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

MAR 12 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#9F3743. Clethodim (SELECT) in or on Soybeans, Cottonseed, and Animal Commodities.
Residue Chemistry Review of a New Herbicide.
DEB Nos: 5611, 5612, 5613 HED No.: 9-1868A
MRID Nos: 410301-37 thru -41; 410302-13 thru -23

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TO: J. Miller/M. Erumsele, PM Team 23
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Valent U.S.A. Corporation and Chevron Chemical Company (hereinafter referred to as Valent/Chevron) propose the establishment of tolerances for the combined residues of the herbicide clethodim (ANSI), (E)-2-[1-(((3-chloro-2-propenyl)oxy)imino)propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one, and its metabolites containing the 2-cyclohexen-1-one moiety (calculated as the herbicide) in/on the following raw agricultural commodities:

soybeans	10.0	ppm
cottonseed	5.0	ppm
meat, fat, and mbyp of cattle, goats, hogs, horses, poultry, and sheep	0.2	ppm
milk	0.05	ppm
eggs	0.5	ppm

Other names for clethodim include RE-45601 and SELECT Herbicide. This is the first request for tolerances for this chemical. No temporary tolerances have been established for this herbicide, and no state registrations or emergency exemptions have been granted.

Clethodim is similar to sethoxydim in chemical structure, metabolic breakdown, proposed use, and proposed enforcement method. Sethoxydim is a registered pesticide (POAST Herbicide) with tolerances (40 CFR 180.412) that include cottonseed, soybeans, and animal products. The tolerance expression and levels for clethodim mimic those of sethoxydim.

SUMMARY OF DEFICIENCIES TO BE RESOLVED FOR DEB

- **Address Product Chemistry deficiencies.**
- **Submit a revised Write-up of Proposed Enforcement Method [RM-26A-1] incorporating directions for animal commodity matrices.**
- **Submit a Specific Confirmatory Procedure.**
- **Run Method Validation Trial(s) by the Agency.**
- **Submit Multiresidue Test Data via FDA Protocol B. [Note: May be deferred until a future petition submission.]**
- **Submit freezer storage stability studies for soybean processing fractions; cottonseed processing fractions; cattle tissues and milk; poultry tissues and eggs.**
- **Submit a revised Section F incorporating the following changes: soybean soapstock @ 15 ppm; cottonseed @ 1.0 ppm; cottonseed meal @ 2.0 ppm; and, eggs @ 0.2 ppm.**

CONCLUSIONS

1. The deficiencies associated with the product chemistry of clethodim will need to be resolved prior to the establishment of the proposed tolerances of this petition. These are discussed in DEB's companion review: "PP#9F3743. Clethodim Product Chemistry Data Submitted in Support of Registration", M. Nelson, DEB# 5681, dated 3/12/90, which see, for details.

2. DEB concludes the proposed label directions adequately delineate the proposed uses on cotton and soybeans and the restrictions/limitations associated with those uses.

3. DEB concludes the nature of the residue in plants has been adequately delineated. The residue of concern is clethodim and its metabolites containing the 2-cyclohexen-1-one moiety.

4. DEB concludes the nature of the residue in ruminants has been adequately delineated. The residue of concern is clethodim and its metabolites containing the 2-cyclohexen-1-one moiety.

5. DEB concludes the nature of the residue in laying hens has been adequately delineated. The residue of concern is clethodim and its metabolites containing the 2-cyclohexen-1-one moiety.

6. DEB concludes that suitable regulatory method(s) for the enforcement of the proposed tolerances of this petition have not yet been submitted. The petitioner needs to (1) submit a revised version of the "common moiety" method which incorporates detailed directions for handling animal products; and, (2) submit a "specific" confirmatory procedure which can be used to differentiate between residues arising from clethodim and sethoxydim. The "common moiety" method will need to successfully pass an EPA method validation trial; the "specific" procedure may also undergo such a trial if the Agency deems it advisable to conduct one.

7. The petitioner is requested to submit test data for clethodim and selected metabolites via Protocol B. Since submission of this petition (3/89) pre-dates the revision of the FDA Multiresidue Method Decision Tree, the request for this data is <u>not</u> being made a data deficiency of this petition. The petitioner is given the option of generating the data as an amendment to this petition, or of submitting the data as part of the next petition proposing clethodim tolerances.

8. <u>Contingent upon</u> the satisfactory resolution of analytical methods issues, DEB concludes that total clethodim residues are stable in soybean seed macerates stored frozen (-20°C) for up to 6½ months.

9. DEB concludes the petitioner must demonstrate via a freezer storage stability study that total clethodim residues (DME + DME-OH) are stable in soybean processing fractions (as listed in Table F) stored frozen (-20°C) for up to 3½ months.

10. Contingent upon the satisfactory resolution of analytical methods issues, DEB concludes that total clethodim residues are stable in fuzzy cottonseed macerates stored frozen (-20°C) for up to 6 months.

11. DEB concludes the petitioner must demonstrate via a freezer storage stability study that total clethodim residues (DME + DME-OH) are stable in cottonseed processing fractions (as listed in Table G) stored frozen (-20°C) for up to 2 months.

12. DEB concludes the petitioner must demonstrate via a freezer storage stability study that total clethodim residues (DME + DME-OH + S-MeDME) are stable in cattle tissues (liver, fat, muscle, kidney) and milk stored frozen (-20°C) for up to 3¼ months.

13. DEB concludes the petitioner must demonstrate via a freezer storage stability study that total clethodim residues (DME + DME-OH + S-MeDME) are stable in poultry tissues (liver, fat, muscle, gizzard) and eggs stored frozen (-20°C) for up to 2 months.

14. Contingent upon the satisfactory resolution of analytical methods issues, DEB concludes the field trial data on soybeans provide adequate geographical representation and are sufficient to support the requested tolerance of 10.0 ppm in conjunction with the proposed use.

15. Contingent upon the satisfactory resolution of freezer storage stability and analytical methods issues, DEB concludes the processing trial data on soybeans are adequate, and that a revised Section F needs to be submitted to include a food additive tolerance proposal of 15 ppm for soybean soapstock in conjunction with the proposed tolerance level of 10.0 ppm on soybeans.

16. Contingent upon the satisfactory resolution of analytical methods issues, DEB concludes the field trial data on cotton provide adequate geographical representation. However, the requested tolerance of 5.0 ppm is too high in conjunction with the proposed use. A tolerance level of 1.0 ppm for cottonseed would be more appropriate, and should be proposed via a revised Section F.

17. Contingent upon the satisfactory resolution of freezer storage stability and analytical methods issues, DEB concludes the processing trial data on cottonseed are adequate, and that a revised Section F needs to be submitted to include a food additive tolerance proposal of 2.0 ppm for cottonseed meal in conjunction with a revised tolerance proposal of 1.0 ppm on cottonseed.

18. Contingent upon the satisfactory resolution of freezer storage stability and analytical methods issues, DEB concludes the proposed tolerance levels of 0.05 ppm for milk and 0.2 ppm for meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep are appropriate to cover any secondary residues which might occur therein as a result of the dietary ingestion of up to tolerance level amounts of total clethodim residues present in treated soybeans, cottonseed, and/or their processed by-products.

19. Contingent upon the satisfactory resolution of freezer storage stability and analytical methods issues, DEB concludes the proposed tolerance level of 0.2 ppm for the meat, fat, and meat by-products of poultry is appropriate to cover any secondary residues which might occur therein as a result of the dietary ingestion of up to tolerance level amounts of total clethodim residues present in treated soybeans, cottonseed, and/or their processed by-products. The proposed tolerance level of 0.5 ppm for eggs is too high; a tolerance level of 0.2 ppm for eggs would be more suitable, and should be proposed via revised Section F.

20. There are no Codex proposals at Step 6 or above, and no Canadian or Mexican limits established for this chemical on any commodity. Thus, the question of compatibility of tolerance expression and levels proposed by this petition with those of IRLs does not apply.

21. If/when DEB can recommend for the establishment of the tolerances proposed by this petition, a dietary risk assessment should be conducted by the Dietary Risk Evaluation Section (DRES), Science Analysis and Coordination Branch (SACB), HED.

RECOMMENDATIONS

DEB recommends **against** the establishment of the proposed tolerances for combined residues of the herbicide clethodim and its metabolites containing the 2-cyclohexen-1-one moiety in or on the commodities of this petition for the reasons stated in **Conclusions 1, 6, 9, 11, 12, 13, 15, 16, 17, and 19.**

DEB also notes the contingent nature of its Conclusions 8, 10, 14, 15, 16, 17, 18, and 19; the need for the petitioner to (eventually) address the issue in Conclusion 7; and DEB's Conclusion 21.

DETAILED CONSIDERATIONS

FORMULATION AND MANUFACTURING PROCESS

Technical clethodim is formulated as SELECT 2 EC Herbicide (aka SELECT 2 EC; SELECT Herbicide), an emulsifiable concentrate containing 2 lbs of the active ingredient (ai), clethodim, per gallon of product.

The Product Chemistry of clethodim, including its manufacturing process, is discussed in DEB's companion review: "PP#9F3743. Clethodim Product Chemistry Data Submitted in Support of Registration", M. Nelson, DEB# 5681, dated 3/12/90, which see. The deficiencies raised there need to be addressed by the petitioner.

The deficiencies associated with the product chemistry of clethodim will need to be resolved prior to the establishment of the proposed tolerances of this petition.

PROPOSED USE

SELECT Herbicide is a new selective postemergence herbicide for the control of annual and perennial grasses in cotton and soybeans.

Apply SELECT postemergence to actively growing grasses according to rate table recommendations (6-16 fl. oz. aka 0.10-0.25 lb ai/A/application, depending on grass species, height, and geographic region). A second application may be needed in arid regions.

When applying by ground equipment, use 10-40 gallons of spray solution/A; for applications by air, use 3-10 gallons of spray solution/A.

Always add a non-phytotoxic petroleum-based crop oil concentrate containing at least 15% emulsifier to the spray tank at 1 qt/A by ground equipment or 1 pt/A by air.

For spot treatments, mix 0.5% SELECT and 1% of the non-phytotoxic crop oil concentrate (per table directions) and treat to wet vegetation, while not allowing runoff of spray solution.

Restrictions and Limitations:

Do not graze treated fields or feed treated forage or hay to livestock.

