The above 5 points were discussed in RCB's memo of 6/26/85 (K. Arne). We should add here that reduction of the sulfoxide may occur, which is somewhat unusual, reverting back to the parent compound, sethoxydim, referred to as MS. With this information in mind, the following conclusions are extrapolated:

1. Sethoxydim residues in ruminant milk consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 25% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfinyl)propyl]-3-hydroxy2-cyclohexene-1-one, referred to as nor-MSO, accounting for 5% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy2-cyclohexene-1-one, referred to as MSO_2, accounting for 10% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO_2, accounting for <3% of the total radioactivity.

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2. Sethoxydim residues detectable in ruminant liver as reported in the 6/26/85 amendment consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MS, accounting for 12% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(methylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MS, accounting for 7% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 8% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO, accounting for 3% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 21% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO_2, accounting for 4% of the total radioactivity; for a total of 55% identified activity. In this amendment, it was shown that MSO_2 and MSO are two major metabolites in the goat liver accounting for up to 48 and 25% of the total radioactivity, respectively; for a total of 73% identified activity.

3. Sethoxydim residues detectable in ruminant kidney as reported in the 6/26/85 amendment consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MS, accounting for 2.5% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(methylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MS, accounting for <2% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 21% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO, accounting for 12% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 16% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO_2, accounting for 5% of the total radioactivity; for a total of 58% identified activity.

4. Sethoxydim residues in ruminant meat and fat were very low to permit characterization of their nature.

Since known sethoxydim metabolites contain the 2-cyclohexene-1-one moiety, RCB considers the nature of the residues in ruminants to be adequately delineated. The residues of concern in ruminants consist of the parent and its metabolites containing the 2-cyclohexene-1-one moiety as expressed in 40CFR§180.412.

Notes:

1. For more details on the names and structural formulas of sethoxydim metabolites, please refer to Figures #2 and #3 in this review.

2. Both BWC-30 and the Direct Oxidation methods are capable of determining the nor-series of sethoxydim and metabolites (personal communication with Dr. Ed Tanek of BASF, 5/29/86).

Deficiency #2

RCB requires that additional attempts be made to characterize activity in poultry fat, muscle, and liver. The extracted activity from the fat and muscle should be subjected to hydrolysis to release any polar conjugates. Any released activity should be characterized.

Petitioner's Response

Additional data on the metabolism of sethoxydim in poultry are included in Reports Lab Com. 1068 and 1070.

The study reported in Lab Com. 1068 is entitled "Further Investigations on The Metabolism of ^{14}C-BAS 9052 H Sulfoxide in Laying Hens," dated September 1985. In this study, liver, muscle, fat, and skin samples were taken from two laying hens sacrificed 6 hours after the last dose. These are the same hens discussed in K. Arne's memo of 6/26/85 that were kept frozen (-21°C). In the original 6/26/85 amendment, four groups of five laying hens each were administered a daily dose for seven consecutive days using 5 mg/bird, equivalent to about 50 ppm in the diet, using the sulfoxide metabolite (^{14}C-labeled BAS 9052 H sulfoxide, designated as ^{14}C MSO). Samples were analyzed on 8/12/85 after approximately eight months in storage. By comparing the 1984 data, it was shown that the metabolites are stable for approximately one year when fortified animal commodities were frozen under -21 °C (see Lab Com. 1068 and 1069 of this amendment, Acc. # 260543). Samples were analyzed using BWC30 method and a variation of this method, designated as the Direct Oxidation (DO) method. In both methods, the oxidative/ hydrolysis or enzymatic cleavage conditions convert the radioactive residues of parent and metabolites (including the nor-metabolites) to glutaric acid derivatives. This in turn is derivatized to the corresponding dimethyl ester, referred to as ^{14}C-DME, OH-DME, and norDME. The nor-series uncovered in ruminant's milk and tissues differ from their corresponding precursors by one CH_2-group less attached to the S-atom. Identification of metabolites was accomplished by the use of radio-TLC against 9 known reference standards, not including the nor-series of standards. The names and structural formulas of the nine standards are shown in Figure-1. More details on the names and structural formulas of sethoxydim and related reference standards are given in Figures-2 and 3 in this review.

