A Copy went to DRES for Review

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

8/19/91

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP#9F3743 - Clethodim (Select®) on Soybeans, Cottonseed, and Animal Commodities. Anticipated Residues Expected in Meat and Milk (No MRID No.) [CB No. 8214] (HED INTRA-0202)

FROM: Francis D. Griffith, Jr., Chemist
Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

TO: James P. Kariya, Chief
Dietary Exposure Section/SACB
Health Effects Division (H7509C)

and

Joanne I. Miller, Acting PM 23
Fungicide-Herbicide Branch
Registration Division (H7505C)

THRU: Richard D. Schmitt, Ph.D., Chief
Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

Background

The purpose of this memorandum is to present estimates of residues or anticipated residues of clethodim and its metabolites in human food and animal feed items based on the residue data presented to register this chemical. These data include crop field trial residue data, processing studies, and livestock feeding studies which were all submitted as part of this petition and adequately reviewed by M.J. Nelson in her March 12, 1990, memorandum. The residue estimates will then be used to estimate the chronic dietary exposure for chronic non-carcinogenic or carcinogenic dietary risk assessment.

The Plant Science Section of the Biological Analysis Division confirmed that a maximum of 8 percent of the soybean crop would be treated with the new herbicide Clethodim. Joanne Miller, PM 23, requested the Dietary Exposure Section (DES) rerun its Dietary Exposure Analysis on soybeans based on 8 percent of the soybean crop likely to be treated with Select. DES then

1/10 379

requested CB to generate anticipated clethodim and its metabolite residues in meat and milk.

Clethodim is a **new chemical** with no established permanent tolerances.

CONCLUSIONS

All anticipated residue data generated were based on crop field trial and feeding studies residue data. These data were generated using an analytical method that has completed a PMV. The anticipated residues for the local milk shed were based on maximum residues detected and for national market were based on average residues.

Our anticipated residues estimates are tabulated as follows:

Soybeans 7.8 ppm (max) and 3.5 ppm (avg.)

	concentration/reduction factor
soybean hulls	0.98
soybean meal	1.02
soybean crude oil	0.1
soybean soapstock	1.25

Cottonseed 0.48 ppm (max) and 0.21 ppm (avg.)

	concentration/reduction factor
cottonseed hulls	1.22
cottonseed meal	1.69
cottonseed crude oil	0.22
cottonseed refined oil	0.1
cottonseed soapstock	1.06

Dairy Cattle, Local Milk Shed

milk	0.0006 ppm
liver	0.0024 ppm
kidney	0.0034 ppm
fat	0.0010 ppm
muscle	< 0.011 ppm (based on 1/2 L.O.D.)

Dairy Cattle, National Market

milk	0.0001 ppm
liver	0.0007 ppm
kidney	0.0009 ppm
fat	0.0002 ppm
muscle	< 0.011 ppm (based on 1/2 L.O.D.)

Beef Cattle, National Market

liver	0.0007 ppm

380

kidney	0.0008 ppm
fat	0.0002 ppm
muscle	0.0001 ppm

Poultry

eggs	0.0006 ppm
liver	0.0010 ppm
other poultry tissues, e.g., thigh and breast muscle, fat, and gizzard	< 0.011 ppm (1/2 L.O.D.)

RECOMMENDATION

The anticipated residues presented in this memorandum are to be used by DES in their Dietary Exposure Analysis to assess risks of clethodim and its metabolites exposure.

DETAILED CONSIDERATIONS

TOLERANCES

No clethodim and its metabolites tolerances have been established. Tolerances as proposed in PP#8F 3743 are for clethodim and its metabolites containing the 2-cyclohexen-1-one moiety in or on the following raw agricultural and processed commodities:

soybeans	10 ppm
cottonseed	1 ppm
soybean soapstock	15 ppm
cottonseed meal	2 ppm
milk	0.05 ppm
meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep	0.2 ppm
eggs	0.2 ppm

USES

The proposed use of clethodim on soybeans is at a rate of 0.1 to 0.25 lb. ai/acre/application not to exceed 0.5 lb. ai/acre/growing season. Since this is a new use, it is unlikely producers will vary these proposed uses. CB expects two applications per season at 0.25 lb./ai clethodim/application/acre with a 60-day PHI.