Do not exceed a total of 32 fl. oz. (0.5 lb ai) of SELECT per acre per season.

Do not apply SELECT within 60 days of harvest.

Do not tank mix SELECT with any pesticide or fertilizer not specified on this label. (None are currently specified.)

DEB concludes the proposed label directions adequately delineate the proposed uses on cotton and soybeans and the restrictions/ limitations associated with those uses.

NATURE OF THE RESIDUE - Plants

Metabolism in Carrots, Soybeans, and Cotton. The petitioner submitted a "Plant Metabolism Study of [Ring-4,6-^{14}C]-Clethodim in Carrots, Soybeans and Cotton", 12/22/88, Lab ID# MEF-0004, MRID# 410301-37.

Immature plants of carrots, soybeans, and cotton were treated twice at a 14-day interval with a 50:50 tautomeric mixture of ring [6-^{14}C]-clethodim:[4-^{14}C]-clethodim (purity, 99.7%) at a rate equivalent to 0.25 lb ai/A as a postemergence foliar spray; grown to maturity in a greenhouse; and, harvested with preharvest intervals (PHI) of 20, 30 and 70 days, respectively.

At harvest, plants were separated into leaves, stems, roots, beans, pods, seeds, fiber and shell fractions, and pooled by species. Each fraction was pulverized, and aliquots combusted to $^{14}CO_2$ to determine ^{14}C concentration and distribution.

The pulverized fractions were subjected to a series of solvent extraction steps to remove polar and non-polar residue components, and the radioactivity determined by liquid scintillation counting (LSC); non-extractable residues were combusted to $^{14}CO_2$ prior to LSC.

Table A shows the ^{14}C concentration and distribution in soybeans, cotton, and carrot plants.

Since leaves contained most of the total ^{14}C, both leaves and edible fractions were taken for metabolite characterization, which was accomplished for clethodim and its free metabolites by two-dimensional thin-layer chromatography (TLC), autoradiography, and/or high performance liquid chromatography (HPLC) cochromatography with authentic standards.

Polar and/or conjugated metabolites were isolated by preparative TLC, subjected to enzyme, acid, and base hydrolysis, and the aglycones released characterized by TLC cochromatography. Major metabolites were confirmed by liquid chromatography/mass spectrometry (LC/MS). Authentic reference standards were used to verify identification.

The remaining non-extractable residue was subjected to acid/base hydrolysis, analysis by TLC, and the radioactivity attributed to the incorporation of activity into the plant matrix.

TABLE A: ^{14}C CONCENTRATION AND DISTRIBUTION IN PLANT TISSUES

	% ^{14}C Distribution (ppm, calculated as ^{14}C-Clethodim)		
Matrix	Soybeans	Cotton	Carrots
Leaves	83.8 (27.9)	93.2 (13.5)	97.3 (22.3)
Roots	0.2 (0.45)	0.3 (0.10)	2.7 (0.40)
Stems	0.8 (0.89)	2.6 (0.66)	
Pods	5.1 (1.83)		
Beans	10.1 (3.87)		
Fiber		0.1 (0.056)	
Seeds		0.2 (0.068)	
Shell		3.6 (1.36)	

Characterization of the ^{14}C in soybean bean/foliage, cotton seed/ foliage, and carrot roots/leaves is given in Table B.

TABLE B: CHARACTERIZATION OF ^{14}C ACTIVITY IN PLANT TISSUES

	ppm ^{14}C Calculated as Clethodim					
	Soybean		Cotton		Carrot	
Component	Bean	Foliage	Seed	Foliage	Root	Leaves
C	---	---	---	---	0.003	---
CSO	1.24	1.65	0.003	0.55	0.11	3.50
CSO_2	0.178	0.25	0.002	0.054	0.014	0.13
ISO	0.302	3.88	0.004	2.40	0.040	4.93
ISO_2	0.314	2.43	0.002	0.55	0.034	1.32
5OH-SO	0.275	<0.05	<0.001	0.19	0.026	0.36
5OH-SO_2	0.414	0.86	0.001	0.054	0.030	0.42
Arom. SO_2	0.058	0.14	<0.001	0.068	0.006	0.067
Others	0.271[a]	3.63[a]	0.0045[b]	4.22[a]	0.052[a]	2.419[a]
CSO Conj.	0.329	6.92	<0.001	0.37	0.024	1.90
CSO_2 Conj.	0.050	0.56	<0.001	0.18	0.002	0.11
Other Conj.	0.383[a]	5.11[a]	0.020[c]	4.25[a]	0.041[b]	5.98[a]
Nonextractable	0.058	2.48	0.032	0.62	0.015	1.18
TOTALS	3.872	27.94	0.069	13.51	0.397	22.32

[a] Composed of ≥9 ^{14}C metabolites.
[b] Composed of ≥4 ^{14}C metabolites.
[c] Contained too low radioactivity to allow further characterization.

The major metabolic pathways of clethodim (C) in plants were initial sulfoxidation to clethodim sulfoxide (CSO) followed by further oxidation to clethodim sulfone (CSO_2), elimination of the chloroallyloxy side chain to give the imine sulfoxide (ISO) and sulfone (ISO_2), and hydroxylation to form the 5-OH sulfoxide (5OH-SO) and sulfone ($5OH-SO_2$). Clethodim sulfoxide and clethodim sulfone conjugates (CSO Conj.; CSO_2 Conj.) were also detected as major or minor metabolites, depending on plant species and subfractions. Also present as a minor metabolite was aromatic sulfone (Arom. SO_2).

Figure 1 (see Appendix) shows the proposed metabolic pathways of clethodim in plants and animals.

Table I (see Appendix) lists the names and structures of clethodim and its possible metabolites.

The solvent extractable ^{14}C was also analyzed by the residue enforcement method of the US FDA Pesticide Analytical Manual, Volume II (PAM II), §180.412 (Sethoxydim). The total extractable residue in soybeans was oxidized, methylated, and then analyzed as the dimethyl ester (DME) and 5-OH dimethyl ester (DME-OH) derivatives (structures and nomenclature are given in Table I; see Appendix), using TLC/autoradiography to quantitate DME and DME-OH instead of gas-liquid chromatography (GLC). The results correlated closely with those obtained from ^{14}C measurements.

Since one of the major plant metabolic pathways is elimination of the chloroallyloxy side chain, ^{14}C-allyl-labeled clethodim was used to conduct a "Plant Metabolism Study (carrots, soybeans, and cotton) of [Allyl-2-^{14}C]-Clethodim", 12/22/88, Lab ID# MEF-0005, MRID# 410301-38.

The study, which was designed to follow the fate of the chloroallyloxy group, was done side-by-side with the ^{14}C-ring-labeled clethodim study discussed above. The results showed that the chloroallyloxy moiety cleaved from clethodim underwent extensive metabolism, eliminating the chlorine atom and incorporating the three carbon moieties into natural plant components (with some being evolved as $^{14}CO_2$).

DEB concludes that the nature of the residue in plants has been adequately delineated. The residue of concern is clethodim and its metabolites containing the 2-cyclohexen-1-one moiety.

NATURE OF THE RESIDUE - Animals

Metabolism in Goats. The petitioner submitted a study, "The *in vivo* Metabolism of [Propyl-1-^{14}C]-Clethodim in a Lactating Goat", 12/29/88, Lab ID# MEF-0038, MRID# 410301-39.

Following a 1-day acclimation period, a lactating goat (39 kg) was dosed with 1.16 mg/kg/day (equivalent to 24 ppm in alfalfa diet) [propyl-1-^{14}C]-clethodim (purity, >99%) in gelatin capsules for 4 consecutive days, receiving 3 equal daily doses (14.2 mg/dose) for 3 days and 1 dose (14.2 mg) on the morning of day 4. A control goat received the same number of empty gelatin capsules. Both animals were sacrificed within 4 hours after the final dose.

Hindquarter and forequarter muscle, peritoneal and subcutaneous fat, liver, kidneys, heart, and blood were collected for metabolite characterization.

Body weights, food consumption, and general health and behavior were monitored and recorded throughout the test period. Weights and volumes of total production of milk (twice per day), urine and feces (once per day) were recorded and aliquots of each removed for radiochemical analysis.

^{14}C measurements and metabolite isolation/identification were performed using standard extraction and hydrolysis procedures, and radiometric, chromatographic, and spectrometric techniques, using authentic reference standards to verify identification, as discussed under Plant Metabolism.

Approximately 91% of the ^{14}C dose was excreted in urine (56.4%) and feces (34.4%). The milk contained 0.14% of the administered dose; the tissues, 0.38%; and, blood, 0.22%. The total recovery of administered ^{14}C was 92%.

Table C shows the ^{14}C concentration and distribution in goat tissues and blood.

TABLE C: ^{14}C CONCENTRATION AND DISTRIBUTION IN GOAT TISSUES AND BLOOD

Sample	PPM	% of Dose
Liver	0.414	0.24
Kidney	0.378	0.04
Fat, subcutaneous	0.079	0.02
Fat, peritoneal	0.047	0.02
Muscle, hindquarter	0.034	0.03
Muscle, forequarter	0.033	0.02
Heart	0.058	0.01
Blood	0.166	0.22
TOTAL	---	0.60

Because most of the dose was excreted in the urine, metabolites in it were identified. The major urinary metabolite was clethodim sulfoxide (**CSO**), varying from 40% of the urinary ^{14}C on day 2 to 67% of the urinary ^{14}C on day 4. The remainder of the urinary ^{14}C was composed of clethodim (**C**) (3.0-27%), S-methyl sulfoxide (**SMSO**) (12-18%), S-methyl (**SM**) (7.0-13%), imine sulfoxide (**ISO**) (1.5-2.8%), clethodim sulfone (CSO_2) (1.5-2.2%), and 5-OH sulfoxide (**5OH-SO**) (0-3.0%).

The ^{14}C in milk plateaued at ca 0.035 ppm by the evening of day 2. The milk was lyophilized for solvent extraction of metabolites. About half the ^{14}C was extractable into organic solvents. It was composed of clethodim (≤0.001 ppm), clethodim sulfoxide (0.006-0.013 ppm), and S-methyl sulfoxide (0.001-0.005 ppm). The other half of the ^{14}C activity was water-soluble and was shown by isotopic dilution to be ^{14}C-lactose (0.014-0.017 ppm, as clethodim equivalents).