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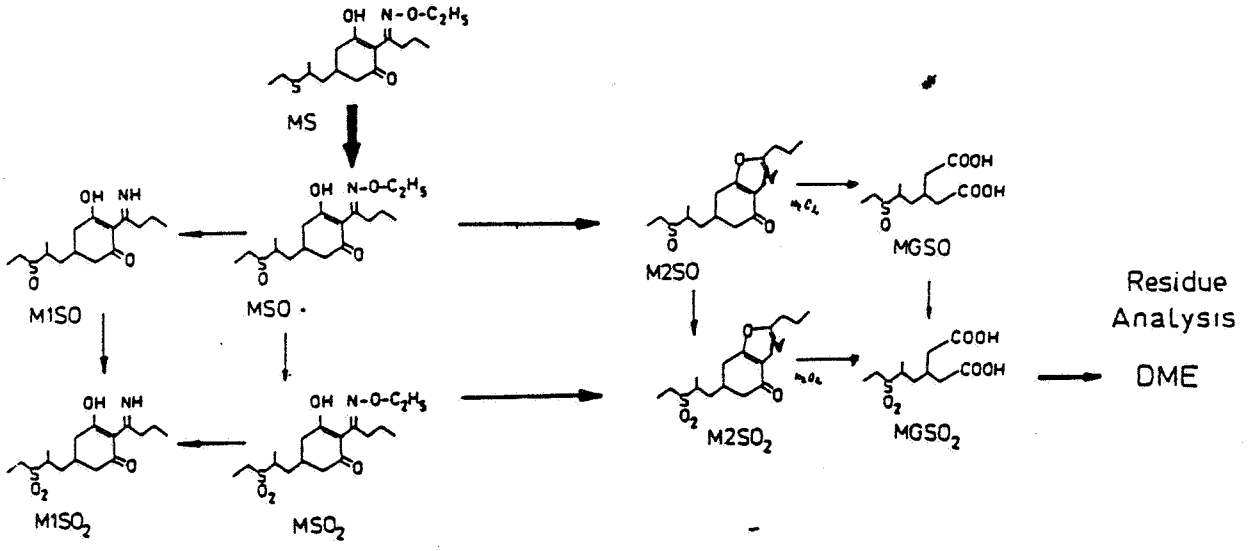
Figure-1: Names and Structural Formulas of Sethoxydim Reference Standards.



Test results are summarized in Tables #1 and #2. Table #1 gives the level of activity recovered in the various extracts, and characterization of residues are given in Table #2.

Table-1. Level of Activity in Poultry Tissue:

Poultry tissue	Total activity 1/	Percent of total residues		
		methanol extracts	DCM phase	aqueous phase
Muscle	0.79	92.4	81.0	13.9
Fat	0.192	96.9	67.7	20.8
Skin	0.94	93.6	93.6	6.4
Liver	1.69	88.8	92.3	0.6

1/ppm sulfoxide equivalent.

Reported total activity are comparable to those previously reviewed by Dr. K. Arne (6/26/85). We note that a minimum of 89% of the activity were extracted in methanol. Also, most of the activity partitioned into dichloromethane (DMC) phase with a minimum of 68% from the fat and a maximum of 94% from the skin. Results from the oxidation reactions has shown that a minimum of 79% of the radioactivity partitioned into the DCM-phase. Thus, the oxidation reaction did not release gaseous $^{14}CO_2$.

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Table-2. Radio-TLC Residue Characterization of Sethoxydim Metabolites in Poultry Tissues, Expressed in Percentage of Total Radioactivity:

Tissue	MSO	MSO_2	M1SO	Polar compounds	Sum
Muscle	50	27	5	ND	82
Fat	39	23	6	ND	68
Skin	57	37	ND	ND	94
Liver	37	35	14	6	92
Liver[1]/	24	17	14	11	66

ND = Not Detected (<0.05 ppm).
1/ Previous data in K. Arne memo of 6/26/85.

Table #2 shows that the main methanolic extractable metabolites identified in poultry muscle, fat, skin, and liver are comprised of MSO, MSO_2, and small amounts of M1SO. These three metabolites accounted for more than 68% of the radioactivity applied onto TLC-plates for the four tissue-types. By using strong hydrolysis and oxidative conditions, practically all of the radioactive residues in the methanol extracts were converted to a single product ($MGSO_2$) which was derivatized to pure ^{14}C-DME. Hydrolysis released 6% of polar conjugates in the liver, but no polar compounds were released from the chicken muscle, fat and skin.

The study reported in Lab Com 1070 entitled "Investigation of Radioactive Residues from BAS ^{14}C-BAS 9052H Treated Chicken-Newly Generated Tissue Samples," dated September, 1985.

In this study, laying hens were dosed daily for five consecutive days using one capsule containing 20 mg of ^{14}C-BAS 9052H, equivalent to 200 ppm/bird/day (used parent since the sulfoxide metabolite was not available). Birds were sacrificed at 4 hours after the final dose. Liver, muscle, and fat samples were removed and packed on solid CO_2 until analyzed. Analysis and identification of metabolites was conducted in a manner similar to that described in study #1068.

Test results are summarized in Tables #3 and #4. Table #3 gives the level of activity recovered in the various extracts, and characterization of residues in the DCM-phase is given in Table #4.

Table-3. Level of Activity in Poultry Tissue:

Poultry tissue	Total activity[1]/	Percent of total residue methanol extracts	DCM phase	aqueous phase
Muscle	3.66	98.6	94.5	4.1
Fat	2.62	98.1	92.7	1.1
Liver	9.12	90.2	81.8	6.6

1/ ppm sulfoxide equivalent.

Table-4. Main Metabolites in the DCM-Phase, Expressed in Percentage of Total Radioactivity.