381

ANALYTICAL METHOD

The analytical method used to generate all of the residue data is the common moiety method, RM-26B-2. In this procedure clethodim and its various metabolites are oxidized to one of three dicarboxylic acids then derivatized to its dimethyl ester (DME) and determined by gas chromatography using a FPD-S detector. This method completed a successful petition method validation (PMV) in EPA laboratories. The method is suitable to gather the residue data for the anticipated residues.

The limits of detection as determined by EPA in the PMV are as follows:

- 0.05 ppm in soybeans for each component equals the sum of 0.15 ppm total clethodim.
- 0.0075 in milk for each component equals the sum of 0.022 ppm.
- 0.025 ppm in beef liver for each component equals the sum of 0.075 ppm.

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

Soybeans

There are adequate geographically representative crop field trial residue data for a 3-year period to support the proposed tolerance. The 1988 field trial data was from two applications of 0.25 lb. ai clethodim and a 60-day PHI. The maximum residue was 7.3 ppm and the average residue was 3.5 ppm.

The 1986 residue data were considered only as supplemental data because the data did not reflect total residue; only DME related residues were determined in the 1986 trials. The 1987 trials did not reflect the use now being proposed. In addition, many of the 1987 samples were stored for peroids of more than 6 1/2 months; the storage stability data would only support samples stored 6 1/2 months.

Cottonseed

There are adequate geographically representative crop field trial residue data for a 3-year period to support the proposed tolerance. The 1988 field trial data was from two applications of 0.25 lb. ai clethodim and a 60-day PHI. The maximum residue was 0.48 ppm and the average residue was 0.21 ppm.

382

MAGNITUDE OF THE RESIDUE - PROCESSED FOOD/FEED

Soybeans

A single soybean processing study was conducted using soybeans bearing real residues from two applications of 2.0 lbs ai/acre clethodim (an 8X exaggerated application rate). The results are as follow:

Matrix	Total ppm Clethodim as DME + DME-OH	Concentration/ Reduction Factor
Soybean (rac)	26.7	---
Hulls	26.1	0.98
Meal	27.2	1.02
Crude oil	2.8	0.1
Degummed oil	1.6	0.06
Refined oil	< 0.08	< 0.003
Soapstock	33.5	1.25

Clethodim and its metabolites concentrate in soybean soapstock, a livestock food item. The analytical method cannot repeatably distinguish between concentration factors of 1.00 and 1.02, thus CB does not consider clethodim concentrates in soybean meal.

Cottonseed

A single cottonseed processing study was conducted using cottonseed bearing real residues from two applications of 2.0 lbs ai/acre of clethodim (an 8X exaggerated application rate). The results are as follows:

Matrix	Clethodim as DME + DME-OH Total PPM	Concentration/ Reduction Factor
Fuzzy cottonseed (rac)	0.8	---
Cottonseed hulls	0.98	1.22
Cottonseed meal	1.35	1.69
Cottonseed crude oil	0.18	0.22
Cottonseed refined oil	0.08	0.10
Soapstock	0.85	1.06

Clethodim and its metabolite definitely concentrate in cottonseed meal, a livestock feed item. The concentration factor of 1.2 in cottonseed hulls is at the Agency's threshold at which it considers the need for food/feed additive tolerance. CB reiterates a feed additive clethodim tolerance is not needed for cottonseed hulls.

MAGNITUDE OF THE RESIDUE - MEAT, MILK, POULTRY, EGGS

Ruminants

The bovine feeding study was conducted where groups of four Holstein cows were dosed daily for 28 consecutive days with a mixture of clethodim:clethodim sulfoxide (5/95) at doses of 10, 30, or 100 ppm. The results are as follows:

CLETHODIM RESIDUES[a] IN DAIRY COWS
(Maximum PPM Detected At Any Timing)

10 PPM	Milk[b]	Liver	Kidney	Muscle	Fat
DME	ND[c]	0.06	0.05	ND	ND
DME-OH	ND	ND	ND	ND	ND
S-MeDME	ND	ND	ND	ND	ND
30 PPM					
DME	0.03	0.12	0.17	ND	0.05
DME-OH	ND	ND	ND	ND	ND
S-MeDME	ND	ND	ND	ND	ND
100 PPM					
DME	0.08	0.45	0.54	0.07	0.15
DME-OH	ND	ND	ND	ND	ND
S-MeDME	0.03	0.09	0.08	ND	ND

[a] Measured as DME, DME-OH, and S-MeDME and expressed as clethodim equivalents
[b] Whole milk
[c] ND = Not Detected (< 0.0125 ppm for milk and < 0.05 ppm for tissues)