Most (77-95%) of the ^{14}C in tissues and blood was extractable into organic solvents, with the acetonitrile and methanol-water fractions containing the highest levels of activity. Those two fractions were pooled for residue characterization, and the metabolic profiles of that extractable activity are given in Table D.

TABLE D: METABOLIC PROFILE (PPM) IN GOAT TISSUES AND BLOOD[a]

Component	Blood	Liver	Kidney	Heart	Muscle		Subcut.
					Fqtr	Hdqtr	Fat
C	0.047	0.114	0.005	0.000	0.000	0.000	0.002
CSO	0.067	0.137	0.139	0.025	0.017	0.014	0.037
CSO_2	0.006	0.013	0.000	0.000	0.000	0.000	0.000
SMSO	0.019	0.025	0.116	0.021	0.009	0.011	0.023
ISO	0.005	0.006	0.016	0.000	0.000	0.000	0.004
5OH-SO	0.004	0.000	0.000	0.000	0.000	0.000	0.000
Unknown[b]	0.005	0.016	0.037	0.000	0.000	0.003	0.006

[a] Values reported as 0.000 ppm are below the level of claimed sensitivity, which is <0.001 ppm.

[b] The unidentified activity was polar in nature and remained at the origin (TLC); it did not correspond to any reference standards.

In the case of liver, 0.064 ppm could not be solubilized, even by refluxing with aqueous acid, and that ^{14}C was presumed recycled into natural cellular constituents. The nonextractable activity in blood and other tissues was only 0.002-0.025 ppm.

Figure I (see Appendix) shows the proposed metabolic pathways for clethodim in animals and plants.

The dominant metabolic process in the ruminant (goat) is oxidation of clethodim to clethodim sulfoxide and, to a lesser extent, clethodim sulfone. Clethodim can also be converted to S-methyl, which can be oxidized to S-methyl sulfoxide and S-methyl sulfone. Cleavage of the oxime N-O bond in clethodim produces the imine, which is rapidly oxidized to imine sulfoxide. In a minor process, clethodim can be hydroxylated to 5-OH, which can be oxidized to 5-OH sulfoxide. Alternately, clethodim sulfoxide may be hydroxylated to 5-OH sulfoxide. (Note: S-methyl is formed only from clethodim; the literature does not support the formation of S-methyl sulfoxide from clethodim sulfoxide. Thus, the S-methyl metabolites have significance only if animals are exposed to clethodim and this is limited because clethodim is rapidly oxidized to sulfoxides and sulfones in plants.)

A comparison was made of the determination of clethodim-, S-Methyl-, and 5-OH related metabolites in the extractable residue of liver and kidney by the residue enforcement method of PAM II, §180.412 (Sethoxydim), and by TLC ^{14}C-quantification. The agreement was good. No 5-OH equivalents were found by either the enforcement method or the metabolism study in these tissues.

DEB concludes the nature of the residue in ruminants has been adequately delineated. The residue of concern is clethodim and its metabolites containing the 2-cyclohexen-1-one moiety.

Metabolism in Laying Hens. The petitioner submitted a study, "[Ring-4,6-^{14}C]-Clethodim: A radiocarbon Metabolism Study in Laying Hens", 12/30/88, Lab ID# MEF-0089, MRID# **410301-40.**

Young laying hens were assigned to one of two test groups (8 hens each) or the control group (12 hens). Following a 12-day acclimation period, each hen in the test groups received an oral dose of a 50:50 tautomeric mixture of ring [6-^{14}C]-clethodim:[4-^{14}C]-clethodim (purity, 99.2%) (either 2.1 mg/kg/day or 51.3 mg/kg/day) contained in a gelatin capsule filled with commercial poultry feed, once daily for 5 consecutive days. Controls received gelatin capsules containing only poultry feed.

During the test period, eggs were collected twice daily and the excreta once daily, and pooled by day and treatment group. All hens were sacrificed beginning approximately 4 hours after administering the final dose.

The following tissues and organs were collected for analysis: Thigh and breast muscles, abdominal fat, gizzard, liver, kidney, heart, skin, gastrointestinal tract with contents, and reproductive organs.

Eggs and tissues from the low dose group (LDG) (2.1 mg/kg/day) were used to quantitate and characterize ^{14}C. The high dose group (HDG) (51.3 mg/kg/ day) egg and tissue samples were used to provide large quantities of metabolites for spectroscopic identification.

^{14}C measurements and metabolite isolation/identification were performed using standard extraction and hydrolysis procedures, and radiometric, chromatographic, and spectrometric techniques, using authentic reference standards to verify identification, as discussed under Plant Metabolism.

Radioanalysis indicated that 77.9% and 84.7% of the administered ^{14}C in the LDG and HDG, respectively, was found in the excreta; 1.9% and 4.2%, respectively, in the tissues; and, 0.1% and 0.3%, respectively, in eggs.

The distribution of ^{14}C in the tissues of the LDG was GI tract, 2.8 ppm > kidney, 1.2 ppm > liver, 0.7 ppm > skin, heart, fat, each 0.3 ppm > reproductive organs, gizzard, thigh muscle, each 0.2 ppm > breast muscle, 0.1 ppm.

The distribution of ^{14}C in eggs of the LDG was egg whites, 0.03-0.22 ppm > egg shells, 0.01-0.10 ppm > egg yolks, 0.01-0.07 ppm.

Distribution of activity in the tissues and eggs of the HDG followed a pattern similar to that of the LDG.

The overall recovery of ^{14}C from solvent extractions of tissues and eggs was 103.1%. Most of the ^{14}C (>80%) was in the acetonitrile fraction. Except for liver and kidney, the nonextractable residue levels were <0.05 ppm.

Attempts to characterize the unextractable residues in the kidney and liver by acid and base hydrolysis were made. <20% of the ^{14}C was released, suggesting low levels of conjugates may have been present; insufficient activity was present to verify this. The remaining activity was attributed to incorporated radiocarbon.

Characterization of the ^{14}C in the tissues and eggs is given in Table E.

At no time was evidence seen to suggest the presence of either 5-OH or S-methyl clethodim or any of its derivatives in any tissue or egg sample.

Figure 1 (see Appendix) shows the proposed metabolic pathways for clethodim in animals and plants.

Clethodim metabolism in laying hens was not as complex as in the lactating goat. The chicken tissues and eggs contained only clethodim (C), clethodim sulfoxide (CSO), and clethodim sulfone

(CSO_2). None of the imine analogs, 5-hydroxy analogs, or S-methyl analogs which were identified in the goat were seen in the chicken.

TABLE E: CHARACTERIZATION OF ^{14}C ACTIVITY IN LAYING HEN TISSUES AND EGGS[a]

	C	CSO	CSO_2	Unknown[b]	Origin[c]
Kidney	0.03	0.51	0.33	0.06	0.06
Liver	0.52	0.22	0.15	0.08	0.02
Skin	0.01	0.17	0.05	0.02	0.02
Heart	0.01	0.14	0.06	0.02	0.07
Fat	0.20	0.04	0.03	0.01	0.01
Gizzard	0.03	0.09	0.43	0.01	0.01
Thigh	<0.01[d]	0.05	0.30	<0.01[d]	0.01
Breast	<0.01[d]	0.04	0.03	0.01	<0.01[d]
Egg White[e]	0.01	0.06	0.03	0.05	0.01
Egg Yolk[e]	0.01	0.02	0.01	<0.01[d]	<0.01[d]

[a] From the Low Dose Group (2.1 mg/kg/day for 5 days).

[b] A composite of multiple TLC bands whose R_f values did not correspond to any authentic standards, each present at too low a residue level to be characterized further.

[c] Residue levels were too low to permit characterization.

[d] The claimed limit of sensitivity is 0.01 ppm.

[e] Day 4 eggs

The presence of clethodim, clethodim sulfoxide, and clethodim sulfone was verified by the residue enforcement method of PAM II, §180.412 (Sethoxydim), and the results were in reasonable agreement with those obtained by TLC-radiometric analysis.

DEB concludes the nature of the residue in laying hens has been adequately delineated. The residue of concern is clethodim and its metabolites containing the 2-cyclohexen-1-one moiety.

Chromatographic Characteristics of Clethodim and Related Compounds. Clethodim and related compounds (metabolites) have isomers of the following three types: geometrical (syn/anti oxime conformers), optical (enantiomers), and tautomers (keto-enol). These isomers usually have different spectral and physical properties. As a result, HPLC and TLC chromatograms often show multiple peaks due to resolution of some of these isomers. This

was taken into account during the identification/quantitation of metabolites in the ^{14}C-clethodim plant and animal metabolism studies.

[Note: Isomerization is not a complicating factor in analyses via the proposed GLC enforcement method (RM-26A-1) since, via that procedure, all components of the residue having the 2-cyclohexen-1-one moiety are converted to two common moieties, **DME** and **DME-OH**, which are acronyms for the dimethyl esters of 3-[2-(ethylsulfonyl)propyl]pentanedioic acid and 3-[2-(ethylsulfonyl)propyl]-3-hydroxypentanedioic acid, respectively, and measured as such. In addition, the method is capable of analyzing for S-methyl analogs of clethodim (such as found in the goat ^{14}C-metabolism study), by oxidation and derivatization to the dimethyl ester of 3-[2-methylsulfonyl)propyl]pentanedioic acid, **S-MeDME**. For further discussion, see Analytical Methods section.]

ANALYTICAL METHODS

Proposed Enforcement Method. The petitioner submitted a volume, "Analytical Method for the Determination of Clethodim Residues", 12/21/88, Lab ID# RM-26, MRID# **410301-41**.

The analytical method used to determine clethodim residues in plant and animal tissues is a gas-liquid chromatographic (GLC) procedure which measures the total toxic residue as two common moieties. The method has been designated RM-26A-1 or RM-26A.

Version **RM-26A-1** is the proposed enforcement method. It is a minor revision of RM-26A with more detailed instructions than is given in RM-26A. The RM-26A-1 procedure is claimed to be essentially the same as that published in PAM II, §180.412, which is used to analyze sethoxydim residues in plant and animal tissues.

RM-26A-1 oxidizes all clethodim-related metabolites retaining the cyclohexen-1-one structure to two common moieties, reported as **DME** and **DME-OH**, which are acronyms for the dimethyl esters of 3-[2-(ethylsulfonyl)propyl]pentanedioic acid and 3-[2-(ethylsulfonyl)propyl]-3-hydroxypentanedioic acid, respectively.