Tissue	MSO	MSO_2	Parent	Sum
Muscle	60	30	4	94
Fat	16	7	69	92
Liver	58	21	3	82

It can be seen from Table #4 that more than 82% of the radioactivity in each of the tissues was characterized. MSO and MSO_2 represented the main metabolites in chicken muscle and liver. Sethoxydim, per se, is the most significant part of fat residues accounting for approximately 69% of the total activity with MSO and MSO_2 accounting for 16 and 7%, respectively. Parent was also detected in liver and muscle as <4% of the total radioactivity. Using mass spectrometry, it was shown that DME was the only oxidation product in poultry liver. The presence of nor-metabolites were not investigated in poultry tissues.

Table-5 gives a summary of the two poultry metabolism studies in which the parent and the sulfoxide metabolites were used in the feed.

Table-5: Sethoxydim and Metabolites in Poultry Resulting from Dosing with Parent or the Sulfoxide Metabolite, Expressed in Percentage of Total Radioactivity.

Tissue	MSO		MSO_2		M1SO		Parent		Total	
	1[a]/	2[b]/	1	2	1	2	1	2	1	2
Muscle	50	60	27	30	5	ND[c]/	---	4	82	94
Fat	39	16	23	7	6	ND	---	69	68	92
Liver	37	58	35	21	14	ND	---	3	92[d]/	82

a/ Poultry dosed with the sulfoxide metabolite.
b/ Poultry dosed with sethoxydim, per se.
c/ ND = Not Detected (<0.05 ppm).
d/ Including 6% polar compounds.

It can be seen from Table-5 that when poultry are dosed with the sulfoxide metabolite, major sethoxydim metabolites identified were MSO and MSO_2 with lesser quantities of M1SO, the latter being largely in the liver. When poultry are dosed with sethoxydim, per se, the major metabolites identified were MSO and MSO_2 with no detectable M1SO, whereas sethoxydim, per se, accounted for minute quantities in poultry tissue and liver, while it is a significant part of the residues (69%) found in the fat. This indicates that the parent compound is fat soluble and that poultry muscle and liver rapidly metabolize the parent to its sulfoxide and sulfone.

RCB's Comments

Using BWC 30 method of analysis and a variation thereof, designated Direct xidation, the petitioner has demonstrated that the oxidation/hydrolysis and enzymatic cleavage convert sethoxydim and metabolites in poultry to a glutaric acid derivative. This in turn is derivatized to its corresponding dimethylester (DME). The method is capable of determining a minimum of 68% of the total radioactivity in poultry muscle, fat, and liver. The major poultry metabolites are MSO and MSO_2 with lesser amounts of M1SO. Although both methods detect the "nor" series, their occurrence in poultry was not investigated in this submission. However, from an evaluation of the available studies including those in the 6/26/85 amendment (TLC and GC chromatograms),it was apparent that the nor-metabolites may not be a part of the poultry metabolism. This issue was discussed with Dr. Ed Tanek of BASF on 5/15/86 (Telecommunication) who indicated that the nor-metabolites were not detected in poultry.

Table-5 should serve as a reference for the basic understanding of sethoxydim metabolism in poultry.

From the available data and considering first that the poultry metabolism study was carried out using the parent compound, the following conclusions were extrapolated:

1. Sethoxydim residues in poultry muscle consist of parent compound sethoxydim, per se, 2-[1-(ethoxyimino)butyl]-5-[2-)(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MS, accounting for 4% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 60% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 30% of the total radioactivity; for a total of 94% identified activity.

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2. Sethoxydim residues in poultry fat consist of parent compound sethoxydim, per se, 2-[1-(ethoxyimino)butyl]-5-[2-)(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MS, accounting for 69% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 16% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy2-cyclohexene-1-one, referred to as MSO_2, accounting for 7% of the total radioactivity; for a total of 92% identified activity.

3. Sethoxydim residues in poultry liver consist of parent compound sethoxydim, per se, 2-[1-(ethoxyimino)butyl]-5-[2-)(ethylthio)propyl]-3-hydroxy2-cyclohexene-1-one, referred to as MS, accounting for 3% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 58% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 21% of the total radioactivity; for a total of 82% identified activity.

When the sulfoxide metabolite is used in the metabolism study, the following conclusions are extrapolated:

1. Sethoxydim residues in poultry muscle consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 50% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 27% of the total radioactivity; and 2-(1-(imino)butyl-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as M1SO, accounting for 5% of the total radioactivity; for a total of 82% identified activity.

2. Sethoxydim residues in poultry fat consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 39% of the total radioactivity; 2-(1-ethoxyimino)butyl-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 23% of the total radioactivity; and 2-(1-(imino)butyl-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as M1SO, accounting for 6% of the total radioactivity; for a total of 68% identified activity.

3. Sethoxydim residues in poultry liver consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 37% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred

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to as MSO_2, accounting for 35% of the total radioactivity; 2-(1-(imino)butyl-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as M1SO, accounting for 14% of the total radioactivity; for a total of 86% identified activity plus 6% unidentified polar compounds.