Ruminants Diets and Dietary Burden from Clethodim Residues

Matrix	Dairy Cattle Max % in Diet	Beef Cattle Max % in Diet
Cottonseed meal	15	15
Cottonseeds	20	25
Cottonseed hulls	5	15
Soapstock	5	5
Soybean seed	25	10
Soybean meal	25	25
Soybean hulls	10	20
Soapstock	5	5

384

Soapstock is a small percentage of any theoretical livestock diet. If we were to include either soapstock in our calculations we would have diets that add up to over 100% ingredients. Thus, soapstock is not included in any of our calculations for clethodim anticipated residues in meat, milk, poultry, or eggs.

The potential clethodim dietary burden for dairy cows in the local milk shed is based on the highest residues detected. Since we were given the percent soybean crop treated, the potential clethodim dietary burden is as follows:

LOCAL MILKSHED

Matrix	Maximum Total Clethodim Res.	X	% in Diet	X	% Crop Treated	X	Concent. Factor	=	Potential Clethodim Dietary Burden
Cottonseed	0.48		20		---		---		0.096
Cottonseed meal	0.48		15		---		1.69		0.122
Cottonseed hulls	0.48		5		---		1.22		0.029
Cottonseed soapstock	0.48		5		---		1.06		0.025
Soybean seed	7.3		25		8		---		0.146
Soybean meal	7.3		25		8		0.98		0.143
Soybean hulls	7.3		10		8		1.02		0.068
Soapstock	7.3		5		8		1.25		0.036

A dairy cattle diet composed solely of cottonseed, soybeans, and their processed commodities is highly unrealistic. While artificial, a dairy cattle diet composed of cottonseed, cottonseed meal, soybean seed, and soybean meal nonetheless maximizes potential dietary burden of clethodim. The anticipated potential clethodim local dairy cattle dietary burden is 0.567 ppm.

Assuming a linear relationship of residues in milk and tissues from a 30 ppm feeding level to a 0.6 ppm feeding level, the anticipated total clethodim residues in dairy cattle in the local milk shed, based on maximum expected residues resulting from the proposed use are:

Milk	Liver	Kidney	Muscle	Fat
0.0006 ppm	0.0024 ppm	0.0034 ppm	< 0.011 ppm (1/2 LOD)	0.001 ppm

The residue value determined for muscle is based on half of the analytical method's limit of detection. No residues were detected in muscle from the 30 ppm feeding.

The potential clethodim dietary burden in beef cattle and dairy cattle in the national market is based on the average residues detected. Therefore, the dietary burden for the national diet will be based on residues in soybeans commodities only in feed commodities available nationwide. Cottonseed feeds are not commodities routinely

385

available nationwide. If limited quantities are available a typical cow won't be eating cottonseed feed commodities. Since we were given the percent soybean crop treated, the potential clethodim dietary burden is as follows:

National Milk Market

Matrix	Average Total Clethodim Residue	X	% in Diet	X	% Crop Treated	X	Concent. Factor	=	Potential Clethodim Dietary Burden
Soybean seed	3.5		25		8		---		0.070
Soybean meal	3.5		25		8		0.98		0.068
Soybean hulls	3.5		10		8		1.02		0.028
Soapstock	3.5		5		8		1.25		0.018

A dairy cattle diet composed solely of soybeans, and its processed commodities is highly unrealistic. While artificial, a dairy cattle diet composed of soybeans, soybean meal and hulls, nonetheless maximizes the potential dietary burden of clethodim. The anticipated potential clethodim national dairy cattle dietary burden is 0.166 ppm.

Assuming a linear relationship of residues in milk and tissues from the 30 ppm feeding to 0.23 ppm feeding the anticipated total clethodim residues in dairy cattle in the national milkshed are as follows (CB used 1/2 LOD for ND residues in muscle at 30 ppm feeding):

Milk	Liver	Kidney	Muscle	Fat
0.0001 ppm	0.0007 ppm	0.0009 ppm	< 0.011 ppm (1/2 LOD)	0.0002 ppm

National Beef Cattle Market

Matrix	Average Total Clethodim Residue	X	% in Diet	X	% Crop Treated	X	Concent. Factor	=	Potential Clethodim Dietary Burden
Soybean seed	3.5		10		8		---		0.028
Soybean meal	3.5		25		8		0.98		0.069
Soybean hulls	3.5		20		8		1.02		0.057
Soapstock	3.5		5		8		1.25		0.018

A beef cattle diet composed solely of cottonseed, soybeans, and their processed commodities is highly unrealistic. While artificial, a beef cattle diet containing soybean seeds, meal, and hulls, nonetheless maximizes the potential dietary burden of clethodim. The anticipated potential clethodim beef cattle dietary burden is 0.15 ppm.