In addition, the method is capable of analyzing for S-methyl analogs of clethodim (such as found in the goat ^{14}C-metabolism study), by oxidation and derivatization to the dimethyl ester of 3-[2-methylsulfonyl)propyl]pentanedioic acid, **S-MeDME**.

In RM-26A-1, residues of clethodim and its metabolites are extracted with methanol and/or water, followed by cleanup with alkaline precipitation and acidic back extraction into methylene chloride. Alkaline hydrogen peroxide oxidation then converts sulfides and sulfoxides to sulfones, and oxidatively cleaves the

cyclohexen-1-one ring to the 3-alkyl and 3-alkyl-3-OH substituted pentanedioic acids, which are derivatized to their corresponding dimethyl esters.

Thus, clethodim, clethodim sulfoxide, clethodim sulfone, and their conjugates, and corresponding imine and oxazole residues are converted to **DME**, while the corresponding 5-OH metabolites are converted to **DME-OH**, and the S-methyl metabolites are converted to **S-MeDME**.

Following partitioning into methylene chloride and, in some cases, further isolation by column chromatography, the dimethyl-pentanedioic acid esters (**DME**, **DME-OH**, and **S-MeDMe**) are quantitated by GLC as three separate peaks using either a packed or a wide-bore fused silica capillary column coated with methyl silicone, with a flame photometric detector operated in the sulfur mode, which allows the calculation of total cyclohexen-1-one moieties in the sample. The total residue is expressed as clethodim equivalents.

The detection limit claimed for residues measured as DME, DME-OH, and (animal matrices) S-MeDME via RM-26A-1 is 0.0125 ppm for milk; 0.05 ppm for other animal commodities, including eggs; and, 0.05-0.20 ppm for soybeans, cotton, and their byproducts.

The petitioner indicates that a set of 8-10 samples may be analyzed in 2-3 days using the RM-26A-1 procedure.

RM-26A-1 (in the form of the PAM II, §180.412 - sethoxydim version) was validated by analysis of crop and animal tissues from the ^{14}C metabolism studies (see Nature of the Residue section) with good agreement between results from this method and from TLC-radiometric analyses.

A further experiment (MRID# **410301-41**) was conducted using the reference standards (**C**, **CSO**, **CSO_2**, **ISO_2**, **5OH-SO**, **5OH-SO_2**, **CO** {clethodim oxazole}, **OSO** {oxazole sulfoxide}, and **OSO_2** {oxazole sulfone}). Untreated control samples of cottonseed and soybean were fortified at 1.0 ppm with each of these standards and then analyzed by method RM-26A-1. Recoveries ranged 67-123% from cottonseed and 52-84% from soybeans, and confirm that each of the standards was converted to DME or DME-OH via RM-26A-1 and quantified as part of the total residue measured.

RM-26A-1 has additionally been validated for recovery of clethodim and selected metabolites from crop and animal substrates by several analytical laboratories, as discussed below.

Craven Laboratories validated RM-26A-1 for C and CSO in cotton and soybean (MRID# **410301-41**; recoveries from fortification at 0.1 ppm and 0.5 ppm with both in both crops ranged 81-97% (n=24).

Craven Laboratories also validated RM-26A-1 for **C** and **CSO** in conjunction with analyses of cotton (MRID# **410302-15**) and soybeans (MRID# **410302-18**) from the 1986 crop field trials. Recoveries of both compounds from cotton fortified at 0.05-5.0 ppm ranged 86-97% (n=10); from soybeans fortified at 0.05-10 ppm, 86-103% (n=8).

Chevron Chemical Company validated RM-26A-1 for **C** and **5OH-SO_2** in conjunction with analyses of cotton and soybean samples from the 1987 (MRID# **410302-14**, cotton; MRID# **410302-17**, soybeans) and 1988 (MRID# **410302-13**, cotton; MRID# **410302-16**, soybeans) crop field trials. Recoveries from cotton fortified at 0.25-1.0 ppm with both compounds ranged 58-129% (n=13); from soybeans fortified with both at 1.0 ppm, 54-138% (n=15). Prior to conducting these analyses, RM-26A-1 was validated for the recovery of **C** from soybeans (MRID# **410301-41**) fortified at 0.1 ppm. Recoveries ranged 68-77% (n=6).

Chevron Chemical Company also validated RM-26A-1 for **C** and **5OH-SO_2** in conjunction with analyses of the processing fractions of soybeans (MRID# **410302-20**) and cottonseed (MRID# **410302-19**). Recoveries from soybean fractions (see listing, Table F) fortified at 0.2-1.0 ppm with both compounds ranged 55-120% (n=1-2, each fraction). Recoveries from cottonseed fractions (see listing, Table G) fortified at 0.2-1.0 ppm with both compounds ranged 57-110% (n=1-3, each fraction).

Analytical Development Corporation validated RM-26A-1 for **C** and **5OH-SO_2** in whole milk and cattle tissues (liver, kidney, muscle, fat) (MRID# **410302-22**) by the analysis in duplicate of controls fortified with both compounds at 0.05 ppm and 0.5 ppm for tissues, and at 0.0125-0.5 ppm in whole milk. Recoveries from tissues ranged 65-123% (n=18); from milk, 74-116% (n=6).

Additional validation of RM-26A-1 was performed by Analytical Development Corporation during the analysis of samples from the cow feeding study (MRID# **410302-22**). Tissue samples (liver, fat, kidney, muscle) were each fortified with **C**, **5OH-SO_2**, and **SMSO** at levels of 0.05 ppm and 0.1 ppm; recoveries ranged 70-109% (n=9). Whole milk was fortified with each compound at 0.0125-0.5 ppm; recoveries ranged 65-115% (n=22). Milk commodities (pasteurized whole milk, cream, skim milk, acid whey) were similarly fortified at 0.05 and 0.1 ppm; recoveries ranged 70-106% (n=4).

EPL Bio-Analytical Services, Inc. validated RM-26A-1 for **C**, **5OH-SO_2**, and **SMSO** in eggs and chicken tissues (liver, fat, gizzard, muscle) (MRID# **410302-21**). Eggs were fortified with these compounds at levels of 0.1-1.0 ppm; recoveries ranged 52-106% (n=16). Tissues were similarly fortified at levels of 0.1-1.0 ppm; recoveries ranged 47-166% (n=37).

RM-26A-1 has not yet been subjected to a method validation trial in EPA laboratories because the method as presently written has been judged to be inadequate (see M. Nelson memo of 10/25/89, this petition) owing to lack of directions for animal commodity matrices. The petitioner was advised to revise and resubmit the method for Agency review. This is an outstanding deficiency.

Upon receipt of a suitably revised version of this proposed enforcement method, the Agency will initiate its in-house method validation trial.

DEB notes that the residue enforcement method for sethoxydim (see PAM II, §180.412, Method I), which is quite similar to that of RM-26A-1, has undergone a successful method validation trial for the recovery of sethoxydim and up to three of its metabolites (the sulfone, 5-OH sulfone, and oxazole sulfone) from soybeans, beef liver, and milk. The range of recoveries was 72-95%. The limit of detection was 0.05 ppm.

DEB further notes that method RM-26A-1 is a common moiety method and, thus, will **not** be able to differentiate between residues arising from clethodim (SELECT Herbicide) and the structurally similar sethoxydim (POAST Herbicide), which already has established tolerances (40 CFR 180.412) for cottonseed, soybeans, and animal products.

This issue is discussed in DEB's memo (M. Nelson) of 1/30/90, this petition. In that memo DEB concurs, in principle, with the petitioner's proposal that the "common moiety" method be used as the primary enforcement method for clethodim residues (assuming it passes an EPA method validation trial), and a "specific" confirmatory procedure (which the petitioner claims to be in the process of developing) be used when differentiation between residues arising from clethodim and sethoxydim is necessary.

The "specific" method, for use as the confirmatory procedure for clethodim residues, is not yet available for Agency review (and possible method validation trial). This is an outstanding deficiency.

DEB concludes that suitable regulatory method(s) for the enforcement of the proposed tolerances of this petition have not yet been submitted. The petitioner needs to (1) submit a revised version of the "common moiety" method which incorporates detailed directions for handling animal products; (2) submit a "specific" confirmatory procedure which can be used to differentiate between residues arising from clethodim and sethoxydim. The "common moiety" method will need to successfully pass an EPA method validation trial; the "specific" procedure may also undergo such a trial if the Agency deems it advisable to conduct one.

Multiresidue Methods. The petitioner submitted a volume, "Multiresidue Method Evaluation", 11/30/88, Lab ID# 129-002, MRID# **410302-23.**

Clethodim (C), clethodim sulfoxide (CSO), and 5-OH clethodim sulfone (5OH-SO_2) were evaluated in accordance with the FDA "Decision Tree for Multiresidue Method (MRM) Testing" (3/88) to meet the residue chemistry data requirements of 40 CFR 158.240 (b)(15).

Via that schema, only Protocol III was appropriate for testing these three compounds. C, CSO, and 5OH-SO_2 were not detected by GLC under test conditions.

This volume of data (MRID# **410302-23**) will be forwarded to FDA for review and use in a future updating of PAM I, Appendix 1.

DEB notes FDA's "Decision Tree for MRM Testing" was revised 4/89. Via the new schema, testing via Protocol B is also applicable to clethodim and its metabolites.

The petitioner is requested to submit test data for clethodim and selected metabolites via Protocol B. Since submission of this petition (3/89) pre-dates the revision of the Decision Tree, the request for this data is not being made a data deficiency of this petition. The petitioner is given the option of generating the data as an amendment to this petition, or of submitting the data as part of the next petition proposing tolerances for clethodim.

FREEZER STORAGE STABILITY DATA

Soybeans. A freezer storage stability study (MRID# **410302-16**) was conducted using frozen (-20°C) macerates of dry shelled soybean seeds from the 1987 residue trials containing weathered, field-incurred clethodim residues. Reanalysis of these macerates at intervals of 86, 141, and 208 days (6½ months) resulted in total clethodim residues (DME + DME-OH) which ranged 71.7-108% of the initial total residues (13.75 ppm) found on day 0.