Note that neither metabolism of the compounds to the corresponding nor-series, nor reduction of the sulfoxide to the parent compound occurred in poultry as it did in the goat. Note, too, that both BWC-30 and the Direct Oxidation methods are capable of determining the nor-series uncovered in ruminant's milk and tissues. For more details on the names and structural formulas of sethoxydim and metabolites, please refer to Figures #2 and #3 in this review.

Since known sethoxydim metabolites contain the 2-cyclohexene-1-one moiety, our conclusion regarding the terminal residues in poultry is consistent with that for ruminant animals. It is our judgement that sethoxydim metabolism in poultry is adequately delinated. The residues of concern in poultry consist of the parent compound, sethoxydim, and its metabolites MSO, MSO_2, and MISO, containing the 2-cyclohexene-1-one moiety as expressed in 40CFR180§412.

We consider deficiency #2 resolved.

Deficiency #3

The petitioner should indicate the type of application (ground or aerial) that was used in the already submitted residue experiments for both soybean and alfalfa. The petitioner should be informed that we require both ground and aerial data reflective of the proposed use. In addition, we require additional residue data for soybean forage that represent the maximum proposed rate and minimum PHI. The latter requirement is because too few available data reflect the proposed PHI.

Petitioner's Response

The petitioner reported that all treated samples thus far submitted were taken from plots sprayed with ground equipment. Additional residue data are included in this amendment (acc. # 260543, dated 12/6/85) for alfalfa forage and comparability data between ground and aerial applications.

(a). Ground vs. Aerial Applications of Sethoxydim

The petitioner submitted comparability residue data reported in CR-12, CR-13, and PR-255. Tests are from side-by-side field trials demonstrating the differences between aerial vs. ground applcations of sethoxydim. Table #6 gives a summary of test results from 19 trials.

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Table-6: Ground vs. Aerial Applications of Sethoxydim Residues in/on Plant Commodities.

Commodity	Test Loc.	Lb Act/ Acre	# of Appl	PHI (Days)	Total Residues in ppm Ground	Aerial
Soybean grains	IN	0.3	1	43	3.7*	12.4
	MS	0.3	1	104	2.1	1.5
		0.3	1	104	2.7	<0.1
		0.3+0.2	2	104	0.28	0.58
	MN	0.2	1	64	0.7	0.89
		0.3	1	64	0.52	0.3
		0.3+0.2	2	64	2.2	0.39
	SC	0.2	1	81	3.1	1.4
		0.3	1	81	4.4	1.3
		0.3+0.2	2	81	5.0	0.87
Cottonseed	CA	0.5+0.5+0.3	3	139	<0.1	0.28
				120	<0.1	0.14
				64	0.18	0.59
Sugarbeet	CA	0.5+0.5	2	104-121	<0.1	<0.1
Roots				101-104	<0.1	<0.1
				76	<0.1	<0.1
Tops				104-121	1.44	<0.11
				101-104	1.6	0.7
				76	<0.1	<0.14

(b). Additional Residue Data on Alfalfa Forage

The petitioner submitted additional residue data on alfalfa forage. We presume that applications were made using ground equipment since the petitioner reported that all treated samples thus far were taken from plots sprayed with ground equipment. Samples were analyzed using method 30G. At the 0.5 to 30 ppm fortification levels to alfalfa forage, recoveries were reported in the range of 71 to 128%. Table-6 gives a summary of sethoxydim residues in/on alfalfa forage.

Table-7: Sethoxydim residues in/on Alfalfa Forage-New Data.

Test Location	Lb Act/A	# of Appl	PHI (Days)	Residues in ppm 1/ From DME	From DME-OH	Total
CA: Medara	0.5	1	8	17.2	1.3	18.5
	0.5+0.5	2	10	7.6	0.81	8.4
	0.5+0.5+0.5	3	9	4.3	0.48	4.8
Imperial Valley	0.5	1	7	11.9	<0.5	12.4
	0.5+0.5	2	7	11.5	<0.5	12.0
	0.5+0.5+0.5	3	18	11.6	<0.5	12.1
Bakersfield	0.5	1	8	10.0	<0.5	10.5
	0.5+0.3	2	7	<0.5	<0.5	<1.0
	0.5+0.3+0.3	3	9	14.7	0.82	15.5
Rio Vista	0.5	1	6	25.3	2.2	27.5
	0.5+0.3	2	18	<0.5	<0.5	<0.1
	0.5+0.3+0.3	3	7	19.2	1.5	20.7
Courtland	0.5	1	7	9.3	0.88	10.2
	0.5+0.3	2	7	8.6	0.66	9.3
	0.5+0.3+0.3	3	6	10.6	0.6	11.2
Arizona: Yuma	0.5	1	7	0.5	<0.5	<0.1
	0.5+0.3	2	7	13.2	0.67	13.9
	0.5+0.3+0.3	3	7	1.0	<0.5	1.5
				7.3	<0.5	7.8
				16.7	0.65	17.4
				2.9	<0.5	3.4
				<0.5	<0.5	<1.0
				20.0	0.58	20.6
				0.65	<0.5	1.2
New Mexico Las Cruces	0.5	1	6	14.1	0.79	14.9
	0.5+0.3	2	8	7.2	0.62	7.8
	0.5+0.3+0.3	3	6	13.2	0.63	13.8
				17.6	0.84	18.4
				9.9	0.59	10.5
				10.9	0.54	11.4