Assuming a linear relationship of residues in tissues from the 100 ppm feeding to the 0.25 ppm feeding, the anticipated total clethodim residues in beef cattle on the national market are as follows:

386

Liver	Kidney	Muscle	Fat
0.0007 ppm	0.0018 ppm	0.0001 ppm	0.0002 ppm

Poultry

The poultry feeding study was conducted where groups of 20 laying hens were dosed daily for 28 consecutive days with a mixture of clethodim:clethodim sulfoxide (5/95) at doses of 10, 30, or 100 ppm. The results are as follows:

CLETHODIM RESIDUES IN LAYING HENS
(Maximum PPM Detected at Any Timing)

	Feeding Level					
	10 ppm		30 ppm		100 ppm	
	Egg	Tissue	Egg	Tissue	Egg	Tissue
DME[a]	ND[d]	ND	0.09	ND	0.24	0.06[e]
DME-OH[b]	ND	ND	ND	ND	ND	ND
S-MeDME[c]	ND	ND	ND	ND	ND	ND

[a] Expressed as clethodim (C)
[b] Expressed as 5-OH clethodim sulfoxide (5OH-SO_2)
[c] Expressed as S-methyl clethodim sulfone (SMSO)
[d] ND = no detectable residue (< 0.05 ppm)
[e] 29-Day liver

Poultry Diets and Dietary Burden from Clethodim Residues

Poultry production in the United States today involves both an extensive local market as well as a national market. CB recognizes that cottonseed may not be available in all poultry feeds, but for those local feed mills which use it, cottonseed seed residues can be transferred to national poultry products.

Poultry diets could contain the following percent soybean cottonseed and their processed commodities:

Matrix	% in Diet Broilers	% in Diet Laying Hens
Cottonseed meal	10	3
Soapstock	5	5
Soybean seed	20	50
Soybean meal	30	20
Soapstock	5	5

The potential clethodim dietary burden in poultry in either the national market or local market is based on average residues detected in the rac. Since we were given the percent soybean crop treated the potential clethodim dietary burden in poultry is as follows:

National Poultry Market

Matrix	Average Total Clethodim Residue	X	% in Diet	X	% Crop Treated	X	Concent. Factor	=	Potential Clethodim Dietary Burden
Soybean seed	3.5		50		8		---		0.140
Soybean meal	3.5		20		8		0.98		0.055
Soapstock	3.5		5		8		1.25		0.018

While artificial, a poultry diet composed solely of cottonseed and soybean processed feed items, it nonetheless maximizes the potential dietary burden of clethodim. The anticipated clethodim poultry dietary burden from consumption of average residues of cottonseed and soybean commodities is 0.26 ppm. If we don't consider cottonseed commodities then the poultry dietary burden becomes 0.21 ppm total clethodim.

Assuming a linear relationship of residues in eggs and poultry tissues; i.e., thigh and breast muscle, liver, gizzard, subcutaneous and abdominal fat, from the 100 ppm feeding to the 0.26 ppm feeding, the anticipated total clethodim residues in poultry are:

Eggs	Liver	Other Tissues
0.0006 ppm	0.0002 ppm	< 0.011 ppm (1/2 LOD)

Ther were no detectable residues in any tissue at any feeding level, except for one positive value at 29 days in liver.

The anticipated residues of total clethodim residues in poultry assuming no cottonseed in the poultry diets are:

Eggs	Liver	Other Tissues
0.0005 ppm	0.0001 ppm	< 0.011 ppm (1/2 LOD)

H7509C:CBTS:Reviewer(FDG):CM#2:Rm814B:557-0826:
63426:I:WP5.0:C.Disk:KEVRIC:08/05/91:aw;dd:aw:ed:fdg:8/11/91.

cc: R.F.,Circu(7),Reviewer(FDG),CBRS(Hummel),ACB/BEAD (D.Marlow),PP#8F3743,PIB/FOD(Furlow).

RDI:SecHd:RSQuick:8/9/91:BrCh:RDESchmitt:8/12/91.

386