The stability of total clethodim residues (DME + DME-OH) is also demonstrated (MRID# **410302-20**) by comparing the results of analysis of a split sample (from 1987 IA trial T-6921): the dry shelled soybeans used for processing (27 ppm) and those used to provide field trial residue data (27, 30 ppm). The total clethodim residue (DME + DME-OH) level in the two portions of that soybean sample is essentially the same, even though the analysis dates of the two portions differ by 6½ months.

Contingent upon the satisfactory resolution of analytical methods issues, DEB concludes that total clethodim residues are stable in soybean seed macerates stored frozen (-20°C) for up to 6½ months.

Soybean Processing Fractions. No freezer storage stability data have been provided to validate the stability of total clethodim residues (DME + DME-OH) in soybean processing fractions.

Soybean processing fractions (MRID# **410302-20**) were frozen stored at -20°C for 10-101 days prior to residue analysis (see Table F). Supporting validation data are recommended by the Agency when samples are frozen stored for more than 2 weeks before analysis (see EPA Position Document on Storage Stability, August 1987).

DEB concludes the petitioner must demonstrate via a freezer storage stability study that total clethodim residues (DME + DME-OH) are stable in soybean processing fractions (as listed in Table F) stored frozen (-20°C) for up to 3½ months.

Cottonseed. A freezer storage stability study (MRID# **410302-13**) was conducted using frozen (-20°C) macerates of fuzzy cottonseed from the 1987 residue trials containing weathered, field-incurred clethodim residues. Reanalysis of these macerates at intervals of 55, 110, and 172 days (6 months), resulted in total clethodim residues (DME + DME-OH) which ranged 79.9-128% of the initial total residues (0.38-1.44 ppm) found on day 0.

Contingent upon the satisfactory resolution of analytical methods issues, DEB concludes that total clethodim residues are stable in fuzzy cottonseed macerates stored frozen (-20°C) for up to 6 months.

Cottonseed Processing Fractions. No freezer storage stability data have been provided to validate the stability of total clethodim residues (DME + DME-OH) in cottonseed processing fractions.

Cottonseed processing fractions (MRID# **410302-19**) were frozen stored at -20°C for up to 2 months prior to residue analysis (see Table G). Supporting validation data are recommended by the Agency when samples are frozen stored for more than 2 weeks before analysis (see EPA Position Document on Storage Stability, August 1987).

DEB concludes the petitioner must demonstrate via a freezer storage stability study that total clethodim residues (DME + DME-OH) are stable in cottonseed processing fractions (as listed in Table G) stored frozen (-20°C) for up to 2 months.

Bovine Tissues and Milk. No freezer storage stability data have been provided to validate the stability of total clethodim residues (DME + DME-OH + S-MeDME) in bovine tissues and milk.

Tissue and milk samples from the dairy cow feeding study (MRID# **410302-22**) were frozen stored at -20°C for up to 3¼ months prior to residue analysis. Supporting validation data are recommended

by the Agency when samples are frozen stored for more than 2 weeks before analysis (see EPA Position Document on Storage Stability, August 1987).

DEB concludes the petitioner must demonstrate via a freezer storage stability study that total clethodim residues (DME + DME-OH + S-MeDME) are stable in bovine tissues (liver, muscle, kidney, and fat) and milk stored frozen (-20°C) for up to 3½ months.

Poultry Tissues and Eggs. No freezer storage stability data have been provided to validate the stability of total clethodim residues (DME + DME-OH + S-MeDME) in poultry tissues and eggs.

Tissue and egg samples from the laying hen feeding study (MRID# 410302-21) were frozen stored at -20°C for up to 2 months prior to residue analysis. Supporting validation data are recommended by the Agency when samples are frozen stored for more than 2 weeks before analysis (see EPA Position Document on Storage Stability, August 1987).

DEB concludes the petitioner must demonstrate via a freezer storage stability study that total clethodim residues (DME + DME-OH + S-MeDME) are stable in poultry tissues (liver, fat, muscle, and gizzard) and eggs stored frozen (-20°C) for up to 2 months.

RESIDUE DATA

Crop field trials with SELECT 2EC Herbicide were conducted in cotton and soybeans in 1986, 1987, and 1988. All postemergence applications included the crop oil concentrate, as specified on the proposed label.

The data for 1986 and 1987 are provided as supplemental information since only DME-related residues were analyzed in the 1986 crop samples, and the rate (2 x 0.4 lb ai/A) and PHI (40-41 days) used in the 1987 trials are not consistent with the label submitted with this petition. Also, many of the samples from the 1987 trials were frozen stored for >6½ months prior to analysis; the stability of residues has only been validated for ≤6½ months.

Crop Field Trials - Soybeans. In the 1986 trials (MRID# 410302-18), a total of 48 dry shelled soybean seed samples (3 varieties) were analyzed from 4 trials (IL, IA, MS, NC). Of this total, 18 samples (2 varieties) were from 3 trials (IA, MS, NC) that received 2 x 0.25 lb ai/A postemergence applications by ground sprayer equipment (20-30 gallons diluted spray per acre) and were harvested 61-63 days after the last application. Clethodim residues, determined as DME, in these 18 soybean samples ranged 0.11-6.1 ppm (average, 1.4 ppm); control values were ≤0.04 ppm DME. All soybean seed samples from the 1986 trials were analyzed within 3 months of harvest.

The 5-OH clethodim metabolites, measured as DME-OH, were not quantitated for the 1986 trials. [Data from the 1987 and 1988 soybean trials demonstrate that residue levels of 5-OH clethodim metabolites range from 21-61% of the total combined (DME + DME-OH) clethodim residue.]

In the **1987** trials (MRID# **410302-17**), a total of 36 dry shelled soybean seed samples (5 varieties) were analyzed from 9 trials in 6 states (MN, MO, IL, IA-4, MS, GA). Of this total, 18 samples (4 varieties) were from 8 trials (5 states) that received 2 x 0.4 lb ai/A postemergence applications by ground sprayer equipment (20-40 gallons diluted spray per acre) and were harvested with a 40-41 day PHI. Total clethodim residues, determined as DME + DME-OH, in those 18 soybean seed samples ranged 1.1-16.2 ppm, average 8.4 ppm; however, only 12 of those 18 soybean seed samples (3 varieties) were analyzed within 6½ months of harvest (the timeframe for which supporting frozen storage stability data are currently available). Total clethodim residues in those 12 samples ranged 3.8-16.2 ppm, 9.7 ppm average. Detectable residues (≥0.20 ppm) of DME or DME-OH were not found in the controls.

Other available data (not being discussed) from those 1987 soybean trials are mainly from samples receiving 2 x 2.0 lbs ai/A applications; one study contains data from PHIs of 14 and 28 days. In 6 of the 9 trials (6 states), data for soybean forage and hay are also submitted; the feed use of these is being label restricted, and no tolerances are being proposed. All samples from the 1987 soybean trials were analyzed within 5-14 months of harvest.

In the **1988** trials (MRID# **410302-16**), a total of 30 dry shelled soybean samples (11 varieties) were analyzed from 12 trials in 10 states (MN, NE, MO, IN, IL, OH, IA-2, AR, LA, MS-2), representing 77% of the total U.S. soybean acreage (Ag. Stat. 1988). Of this total, 24 samples (11 varieties) were from 12 trials (10 states) receiving 2 x 0.25 lb ai/A postemergence applications, either by air (5 gallons spray volume per acre) or ground sprayer equipment (10-40 gallons diluted spray per acre), and harvested 58-69 days after the last application. Total clethodim residues, determined as DME + DME-OH, in those 24 soybean seed samples ranged <0.4-16.4 ppm, with an average of 3.5 ppm. Detectable residues (≥0.20 ppm) of DME or DME were not found in the controls. Residues >7.3 ppm were found in only one trial (MN), which was claimed to be atypical due to adverse environmental conditions. Higher residues did not result from the use of aerial application equipment. All samples from the 1988 soybean trials were analyzed within 3 months of harvest.

Residue data were also submitted for soybean forage and hay in 11 of the 12 1988 trials. These data are not needed to support this petition since the proposed label for SELECT Herbicide restricts

the grazing of treated fields and the feeding of treated forage and hay to livestock. The Residue Chemistry Guidelines (Subdivision O) do consider this to be a practical restriction (under grower control).

Contingent upon the satisfactory resolution of analytical methods issues, DEB concludes the field trial data on soybeans provide adequate geographical representation and are sufficient to support the requested tolerance of 10.0 ppm in conjunction with the proposed use.

Processing Trials - Soybeans. A soybean processing study (MRID# 410302-20) was run (at the Seed Fractionation Laboratory of Texas A & M University) using field-grown soybean seeds treated with 2 x 2.0 lb ai/A postemergence applications of SELECT 2EC Herbicide and harvested at 40 day PHI (from 1987 IA soybean trial T-6921).

These fractions were analyzed for total clethodim residues (DME + DME-OH) 10-101 days after being processed. The results are summarized in Table F.

TABLE F: CONCENTRATION IN PROCESSED SOYBEANS

Matrix	Clethodim[a] (ppm)	Concentration Factor	Storage[b] (months)
Dry Shelled Soybeans	26.7	--	--
Hulls	26.1	0.98	3¼
Meal	27.2	1.02	<½
Crude Oil	2.8	0.10	1½
Crude Lecithin	42.1	1.58	3¼
Degummed Oil	1.6	0.06	3¼
Refined Oil	<0.08	<0.003	1½
Soapstock	33.5	**1.25**	3½

[a] Total residue: DME + DME-OH, expressed as clethodim.
[b] Frozen storage after processing, prior to residue analysis.

Concentration of residues is demonstrated in soybean soapstock (1.25X); a food additive tolerance at 15 ppm should be proposed by the petitioner for this processing fraction. [We note that concentration also occurs in the crude lecithin fraction (1.6X); however, the Agency does not establish food additive tolerances for this fraction.

Detectable residues (≥0.02-≥0.20 ppm, depending on matrix) of DME or DME-OH were not found in any processed fraction from controls.

No data were provided for soybean grain dust. However, since clethodim has been shown to be a systemic herbicide (see Nature of the Residue), and since clethodim residues do not concentrate in soybean hulls (see Table F), DEB can conclude no concentration of clethodim residues would be expected in soybean grain dust.

Contingent upon the satisfactory resolution of freezer storage stability and analytical methods issues, DEB concludes the processing trial data on soybeans are adequate, and that a revised Section F needs to be submitted to include a food additive tolerance proposal of 15 ppm for soybean soapstock in conjunction with the proposed tolerance level of 10.0 ppm on soybeans.