1/ Sethoxydim equivalents. residues are not corrected for

It can be seen from Table-7 that total sethoxydim residues in/on alfalfa forage ranged from non-detectable (<1.0 ppm) to a maximum of 27.5 ppm. Eight of 30 residue trials summarized in Table-6 reflect the proposed use. Total sethoxydim residues in these trials ranged from 1.5 to 20.7 ppm, averaging 9.5 ppm,

not corrected for control or recovery. With the exception of two control samples in which sethoxydim residues were reported at 1.5 and 3.3 ppm, six additional control samples had no detectable residues (<0.1 ppm).

Alfalfa Hay

Because a conclusion on the requested tolerance for this commodity has not been reached, it is appropriate to briefly discuss the available residue data in this section.

No data are included in this amendment for this commodity. Data are available for 24 alfalfa hay samples (PP#3F2904, memo of J. Onley, 1/12/85) in which sethoxydim residues ranged up to 12.7 ppm when analyzed by method 30B. Upon re-analyses of the same samples using a modification to method 30B, designated as 30H, sethoxydim residues ranged up to 28 ppm (K. Arne memo of 6/26/85). The validation studies discussed in K. Arne memo suggest that higher residue values would be uncovered by the use of method 30H. Dr. Arne stated that residue data submitted earlier for alfalfa hay are generally lower.

RCB's Comments

(a). We note that in the previous amendment (accession #073398, dated 3/12/85), the petitioner deleted the proposed tolerance for residues of sethoxydim residues in/on soybean forage and imposed a restriction prohibiting grazing of treated soybean fields and feeding treated soybean forage or ensilage to livestock. Since soybean forage is considered under control of the grower and thus subject to label restrictions, it is our judgement that additional residue data on soybean forage are not needed.

(b). Data in Table #6 demonstrate that in 19 residue trials, ground applications resulted in higher sethoxydim residues in/on plant commodities in 9 trials and aerial applications in 7 trials with the remaining 3 trials being of equal residues. Of the trials from aerial application with higher residues than ground application, one in particular had an unusually higher residues in/on soybean grains (12.4 vs. 3.7 ppm) exceeding the present tolerance of 10 ppm for this commodity. Note, however, that this test reflects a 43 day PHI, whereas the proposed PHI is 90 days. In general, the comparability residue data between ground and aerial applications can be seen in about 70% of the tests. Therefore, RCB concludes that there are little or no differences in sethoxydim residues in/on plant commodities resulting from ground or aerial applications.

(c). Residues of sethoxydim in/on alfalfa forage discussed in this amendment are in agreement with those discussed in the earlier amendment (K. Arne, 6/26/85), where in 24 alfalfa forage samples from treatments which approximate the proposed use, total sethoxydim residues ranged up to 11.4 ppm.

(d). Evaluation of the meat, milk, poultry and eggs tolerances

No feeding studies were submitted with this amendment. Two feeding studies, one for goats and one for poultry, were previously submitted in connection with this petition in the previous amendment (K. Arne, 6/26/85). The following is a summary of the feeding studies.

A. Ruminants

Sethoxydim Residues in/on Ruminant Commodities at Various Feeding levels

Feeding Level (ppm)	Sethoxydim residues (ppm) in Milk	Fat	Kidney	Liver	Muscle
30	<0.01-0.03	<0.05	<0.05	<0.05	<0.05
100	<0.01-0.07	<0.05	<0.31	<0.05	<0.05
300	<0.01-0.11	0.07	<0.45	0.17	<0.05
75 (hay)	<0.01-0.18	<0.05	<0.44	0.14	<0.05

B. Poultry

Sethoxydim Residues in/on Poultry Commodities at Various Feeding Levels

Feeding Level (ppm)	Sethoxydim residues (ppm) in Fat	Kidney	Liver	Muscle	Skin
25	<0.05	<0.75	0.4	0.06	0.10
80	0.05	1.4	0.42	0.10	0.23
250	0.17	1.46	1.26	0.21	0.60

Considering the feeding items in this use as well as all uses for which there are tolerances and pending tolerances, the maximum dietary intake for cattle was calculated at 27.25 ppm as follows:

Feed Items	Tolerance (ppm)	Percent in Feed	Maximum Dietary Intake (ppm)
Soybean grain	10	25	2.50
Alfalfa forage	40	25	10.00
Alfalfa hay	40	25	10.00
Cottonseed	5	20	1.00
Peanut Soapstock	75	5	3.75
		Total	27.25

Similarly, the maximum dietary intake for poultry was calculated at 12.25 ppm as follows:

Feed Items	Tolerance (ppm)	Percent in Feed	Maximum Dietary Intake (ppm)
Soybean grain	10	50	5.00
Cottonseed	5	10	0.50
Peanut Soapstock 1/	75	5	3.75
Sunflower meal 1/	20	15	3.00
		Total	12.25

1/ Tolerances on these commodities are pending

From the available data, we conclude that the present tolerances for residues of sethoxydim in/on the meat, milk, poultry and eggs will not be exceeded as a result of this use as well as registered and pending uses.