Crop Field Trials - Cotton. In the 1986 trials (MRID# 410302-15), a total of 44 fuzzy cottonseed samples (3 varieties) were analyzed from 4 trials (CA, TX, MS, GA). Of this total, 14 samples (3 varieties) were from 3 trials (CA, MS, GA) that received 2 x 0.25 lb ai/A postemergence applications by ground sprayer equipment (20-30 gallons diluted spray per acre) and were harvested 59-62 days after the last application. Clethodim residues, determined as DME, in these 14 cottonseed samples ranged <0.05-0.48 ppm (average, 0.18 ppm); in controls, 0.003-0.21 ppm. All fuzzy cottonseed samples from the 1986 trials were analyzed within 5 months of harvest.

The 5-OH clethodim metabolites, measured as DME-OH, were not quantitated for the 1986 trials. [Data from the 1987 and 1988 cotton trials demonstrate that residue levels of 5-OH clethodim metabolites are generally below or at the limit of detection (0.05 ppm) in fuzzy cottonseed harvested up to 60 days after the last of 2 postemergence applications at 0.25 or 0.40 lb ai/A/application. Residues of 5-OH clethodim metabolites (measured as DME-OH) were found in only 2 of the 19 trials conducted in 1987 and 1988.]

In the 1987 trials (MRID# 410302-14), a total of 36 fuzzy cottonseed samples (7 varieties) were analyzed from 10 locations in 7 states (CA, AZ, NM, TX, FL-3, MS-2, GA). Of this total, 20 samples (6 varieties) were from 9 trials (5 states) receiving 2 x 0.2-0.4 lb ai/A postemergence applications by ground sprayer equipment (10-40 gallons diluted spray per acre), and harvested with a 40-41 day PHI. Total clethodim residues, determined as DME + DME-OH, in those 20 fuzzy cottonseed samples ranged <0.24-<0.73 ppm, with an ≤0.46 ppm average; residues in controls were non-detectable (≤0.05-≤0.20 ppm) of DME-OH and non-detectable (≤0.05-≤0.20 ppm) to 0.13 ppm of DME. Only 6 of those 20 fuzzy cottonseed samples were analyzed within 6½ months of harvest (the timeframe for which supporting frozen storage stability data are currently available). Total clethodim residues in those 6 samples ranged <0.29-<0.68 ppm, with an ≤0.47 ppm average.

Other available data (not being discussed) from those 1987 cotton trials are mainly from samples receiving 2 x 2.0 lbs ai/A applications; one study contains data from PHIs of 14 and 28 days. In 2 of the 10 trials (2 states), data for cotton forage are also submitted; the feed use of this is being label-restricted, and no tolerance is being proposed. All samples from the 1987 cotton trials were analyzed within 6-9 months of harvest.

In the **1988** trials (MRID# **410302-13**), a total of 22 fuzzy cottonseed samples (5 varieties) were analyzed from 9 locations in 6 states (CA-2, TX-2, AR, LA, MS-2, TN), representing 81.7% of the total U.S. cotton acreage (Ag. Stat. 1988). Of this total, 18 samples (5 varieties) were from 9 trials (6 states) that received 2 x 0.25 lb ai/A postemergence applications, either by air (5 gallons spray volume per acre) or ground sprayer equipment (10-40 gallons diluted spray per acre), and were harvested with a 60 day PHI. Total clethodim residues, determined as DME + DME-OH, in those 18 fuzzy cottonseed samples ranged <0.11-0.48 ppm, ≤0.21 ppm average; residues in controls ranged <0.05-0.07 ppm of DME and <0.05-0.08 ppm of DME-OH. Higher residues did not result from the use of aerial application equipment. All samples from the 1988 cotton trials were analyzed within 2 months of harvest.

Residue data are not submitted for cottonseed forage. These data are not needed to support this petition since the proposed label for SELECT Herbicide restricts the grazing of treated fields and the feeding of treated forage to livestock. The Residue Chemistry Guidelines (Subdivision O) do consider this to be a practical restriction (under grower control).

Contingent upon the satisfactory resolution of analytical methods issues, DEB concludes the field trial data on cotton provide adequate geographical representation. However, the requested tolerance of 5.0 ppm is too high in conjunction with the proposed use. A tolerance level of 1.0 ppm for cottonseed would be more appropriate, and should be proposed via a revised Section F.

Processing Trials - Cottonseed. A cottonseed processing study (MRID# **410302-19**) was run (at the Seed Fractionation Laboratory of Texas A & M University) using field-grown fuzzy cottonseed treated with 2 x 2.0 lb ai/A postemergence applications of SELECT 2EC Herbicide and harvested with a 40 day PHI (from 1987 MS cottonseed trial T-6912).

These fractions were analyzed for total clethodim residues (DME + DME-OH) ≤2 months after being processed. The results are summarized in Table G.

Detectable residues (≥0.04-≥0.20 ppm, depending on matrix) of DME or DME-OH were not found in any processed fraction from control samples.

TABLE G: CONCENTRATION IN PROCESSED COTTONSEED

Matrix	Clethodim[a] (ppm)	Concentration Factor	Storage[b] (months)
Fuzzy Cottonseed	0.80[c]	--	--
Hulls	≤0.98[d]	≤1.22	2
Meal	1.35	1.69	2
Crude Oil	≤0.18	≤0.22	1
Refined Oil	<0.08	≤0.10	1
Soapstock	≤0.85	≤1.06	1½
Delinted Cottonseed	0.88	1.1	2

[a] Total residue: DME + DME-OH, expressed as clethodim.

[b] Frozen storage after processing, prior to residue analysis.

[c] Average value, n=3 (≤0.68, 0.95, 0.78 ppm; 3 separate samples)

[d] Residue is comprised of 0.78 ppm DME + <0.20 ppm (limit of detection) DME-OH = ≤0.98 ppm.

Concentration of residues is demonstrated in cottonseed meal (1.69X); a food additive tolerance at 2.0 ppm should be proposed by the petitioner for this processing fraction.

Adding in a limit of detection residue level for DME-OH raises the total clethodim residue (DME + DME-OH) level in cottonseed hulls to ≤0.98 ppm and the concentration factor for cottonseed hulls to the 1.2X level, which is the threshold the Agency generally uses in its considerations for the need for food additive tolerances. In this particular circumstance, DEB concludes a food additive tolerance for cottonseed hulls is not needed.

Contingent upon the satisfactory resolution of freezer storage stability and analytical methods issues, DEB concludes the processing trial data on cottonseed are adequate, and that a revised Section F needs to be submitted to include a food additive tolerance proposal of 2.0 ppm for cottonseed meal in conjunction with a revised tolerance proposal of 1.0 ppm on cottonseed.

ANIMAL FEEDING STUDIES

Dairy Cattle Feeding Study. The petitioner submitted a study, "Cow Feeding Study: Determination of Residues of Clethodim in Bovine Tissues and Milk", 1/9/89, Lab ID# ADC 1124, MRID# 410302-22.

Fourteen Holstein cows were used for the study (randomly divided into one control group of two cows and three test groups of four cows each). Following an acclimation period of 7 days, each cow in the test groups was given an oral dose of a 5:95 mixture of clethodim:clethodim sulfoxide (purity, 92.7-99.6%) contained in a gelatin capsule, once daily for 28 consecutive days. Controls were dosed with empty gelatin capsules.

Cows received 70-85 lbs wet weight (ca 37-45 lbs dry weight) per day of a commercial dairy ration, with half being given after the morning milking and half after the evening milking. For each cow, the amount of feed offered during the treatment period was approximately equal to that consumed during the acclimation period. Tap water was supplied ad libitum.

The C:CSO mixture was chosen because the major component of the residue in soybean seed was shown to be CSO in the plant metabolism studies (>40% for CSO plus conjugates; see Table B).

The dose levels for the three test groups were 10 ppm, 30 ppm, and 100 ppm equivalency in the diet. (Dosing levels were based on the highest daily food consumption, determined during the acclimation period: 85 lbs/cow/day.)

Information on housing, environmental conditions, body weights, food consumption, milk production, and general health and behavior were monitored and are provided. Raw data and representative chromatograms were also submitted.

Milk samples, consisting of equal parts of morning and evening milkings for a given day, were collected from each cow on days -1, 1, 2, 4, 7, 12, 16, 20, 24, 28, 29, 30, and 31.

Three cows from each dose level and one control cow were sacrificed on test day 29, within 24 hours of the last dose; and the remaining cow in each group on day 31, after 2 days withdrawal. Samples of liver, kidney, composite muscle, and composite fat (peritoneal and subcutaneous) were collected from each carcass for residue analysis.

All tissue and milk samples were maintained under frozen storage (-20°C) until analysis for total clethodim residues (DME + DME-OH + S-MeDME) by a modified version of RM-26A (adapted for milk and bovine tissues).

The results of residue analysis of bovine tissues and milk are summarized in Table H.

No detectable residues (≥0.0125 ppm, milk; ≥0.05 ppm, tissues) of DME, DME-OH, or S-MeDME were found in any control samples of milk or bovine tissues.

TABLE H: 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)

DME residues were found in liver and kidney at all feeding levels; in milk and fat, at the 30 and 100 ppm feeding levels; and, in muscle, at the 100 ppm level only. S-MeDME was found in milk, liver, and kidney at the 100 ppm level. DME-OH was not found in milk or any tissue at any feeding level. Residues in milk plateaued on test days 1 or 2.

No detectable residues of DME, DME-OH, or S-MeDME were reported in any control milk (<0.0125 ppm) or bovine tissue (<0.05 ppm) samples.

Composite whole milk samples collected on test days 25, 26, and 27 from the control group and the 100 ppm dose level group were processed to obtain skim milk (nonfat solids), cream (fat solids), pasteurized milk, and acid whey (lactose). Analysis for total clethodim residues (DME + DME-OH + S-MeDME) was performed on these processing fractions.

A summary of the results of residue analysis of processed milk is presented in Table I.