The proposed 0.05 ppm tolerance for residues of sethoxydim in milk is adequately covered which is also consistent with currently established 0.05(N) tolerance for this commodity. The reason for changing the milk tolerance from 0.05(N) to 0.05 ppm is due to the fact that the validated limit of detection was reported at 0.03 ppm not 0.05 ppm (0.01 ppm for each of DME, DME-OH and nor-DME when using the direct oxidation method). Furthermore, negligible residue tolerances (N) are no longer set.

From the available data thus far submitted, RCB concludes that the proposed 40 ppm tolerance for residues of sethoxydim in/on alfalfa hay and alfalfa forage is adequate. In the earlier amendment (K. Arne, 6/26/85), RCB concluded that the proposed 10 ppm tolerance for residues of sethoxydim in/on soybean hay is adequate.

Deficiency #3 is resolved.

Deficiency #4

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

Petitioner's Response

The petitioner stated that the additional data included in this amendment should address the Agency's concern regarding the methodologies and metabolism of sethoxydim in poultry.

RCB's Comments

RCB agrees with the petitioner's response concerning the feeding studies, in that additional feeding studies are not needed.

Deficiency #4 is resolved.

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Conclusions

1(a). Sethoxydim residues detectable in ruminant milk consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 25% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO, accounting for 5% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl) propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 10% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO_2, accounting for $\leq$3% of the total radioactivity.

1(b). Sethoxydim residues detectable in ruminant liver as reported in the 6/26/85 amendment consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MS, accounting for 12% of the total radioactivity; 2-[1-(ethoxyimino)bytyl]-5-[2-(methylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MS, accounting for 7% of the total radioactivity; 2-(1-ethoxyimino)butyl-5-[2-(ethylsulfinyl) propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 8% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO, acounting for 3% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 21% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(methyl-sulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO_2, accounting for 4% of the total radioactivity; for a total of 55% identified activity. In this amendment, it was shown that MSO_2 and MSO are two major metabolites in the goat liver accounting for up to 48 and 25% of the total radioactivity, respectively; for a total of 73% identified activity.

1(c). Sethoxydim residues detectable in ruminant kidney as reported in the 6/26/85 amendment consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MS, accounting for 2.5% of the total radioactivity; 2-[1-(ethoxyimino)bytyl]-5-[2-(methylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MS, accounting for <2% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)

propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 21% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO, accounting for 12% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 16% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(methylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as nor-MSO_2, accounting for 5% of the total radioactivity; for a total of 58% identified activity.

1(d). Sethoxydim residues in ruminant meat and fat were too low to permit characterization of their nature.

1(e). Since known sethoxydim metabolites contain the 2-cyclohexene-1-one moiety, RCB considers the nature of the residues in ruminants to be adequately delineated. The residues of concern in ruminants consist of the parent and its metabolites containing the 2-cyclohexene-1-one moiety which are: MSO, MSO_2, nor-MSO, and nor-MSO_2.

2(a). When the parent compound is used in the poultry metabolism study, the following conclusions are extrapolated:

2(a)(1). Sethoxydim residues in poultry muscle consist of parent compound sethoxydim, per se, 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MS, accounting for 4% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 60% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 30% of the total radioactivity; for a total of 94% identified activity.

2(a)(2). Sethoxydim residues in poultry fat consist of parent compound sethoxydim, per se, 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MS, accounting for 69% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 16% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 7% of the total radioactivity; for a total of 92% identified activity.

2(a)(3). Sethoxydim residues in poultry liver consist of parent compound sethoxydim, per se, 2-[(1-ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MS, accounting for 3% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 58% of the total radioactivity; and 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred

to MSO_2, accounting for 21% of the total radioactivity; for a total of 82% identified activity.

2(b). When the sulfoxide metabolite is used in the metabolism study, the following conclusions are extrapolated:

2(b)(1). Sethoxydim residues in poultry muscle consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 50% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 27% of the total radioactivity; and 2-(1-(imino)butyl-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as M1SO, accounting for 5% of the total radioactivity; for a total of 82% identified activity.

2(b)(2). Sethoxydim residues in poultry fat consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 39% of the total radioactivity; 2-(1-ethoxyimino)butyl-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 23% of the total radioactivity; and 2-(1-imino)butyl-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as M1SO, accounting for 6% of the total radioactivity; for a total of 68% identified activity.

2(b)(3). Sethoxydim residues in poultry liver consist of 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO, accounting for 37% of the total radioactivity; 2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as MSO_2, accounting for 35% of the total radioactivity; 2-(1-(imino)butyl-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexene-1-one, referred to as M1SO, accounting for 14% of the total radioactivity; for a total of 86% identified activity plus 6% unidentified polar compounds.