TABLE I: CLETHODIM RESIDUES IN PROCESSED MILK[a]

	DME	DME-OH	S-MeDME
Pasteurized Whole Milk	0.06	ND[b]	0.01
Skim Milk (Nonfat Solids)	0.03	ND	ND
Cream (Fat Solids)	0.11	ND	ND
Acid Whey (Lactose)	0.03	ND	ND

[a] Results are from composited 100 ppm dose level milk samples.
[b] ND = Not detected (<0.0125 ppm)

No detectable residues (≥0.0125 ppm) of DME, DME-OH, or S-MeDME were found in any samples of control milk processed fractions.

Analysis of processed milk fractions indicates a propensity for higher residues of DME in cream vis-a-vis skim or whole milk. However, since residues do not concentrate in the oil fractions of soybeans or cottonseed, and since appreciable residues are not detected in fat samples from cattle or poultry, we do not consider it necessary to set the proposed milk tolerance on a "milk fat" basis.

The residue data from this feeding study indicate a §180.6(a)(2) categorization, and the need for tolerances.

The 0.2 ppm proposed tolerance level for total residues of clethodim in the meat, fat, and meat by-products of cattle (and goats, hogs, horses, and sheep) mainly reflects combined method sensitivities (0.05 ppm each for DME + DME-OH + S-MeDME), rounded up to 0.2 ppm. The 0.05 ppm tolerance level proposed for total residues of clethodim in milk also mainly reflects combined method sensitivities (0.0125 ppm each for DME + DME-OH + S-MeDME), rounded up to 0.05 ppm.

These proposed tolerance levels appear to be both adequate and appropriate to cover any secondary residues which might arise in milk or livestock tissues as a result of the dietary ingestion of treated soybeans, cottonseed, and/or their processed by-products containing up to tolerance level amounts of clethodim-related compounds. However, DEB notes the tissue and milk samples from this feeding study were frozen stored (-20°C) for up to 3¼ months prior to analysis for total clethodim residues (DME + DME-OH + S-MeDME), and no frozen storage stability data have been submitted to validate total clethodim residues in animal commodity samples (see Freezer Storage Stability Data section). DEB also notes there are analytical methods issues to be resolved (see Analytical Methods section).

Contingent upon the satisfactory resolution of freezer storage stability and analytical methods issues, DEB concludes the proposed tolerance levels of 0.05 ppm for milk and 0.2 ppm for the meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep are appropriate to cover any secondary residues which might occur therein as a result of the dietary ingestion of up to tolerance level amounts of total clethodim residues present in treated soybeans, cottonseed, and/or their processed by-products.

Laying Hens Feeding Study. The petitioner submitted a study, "Clethodim (5%) & Clethodim Sulfoxide (95%): Meat & Egg Residue Study in White Leghorn Chickens", 12/29/88, Lab ID# 88 EM 9, MRID# **410302-21.**

Young laying hens were randomly assigned (20 hens each) to one of three test groups or the control group. Following an acclimation period of 35 days, each hen in the test groups received an oral dose of a 5:95 mixture of clethodim:clethodim sulfoxide (purity, ≥98.5%) contained in a gelatin capsule, once daily for 28 consecutive days. Controls received gelatin capsules containing only the carrier (corn oil and evaporated acetone). Hens received poultry mash and water ad libitum throughout the dosing period.

The **C:CSO** mixture was chosen because the major component of the residue in soybean seed was shown to be **CSO** in the plant metabolism studies (>40% for **CSO** plus conjugates; see Table B).

The dose levels for the three test groups were 10 ppm, 30 ppm, and 100 ppm equivalency in the diet. (Dosing levels were based on the highest daily food consumption, determined during the 35-day acclimation period: 151.3 grams/hen/day.)

Information on housing, environmental conditions, body weights, food consumption, egg production and quality, and general health (morbidity and mortality) and behavior were monitored and are provided. Raw data and representative chromatograms were also submitted.

Egg samples were retained and pooled by dose group for days -1, 1, 2, 4, 7, 14, 21, 28, 29, and 30.

On day 29, 10 hens from each group were randomly selected for sacrifice; all remaining hens were sacrificed on day 31. Thigh and breast muscle, liver, gizzard, and subcutaneous and abdominal fat were collected for residue analysis from each hen, pooled by tissue and test group, and 2-3 subportions of each taken for analysis.

All tissue and egg samples were maintained under frozen storage (-20°C) until analysis for total clethodim residues (DME + DME-OH + S-MeDME) by a modified version of RM-26A (adapted for eggs and chicken tissues).

The results of residue analysis are summarized in Table J.

TABLE J: 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

No detectable residues (≥0.05 ppm) of DME, DME-OH, or S-MeDME were found in any control samples of eggs or poultry tissues.

C, 5OH-SO_2, and SMSO were not detected (<0.05 ppm) in any of the fat, gizzard, or muscle samples, even at the 100 ppm dose level.

C was found (0.06 ppm) in only one liver sample (day 29), which was from the 100 ppm dose level. 5OH-SO_2 and SMSO were not detected (<0.05 ppm) in any of the liver samples.

No detectable residues (<0.05 ppm) of C were found in eggs from the 10 ppm dose level. C residues were found in eggs from both the 30 ppm (0.05-0.09 ppm) and 100 ppm (0.14-0.24 ppm) dose levels; these residues declined to <0.05 ppm by day 29. 5OH-SO2 and SMSO were not detected (<0.05 ppm) in any of the egg samples.

No detectable residues (<0.05 ppm) of DME, DME-OH, or S-MeDME were reported in any control egg or poultry tissue samples.

The residue data from this feeding study indicate a §180.6(a)(2) categorization, and the need for tolerances.

The 0.2 ppm proposed tolerance level for total residues of clethodim in the meat, fat, and meat by-products of poultry essentially reflects the combined method sensitivities (0.05 ppm each for DME + DME-OH + S-MeDME), rounded up to 0.2 ppm. The 0.5 ppm tolerance level proposed for total residues of clethodim in eggs appears unjustified; 0.2 ppm would be a more suitable level.

These tolerance levels would appear to be both adequate and appropriate to cover any secondary residues which might arise in eggs or poultry tissues as a result of the dietary ingestion of treated soybeans, cottonseed, and/or their processed by-products containing up to tolerance level amounts of clethodim-related compounds. However, DEB notes the tissue and egg samples from this feeding study were frozen stored (-20°C) for up to 2 months prior to analysis for total clethodim residues (DME + DME-OH + S-MeDME), and no frozen storage stability data have been submitted to validate total clethodim residues in animal commodity samples (see Freezer Storage Stability Data section). DEB also notes there are analytical methods issues to be resolved (see Analytical Methods section).

Contingent upon the satisfactory resolution of freezer storage stability and analytical methods issues, DEB concludes the proposed tolerance level of 0.2 ppm for the meat, fat, and meat by-products of poultry is appropriate to cover any secondary residues which might occur therein as a result of the dietary ingestion of up to tolerance level amounts of total clethodim residues present in treated soybeans, cottonseed, and/or their processed by-products. The proposed tolerance level of 0.5 ppm for eggs is too high; a tolerance level of 0.2 ppm for eggs would be more suitable, and should be proposed via revised Section F.

OTHER CONSIDERATIONS

International Harmonization of Tolerances. An International Residue Limit (IRL) Status Sheet for clethodim is included in the Appendix of this review.

There are no Codex proposals at Step 6 or above, and no Canadian or Mexican limits established for this chemical on any commodity.

Dietary Risk Evaluation. This petition represents the first food use tolerance request for clethodim.

If/when DEB can recommend for the establishment of the tolerances proposed by this petition, a dietary risk assessment should be conducted by the Dietary Risk Evaluation Section (DRES), Science Analysis and Coordination Branch (SACB), HED.

cc: M. Nelson, Reading File, Circ. (7), PP# 9F3743, Clethodim Reg. Std. File, Clethodim S.F., ISB/PMSD (E. Eldredge).

H7509C:DEB:Reviewer(MJN):CM#2:Rm810:557-7423:typist(mjn):
CLET3743.RC:3/8/90.
RDI:SecHead:RSQuick:3/8/90:BrSrScientist:RALoranger:3/8/90.

APPENDIX

(1) FIGURE 1: Proposed Metabolic Pathways for Clethodim in Plants and Animals

(2) TABLE 1: Chemical Names, Designations and Structures of Clethodim and Possible Clethodim Metabolites