2(b)(4). Neither metabolism of the compounds to the corresponding nor-series, nor reduction of the sulfoxide to the parent compound occurred in poultry as it did in the goat. Note, too, that both BWC-30 and the Direct Oxidation methods are capable of determining the nor-series uncovered in ruminant's milk and tissues.

2(b)(5). Since known sethoxydim metabolites contain the 2-cyclohexene-1-one moiety, our conclusion regarding the terminal residues in poultry is consistent with that for ruminant animals. It is our judgement that sethoxydim metabolism in poultry is adequately delinated. The residues of concern in poultry consist of the parent compound, sethoxydim, and its metabolites containing the 2-cyclohexene-1-one moiety which are MSO, MSO_2, and M1SO.

3. Adequate analytical methodologies are available for enforcement of the proposed tolerances. PAM II, Method I, designated as BWC-30, is suitable for enforcement of ruminant tissue and milk tolerances. A variation of BWC-30 method, designated as method 30G, is suitable for enforcement of sethoxydim tolerances in alfalfa forage. A variation in method BWC-30, designated as method 30H, is suitable for enforcement of sethoxydim tolerances in alfalfa and soybean hay. Finally, a variation of BWC-30 method, designated as the Direct Oxidation method (DO) is suitable for enforcement of the poultry tissue and eggs tolerances. The BWC-30 and DO methods are capable of determining the nor-series of sethoxydim and metabolites. We recommend that variations in method BWC-30 be included in PAM II as a lettered supplement to Method I for sethoxydim.

   We will initiate a MTO for the nor-metabolites using the existing enforcement methodology. We will not hold up our concurrence in this tolerance request, if the petitioner agrees to submit the following standards to EPA , RTP and COB, Beltsville laboratory: M1SO, nor-MSO, and nor-MSO_2. The petitioner should be informed of this.

4. The grazing restriction should include the term "green succulent" to read "Do not graze treated soybean fields and do not feed treated soybean forage (green succulent) or ensilage to livestock. Treated soybean hay may be fed." The petitioner is requested to submit a revised Section B to this effect.

5. The available comparability data between ground and aerial applications indicate that no significant differences are expected in sethoxydim residues in/on plant commodities from either ground or aerial applications at the proposed use.

6. Additional feeding studies are not needed.

7(a). The proposed 10 ppm tolerance for residues of sethoxydim in/on soybean hay is adequate.

7(b). The proposed 40 ppm tolerance for residues of sethoxydim in/on alfalfa forage and hay is adequate.

8(a). The proposed 0.05 ppm tolerance for residues of sethoxydim in milk is adequate and is consistent with the currently established tolerance of 0.05 (N) for this commodity.

8(b). The present tolerances for residues of sethoxydim in/on the meat, milk, poultry and eggs will not be exceeded as a result of this use as well as registered and currently pending uses.

9. An International Residue Limit Status sheet is included in this petition (PP#3F2904), dated 6/26/85. No Codex, Mexican, or Canadian tolerances are established for sethoxydim in/on subject crops.

Recommendations

TOX considerations permitting, and provided that the petitioner complies with Conclusion #4 (see also under Note to PM), RCB can recommend for amending 40CFR§180.412 to include the following permanent tolerances for residues of sethoxydim and metabolites: 10 ppm for soybean hay, 40 ppm for alfalfa hay and forage.

Note to PM

RCB will initiate a MTO for the nor-metabolites using the existing enforcement methodology. We will not hold up our concurrence in this tolerance request, if the petitioner agrees to submit the following metabolites to EPA , RTP and COB, Beltsville laboratory: M1SO, nor-MSO, and nor-MSO_2. The petitioner should be informed of this.

Attachments: Figures 2 and 3 (2 pages)

cc: RF, Circu, S. Malak, M. Firestone, S.F. (sethoxydim or Poast), PP#2F2670, PP#3F2904, PP#5F3234/FAP#5H5464, PP# 5F3284/FAP#5H5475, TOX, EAB, EEB, BUD (D. Marlow), PM (RD), FDA, Robert Thompson (RTP), and PMSD/ISB.

RDI: P.V. Errico: 6/17/86: R.D. Schmitt: 6/18/86
TS-769:RCB:CM#2:RM810:S.Malak:X557-73330:2/14/86 (revised 6/6/86 & 6/13/86).

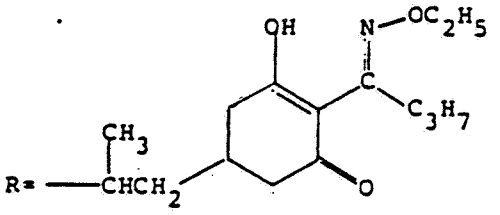
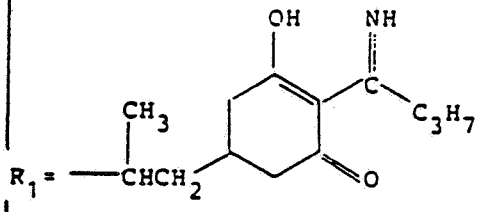
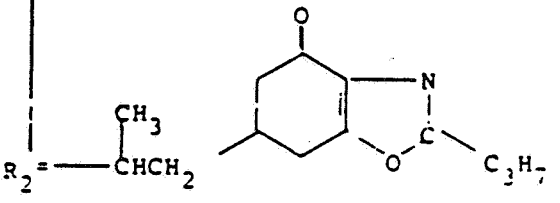
Designation	Abbreviated structure	Group structure
MS	C_2H_5S-R	
MSO	$C_2H_5\overset{O}{\overset{\|}{S}}-R$	
MSO_2	$C_2H_5\overset{O}{\overset{\|}{\underset{O}{\|}S}}-R$	
Nor-MS	CH_3S-R	
Nor-MSO	$CH_3\overset{O}{\overset{\|}{S}}-R$	
$Nor-MSO_2$	$CH_3\overset{O}{\overset{\|}{\underset{O}{\|}S}}-R$	
$5-OHMSO_2$	$C_2H_5\overset{O}{\overset{\|}{\underset{O}{\|}S}}-(5-OH-R)$	
M1SO	$C_2H_5\overset{O}{\overset{\|}{S}}-R_1$	
$M1SO_2$	$C_2H_5\overset{O}{\overset{\|}{\underset{O}{\|}S}}-R_1$	
M2SO	$C_2H_5\overset{O}{\overset{\|}{S}}-R_2$	
$M2SO_2$	$C_2H_5\overset{O}{\overset{\|}{\underset{O}{\|}S}}-R_2$	

Figure 2. Structures of Possible Metabolites (Source: PP#3F2904)

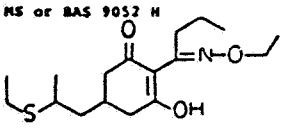
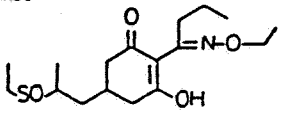
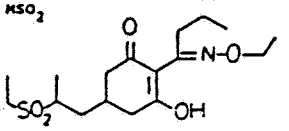
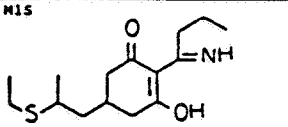
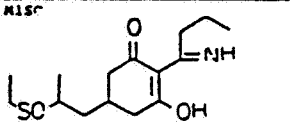
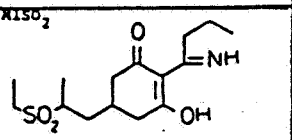
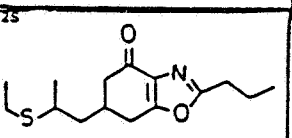
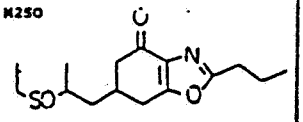
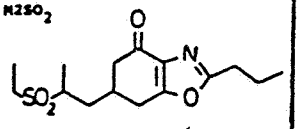
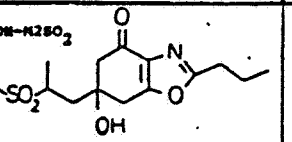
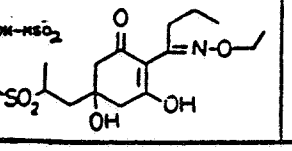
	ABBREVIATION AND STRUCTURAL FORMULA	MOLECULAR WEIGHT	CHEMICAL NAME
M TYPE	MS or BAS 9052 H 	327	2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one
	MSO 	343	2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexen-1-one
	MSO_2 	359	2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-hydroxy-2-cyclohexen-1-one
M1 TYPE	M1S 	283	2-[1-(imino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one
	M1SO 	299	2-[1-(imino)butyl]-5-[2-(ethylsulfinyl)propyl]-3-hydroxy-2-cyclohexen-1-one
	$M1SO_2$ 	315	2-[1-(imino)butyl]-5-[2-(ethylsulfonyl)propyl]-3-2-cyclohexen-1-one
M2 TYPE	M2S 	281	6-[2-(ethylthio)propyl]-6,7-dihydro-2-propyl-4(5H)-benzoxazolone
	M2SO 	297	6-[2-(ethylsulfinyl)propyl]-6,7-dihydro-2-propyl-4(5H)-benzoxazolone
	$M2SO_2$ 	313	6-[2-(ethylsulfonyl)propyl]-6,7-dihydro-2-propyl-4(5H)-benzoxazolone
HYDROXY	6-OH-$M2SO_2$ 	329	6-[2-(ethylsulfonyl)propyl]-6-hydroxy-6,7-dihydro-2-propyl-4(5H)-benzoxazolone
	5-OH-MSO_2 	375	2-[1-(ethoxyimino)butyl]-5-[2-(ethylsulfonyl)propyl]-3,5-dihydroxy-2-cyclohexen-1-one

FIGURE 3: STRUCTURES AND ABBREVIATION OF BAS 9052 H AND ITS RELATED REFERENCE STANDARDS (Source: PP#3F2904)