(3) International Residue Limit Status Sheet

FIGURE 1 PROPOSED METABOLIC PATHWAYS FOR CLETHODIM IN PLANTS AND ANIMALS

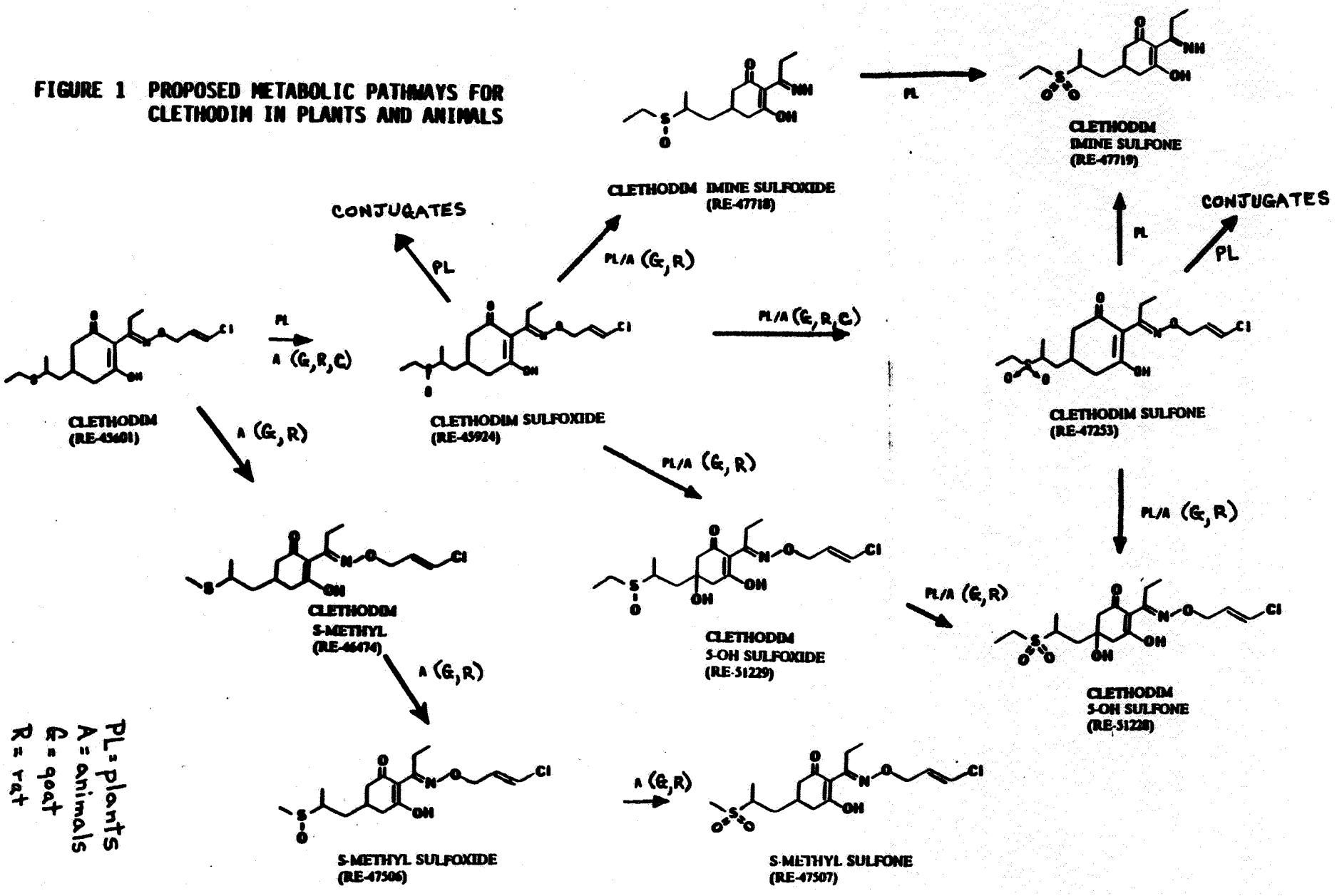


TABLE I

CHEMICAL NAMES, DESIGNATIONS AND STRUCTURES OF POSSIBLE CLETHODIM METABOLITES

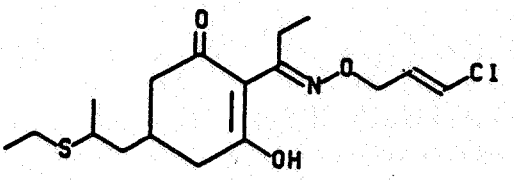
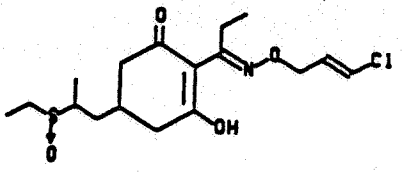
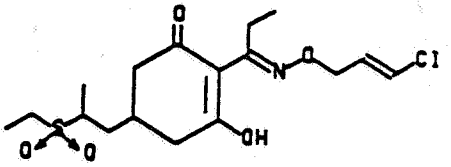
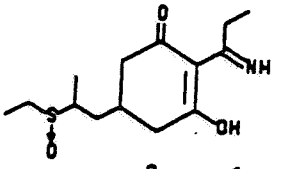
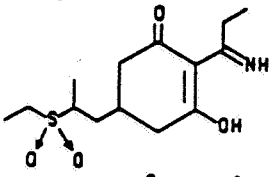
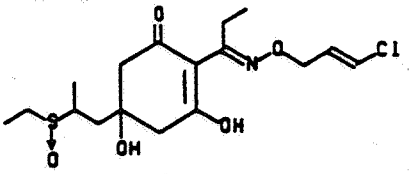
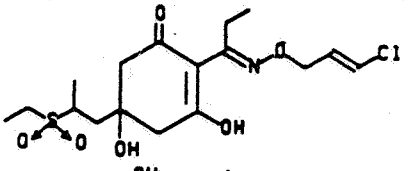
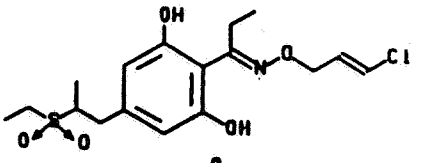
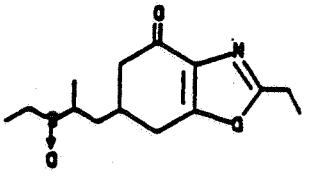
DESIGNATION	CHEMICAL NAME	STRUCTURE
CLETHODIM (RE-45601)	2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one	
CLETHODIM SULFOXIDE (RE-45924)	2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylsulfoxo)propyl]-3-hydroxy-2-cyclohexen-1-one	
CLETHODIM SULFONE (RE-47253)	2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylsulfonyl) propyl]-3-hydroxy-2-cyclohexen-1-one	
IMINE SULFOXIDE (RE-47718)	2-[[1-imino]propyl]-5-[2-(ethylsulfoxo) propyl]-3-hydroxy-2-cyclohexen-1-one	
IMINE SULFONE (RE-47719)	2-[[1-imino]propyl]-5-[2-(ethylsulfonyl) propyl]-3-hydroxy-2-cyclohexen-1-one	
5-OH SULFOXIDE (RE-51229)	2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylsulfoxo)propyl]-5-hydroxy-3-hydroxy-2-cyclohexen-1-one	
5-OH SULFONE (RE-51228)	2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylsulfonyl)propyl]-5-hydroxy-3-hydroxy-2-cyclohexen-1-one	
AROMATIC SULFONE (RE-50419)	2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylsulfonyl) propyl]-1,3-dihydroxybenzene	
OXAZOLE SULFOXIDE (RE-47796)	6,7-dihydro-6-[2-(ethylsulfoxo)propyl]-2-ethyl-4(5H)-benzoxazolone	

TABLE I (CONTINUED)

CHEMICAL NAMES, DESIGNATIONS AND STRUCTURES
OF POSSIBLE CLETHODIM METABOLITES

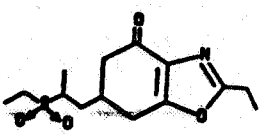
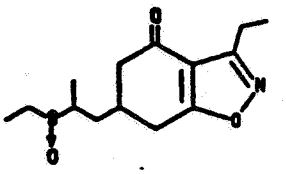
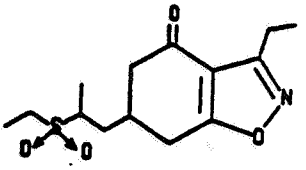
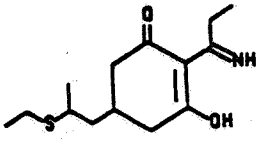
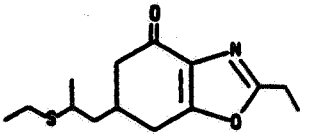
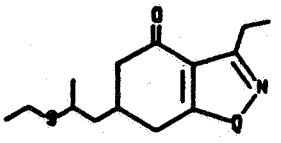
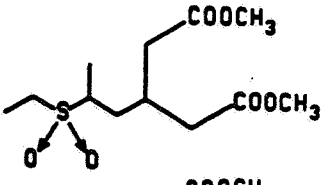
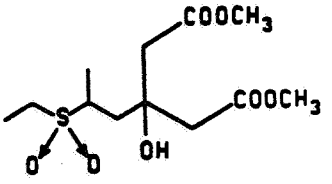
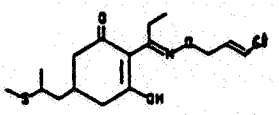
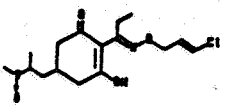
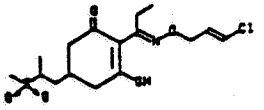
DESIGNATION	CHEMICAL NAME	STRUCTURE
OXAZOLE SULFONE (RE-47797)	6,7-dihydro-6-[2-(ethylsulfonyl)propyl]-2-ethyl-4(5H)-benzoxazolone	
ISOXAZOLE SULFOXIDE (RE-47614)	6,7-dihydro-6-[2-(ethylsulfoxo)propyl]-3-ethyl-1,2-benisoxazol-4(5H)-one	
ISOXAZOLE SULFONE (RE-47615)	6,7-dihydro-6-[2-(ethylsulfonyl)propyl]-3-ethyl-1,2-benisoxazol-4(5H)-one	
IMINE (RE-47686)	2-[[1-imino]propyl]-5-[2-(ethylthio) propyl]-3-hydroxy-2-cyclohexen-1-one	
OXAZOLE (RE-47365)	6,7-dihydro-6-[2-(ethylthio)propyl]-2-ethyl-4(5H)-benzoxazolone	
ISOXAZOLE (RE-47613)	6,7-dihydro-6-[2-(ethylthio)propyl]-3-ethyl-1,2-benisoxazol-4(5H)-one	
DME (RE-50525)	3-[2-(ethylsulfonyl)propyl] pentanedioic acid methyl ester	
DME-OH (RE-50562)	3-[2-(ethylsulfonyl)propyl]-3-hydroxy-pentanedioic acid methyl ester	

TABLE I (CONTINUED)

CHEMICAL NAMES, DESIGNATIONS AND STRUCTURES OF POSSIBLE CLETHODIM METABOLITES

DESIGNATION	CHEMICAL NAME	STRUCTURE
S-METHYL (RE-46474)	2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(methylthio)propyl]-3-hydroxy-2-cyclohexen-1-one	
S-METHYL SULFOXIDE (RE-47506)	2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(methylsulfoxo)propyl]-3-hydroxy-2-cyclohexen-1-one	
S-METHYL SULFONE (RE-47507)	2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylsulfonyl) propyl]-3-hydroxy-2-cyclohexen-1-one	

INTERNATIONAL RESIDUE LIMIT STATUS

J. Nelson 3/2/90

CHEMICAL Clethodim

CODEX NO. ____

CODEX STATUS:

☑ No Codex Proposal Step 6 or above

Residue(if Step 8): ____

Crop(s)	Limit (mg/kg)

PROPOSED U.S. TOLERANCES:

Petition No. 9F3743

RCB Reviewer Nelson

Residue: parent and metabolites w/ 2-cyclohexen-1-one moiety.

Crop(s)	Limit (mg/kg)
soybeans	10
cottonseed	5
mfmb-p of cghhps	0.2
milk	0.05
eggs	0.5

CANADIAN LIMITS:

☑ No Canadian limit

Residue: ____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

☑ No Mexican limit

Residue: ____

Crop(s)	Limit (mg/kg)

NOTES: