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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: 04 OCTOBER, 2000

Subject: Occupational and Residential Risk Assessment to Support Request for New Uses of Clethodim on Potatoes, Sugar Beets, Sunflower, Canola, Cucumbers, Bell Peppers and Non-Bell Peppers

DP Barcode:	PC Code:	Trade Name:	EPA Reg#	MRID#	PRAT Case	Class	Caswell#	40 CFR
D268761	121011	Select®	59639-3, 59639-78	N/A	289025	Herbicide	None	180.458

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This memorandum contains an occupational and residential exposure assessment based on the use of clethodim on potatoes, sugar beets, sunflower, canola, cucumbers, bell peppers and non-bell peppers in addition to currently registered use sites. This memo has been peer reviewed by Jack Arthur of RAB3, Timothy Leighton of CEB2 and Susan Hanley of RRB1.

1.0 Executive Summary

Clethodim (Select®) is a cyclohexenone herbicide used for control of annual and perennial grass weeds in broad leaf crops. Other chemicals with similar molecular structure include sethoxydim, tralkoxydim and cycloxydim. The current petition (PP#289025) is for two

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emulsifiable concentrate formulations, Select®, 12 % active ingredient (ai), EPA Reg. No. 59639-78 and Select 2 EC, 26 % ai, EPA Reg. No. 59639-3.

Select® products are currently registered for a variety of use sites including agricultural crops and non-crop areas. The labels for both products permit application to commercial and residential sites and on other non-crop or non-planted areas including rights of way such as railroads, highways, roads, dividers, medians, pipelines, public utility lines, pumping stations, transformer stations and substations, around airports, electric utilities, commercial buildings, manufacturing plants, storage yards, rail yards, fence lines, parkways, ornamental gardens, walkways, patios, greenhouse benches, along driveways and around golf courses.

No chemical-specific exposure data for handlers or postapplication activities were submitted to support the registration of clethodim on the proposed new uses. Based on clethodim labels, Select® and Select® 2EC, are both available for weed control use in residential and/or public areas. However, the registrant has indicated that the product is not for use by homeowners (personal communication with D. Kenny, Registration Division, 08/30/00). Therefore, there will be no non-occupational handlers of clethodim products and a non-occupational handler exposure assessment is not necessary. **RD must ensure that a statement prohibiting use by homeowners will be added to all clethodim labels.**

Following treatment by professional applicators, the public could potentially come into contact with clethodim residues in areas such as patios, along driveways and around golf courses and fence lines. However, weed control with clethodim in these areas generally consists of a spot treatment, resulting in a very small treated area, and it is unlikely that adults and children would be exposed to these treated areas. Therefore, a non-occupational postapplication exposure assessment was not performed.

There is a potential for occupational exposure to clethodim during mixing, loading, application, and postapplication activities. Select® products are proposed for use by ground or aerial equipment. For occupational handlers and those involved in postapplication activities such as scouting, irrigation and hand harvesting, short-term or intermediate-term exposures may occur. Chronic exposures are not expected.

No chemical-specific exposure data were submitted for this action. In accordance with HED policy, occupational handler exposures were estimated using the Pesticide Handlers Exposure Database (PHED) Surrogate Exposure Guide (revised August, 1998). Short-and intermediate-term dermal MOEs for occupational handlers were greater than the target of 100. Short- and intermediate-term postapplication MOEs were greater than 100 on the day of treatment, and do not exceed HED's level of concern. Based on the use pattern, long-term or chronic exposure is not expected. Clethodim is categorized in acute toxicity category I for primary dermal irritation. Registration Division must ensure that the correct REI appears on the label.

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2.0 Hazard Profile

Table 1. Acute Toxicity of Clethodim Technical

Study Type	MRID	Dose	Results	Tox Catagory
Acute Oral (Rat)	409745-07	0.25 g/kg tech. 83.3% ai	LD50: ♂: 1.63 g/kg ♀: 1.36 g/kg	III
Acute Oral (Mice)	409745-08	.35 g/kg tech 83.3% ai	LD50: ♂: 2.57 g/kg ♀; 2.43 g/kg	III
Acute Dermal (Rabbit)	409745-10	2 & 5 g/kg tech 83.3% ai	LD50 > 5.0 g/kg for ♂ and ♀	IV
Acute Inhalation (Rat)	409745-12	3.9 mg/l, MMAD= 2.8 um	LC50: . 3.9 mg/L	III
Primary Eye Irritation (Rabbit)	409745-14	0.1 ml tech 83.3% ai	mild ocular irritation	III
Primary Dermal Irritation (Rabbit)	409745-16	0.5 ml tech 83.2% ai	severe erythema observed at 72 hours	I*
Dermal Sensitization (Guinea Pig)	409745-18	0.5 & 5% induction; 0.5% challenge	not a sensitizer	

* In the rat 21-day dermal toxicity study (conducted at doses of 0, 10, 100 or 1,000 mg/kg/day), the LOAEL for skin irritation was 10 mg/kg/day and no NOAEL for dermal irritation was established. Thus, the TESC recommended that for occupational or residential exposure concerns, the chemical should be placed in TOX Catagory 1 (Toxicology Endpoint Selection Document, February 6, 1996).

Clethodim falls into acute toxicity category I for primary dermal irritation and categories III and IV for all other types of acute toxicity.

The Hazard Identification Assessment Review Committee (HIARC) met to evaluate the toxicology data base for clethodim on October 16, 1997 (Attachment 1). The HIARC identified endpoints for short-, intermediate- and long-term risk assessment for dermal and inhalation routes of exposure. The short-term dermal and inhalation endpoint was chosen based on the results of an oral developmental rat study in which reductions in fetal body weight and an increase in the incidence of skeletal anomalies were observed. The intermediate-term dermal and inhalation endpoint was based on the results of an oral subchronic toxicity study in dogs in which increased absolute and relative liver weights were observed. The long-term dermal and inhalation endpoint was based on the results of a chronic toxicity study in dogs in which alterations in hematology and chemistry parameters were observed. Based on proposed and existing use patterns, long-term dermal or inhalation exposure is not expected and a long-term

risk assessment was not conducted. The doses and toxicological endpoints selected for various scenarios are summarized below.

Table 2. Summary of Toxicological Endpoints for Use in Human Risk Assessment

Exposure Scenario	Dose (mg/kg/day)	UF	Endpoint	Study
Acute Dietary (All Populations)	None Selected. There were no effects observed in oral toxicity studies including developmental toxicity studies in rats and rabbits that could be attributable to a single dose (exposure). Therefore, a dose and endpoint were not selected for this risk assessment.			
Chronic Dietary (All Populations)	**NOAEL = 1.0**	100	Alterations in hematology and clinical chemistry parameters and increased absolute and relative liver weights observed at the LOAEL of 75 mg/kg/day.	Chronic Toxicity-Dog (1 year)
			Chronic RfD = 0.01 mg/kg/day	
Short-Term (Dermal)[1]	**NOAEL = 100** (oral)	100	Decreased body weight gain and clinical signs of toxicity (salivation).	Developmental - Rat
Intermediate-Term (Dermal)[1]	**NOAEL = 25** (oral)	100	Increased absolute and relative liver weights.	Subchronic Toxicity - Dog (90 days)
Long-Term (Dermal)[1]	**NOAEL = 1.0** (oral)	100	Alterations in hematology and clinical chemistry parameters as well as increases in absolute and relative liver weights.	Chronic Toxicity - Dog (1 year)
Short-Term Inhalation	Maternal **NOAEL = 100**	100	Decreased body weight gain and clinical signs of toxicity (salivation).	Developmental - Rat
Intermediate-Term Inhalation	**NOAEL = 25**	100	Increased absolute and relative liver weights.	Subchronic Toxicity - Dog (90 days)
Long-Term Inhalation	**NOAEL = 1.0**	100	Alterations in hematology and clinical chemistry parameters as well as increases in absolute and relative liver weights.	Chronic Toxicity - Dog (1 year)

[1]A dermal absorption factor of 30% is used for these risk assessments, based on the results of a dermal absorption study (MRID 41030202).
Reference: *CLETHODIM: Report of the Hazard Identification Assessment Review Committee.* 10/24/97.

The Food Quality Protection Act (FQPA) Safety Factor Committee evaluated the hazard and exposure data for clethodim on July 31, 2000. The Committee concluded that the FQPA safety factor could be removed (1x) for the purposes of risk assessment (Attachment 2). The rationale for removing the FQPA safety factor include:

- There is no indication of quantitative or qualitative increased susceptibility of rats or

rabbits to *in utero* and/or postnatal exposures;

- A developmental neurotoxcity study is not required; and
- The dietary (food and drinking water) and non-dietary (residential) exposure assessments will not underestimate the potential exposures for infants and children.

3.0 Use Profile

The established tolerances for clethodim are published in 40 CFR 180.458. The current petition (PP#289025) is for two emulsifiable concentrate formulations, Select®, 12 % ai, EPA Reg. No. 59639-78 and Select® 2 EC, 26 % ai, EPA Reg. No. 59639-3. Use patterns for all currently registered and proposed uses are presented in Table 4.

Table 3. Proposed and Existing Use Patterns for Clethodim

Formulation Type (Reg. #)	Crops	Weeds controlled (Maximum Rate for Single Application)	Max. Rate per Season (lb ai/ acre/season)	Interval Between Applications (days)	Pre-Harvest Interval (days)
Emulsifiable Concentrate (Select®, 59639-78 and Select® 2EC, 59639-3)	Cotton	Annual and perennial grasses (0.25 lb ai/acre except cucumbers and peppers; Cucumbers and peppers: 0.12 lb ai/acre)	0.5 (except canola); Canola: 0.08	14	60
	Soybeans				
	Sugar beets, onions (dry bulbs), garlic, shallots (dry bulbs), tomatoes, alfalfa, peanuts, dry beans, potatoes, sweet potatoes, yams[1], sunflower, canola, cucumbers, peppers,				Sugar beets and peanuts: 40; Onions and shallots: 45; Tomatoes and peppers: 20; Alfalfa: 15; Dry beans and potatoes and yams: 30; Sunflower: 70; Canola: 60; Cucumbers: 14
	Ornamentals				Maple Syrup: 365
	Conifer trees, non-bearing food crops, fallow land, non-crop or non-planted areas				N/A

1. Includes other tuberous and corm vegetables.

4.0 Occupational Exposure

Workers may be exposed to clethodim during mixing, loading, application, and postapplication activities. Based on the proposed application frequency, short and intermediate-term exposures may occur. Chronic exposures (≥6 months of continuous exposure) are not

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expected.

The highest rate for a single application among the crops included in this assessment is 0.25 lb ai/acre. This application rate was used for estimating exposure and risk for workers.

4.1 Occupational Handler Exposure and Risk

No chemical-specific handler exposure data were submitted in support of this action. It is the policy of the HED to use surrogate data, such as data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 as presented in PHED Surrogate Exposure Guide (8/98) to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available (HED Science Advisory Council for Exposure Draft Policy # 7, dated 1/28/99).

Potential exposure scenarios include mixing/loading liquids for groundboom and aerial applications, groundboom and aerial applications of liquid formulations and mixing/loading and applying for spot treatment (professional applicators).

Standard values established by the HED Science Advisory Council for Exposure were used for acres treated per day. For short-term eposure assessment, a body weight of 60 kilograms was used to represent females because the short-term endpoint is based on developmental effects. A body weight of 70kg, representing males and females was used for the intermediate-term assessment. The level of personal protective equipment worn by handlers is based on the minimal level needed to achieve the targeted MOE of 100 for the endpoint of the active ingredient. The oral NOAEL of 100 mg/kg/day from the developmental rat study was used to estimate short-term dermal and inhalation risks. A dermal absorption rate of 30% was used to estimate the absorbed dermal dose. The dermal absorption rate is based on a dermal absorption study conducted in rats. The oral NOAEL of 25 mg/kg/day from the subchronic toxicity in dogs was used to estimate intermediate-term dermal and inhalation risks. Long-term exposure is not expected based on the use pattern.

A summary of the exposure and risk estimates for occupational handlers is presented in Table 4. All MOEs are above 100. The lowest MOE, 230, was calculated for intermediate-term risk for professional applicators who mix, load and apply clethodim for spot treatment (wearing no gloves). For workers, MOEs of 100 or greater do not exceed HED's level of concern.

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Table 4. Short-term Exposure and Risk for Occupational Handlers

Exposure Scenario	Personal Protective Equipment	Acres Treated per day	PHED Unit Dermal Exposure (mg/lb ai)	Daily Dermal Exposure (mg/kg/day)[1] and Short-term Dermal MOE[3]	PHED Unit Inhalation Exposure (mg/lb ai)	Daily Inhalation Exposure[2] (mg/kg/day) and Short-term Inhal. MOE[3]	PHED Data Confidence	Combined Dermal and Inhalation Daily Exposure[4] (mg/kg/day)	Total Short-Term MOE
Mixer/loader: Liquid, Open Mix (for groundboom)	Long Sleeves, Long Pants, Gloves	200	0.023	0.0058 / 17,000	0.0012	0.001 / 100,000	Dermal: High; Inhal: High	0.0068	15,000
Mixer/loader: Liquid, Open Mix (for aerial)	Long pants, long sleeves, gloves	1200	0.023	0.035 / 2,900	0.0012	0.006 / 17,000	Dermal: High; Inhal: High	0.0405	2,500
Application: Groundboom, Open Cab	Long pants, long sleeves, NO gloves	200	0.014	0.0035 / 29,000	0.00074	0.00062 160,000/	Dermal: High; Inhal: High	0.0041	24,000
Application: Aerial, Fixed Wing, Closed Cab	Long pants, long sleeves, NO gloves	1200	0.0050	0.0075 / 13,000	0.000068	0.00034 / 290,000	Dermal: Medium; Inhal: Medium	0.0078	13,000
Mixing/Loading and Application: Liquid, Low Pressure Handwand	Long pants, long sleeves, NO gloves	1	100	0.13 / 800	0.03	0.00013 / 800,000	Dermal: Low; Inhal: Medium	0.13	800

[1] Dermal Daily Exposure = {Application Rate (0.25 lb ai/A) x Acres Treated (A/day) x Dermal Unit Exposure (mg/lb ai handled) x Dermal Absorption Factor (0.30)}/Body Weight.

[2] Inhalation Daily Exposure = {Application Rate (0.25 lb ai/A) x Acres Treated (A/day) x Inhalation Unit Exposure (mg/lb ai handled)}/Body Weight.

[3] Short-Term MOE = NOAEL (100 mg/kg/day) / Daily Dose.

[4] Combined Dermal and Inhalation Daily Exposure = Dermal Daily Exposure = Inhalation Daily Exposure

[5] Total Short-Term MOE = Short-Term NOAEL (100 mg/kg/day) / Combined Dermal and Inhalation Exposure

Note: Error may occur due to rounding.

Table 5. Intermediate-term Exposure and Risk for Occupational Handlers

Exposure Scenario	Personal Protective Equipment	Acres Treated per day	PHED Unit Dermal Exposure (mg/lb ai)	Daily Dermal Exposure (mg/kg/day)[1] and Int. Dermal MOE[3]	PHED unit Inhalation Exposure (mg/lb ai)	Daily Inhalation Exposure[2] (mg/kg/day) and Int. Inhalation MOE[3]	PHED Data Confidence	Combined Dermal and Inhalation Daily Exposure[4] (mg/kg/day)	Total Intermediate-Term MOE[5]
Mixer/loader: Liquid, Open Mix (for groundboom)	Long Sleeves, Long Pants, Gloves	200	0.023	0.0049 / 5,100	0.0012	0.00086/ 29,000	Dermal: High; Inhal: High	0.0058	4,300
Mixer/loader: Liquid, Open Mix (for aerial)	Long pants, long sleeves, gloves	1200	0.023	0.030 / 830	0.0012	0.0051/ 4,900	Dermal: High; Inhal: High	0.035	720
Application: Groundboom, Open Cab	Long pants, long sleeves, NO gloves	200	0.014	0.003 / 8,300	0.00074	0.00053/ 47,000	Dermal: High; Inhal: High	0.0035	7,100
Application: Aerial, Fixed Wing, Closed Cab	Long pants, long sleeves, NO gloves	1200	0.0050	0.018 / 1,400	0.000068	0.00029/ 86,000	Dermal: Medium; Inhal: Medium	0.018	1,400
Mixing/Loading and Application: Liquid, Low Pressure Handwand	Long pants, long sleeves, NO gloves	1	100	0.107 / 230	0.03	0.000107/ 230,000	Dermal: Low; Inhal: Medium	0.107	230

[1] Dermal Daily Exposure = {Application Rate (0.25 lb ai/A) x Acres Treated (A/day) x Dermal Unit Exposure (mg/lb ai handled) x Dermal Absorption Factor (0.30)}/Body Weight.

[2] Inhalation Daily Exposure = {Application Rate (0.25 lb ai/A) x Acres Treated (A/day) x Inhalation Unit Exposure (mg/lb ai handled)}/Body Weight.

[3] Intermediate-Term MOE = NOAEL (25 mg/kg/day) / Daily Dose

[4] Combined Dermal and Inhalation Daily Exposure = Dermal Daily Exposure + Inhalation Daily Exposure

[5] Total Intermediate-Term MOE = Intermediate-Term NOAEL (25 mg/kg/day) / Combined Dermal and Inhalation Exposure

Note: Error may occur due to rounding.

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4.2 Postapplication Exposure and Risk

Postapplication exposure is possible for workers entering treated fields to tend or harvest crops. Based on the timing of application (throughout all stages of plant growth), workers are expected to have some dermal contact with clethodim residues.

Workers performing post-application activities such as scouting, irrigating, harvesting, etc. may receive dermal exposure to clethodim residues. When calculating the dermal doses for workers, the maximum label application rates from proposed labels was used (0.25 lb ai/acre). These values are based on data analyzed from other pesticides on a variety of crops. Clethodim is registered or proposed for use on many different agricultural crops which can be categorized based upon the characteristics of the crop and postapplication activities of workers. Transfer coefficients ranged from 1000 to 2,500 cm^2/hour, depending on the task performed and the crop. Transfer coefficient values were taken from those appearing in Exposure SAC Policy number 3.1, "Agriculture Transfer Coefficients" (August, 2000). Transfer coefficients are based on studies conducted by the Agriculture Reentry Task Force (ARTF).

Daily dermal absorbed doses (mg/kg/day) were calculated for post-application activities using the following equation:

$$\textbf{Daily dermal absorbed dose}_t = \frac{DFR_t\ (\mu g/cm^2) \times 1E\text{-}3\ mg/\mu g \times Tc\ (cm^2/hr) \times DA \times ET\ (hrs)}{BW\ (kg)}$$

Where,

DFR_t	=	dislodgeable foliage residue on day "t" (ug/cm^2)
Tc	=	transfer coefficient (cm^2/hr)
DA	=	dermal absorption factor (unitless)
ET	=	exposure time (hr/day)
BW	=	body weight (kg)

Dislodgeable foliar residue values on the day of application were calculated using the following equation:

$$\textbf{DFR}_t\ (ug/cm^2) = \text{Application Rate (lb ai/acre)} \times F \times 4.54E8\ \mu g/lb \times 24.7E\text{-}9\ acre/cm^2$$

Where:

DFR_t	=	dislodgeable foliage residue on day "t" (ug/cm^2)
Rate	=	application rate (lb ai/acre)
F	=	fraction of ai retained on foliage (unitless)

The non-cancer risk or margin of exposure (MOE) for all time durations was calculated as follows:

$$\text{MOE} = \frac{\text{NOAEL (mg/kg/day)}}{\text{Daily Absorbed Dose (mg/kg/day)}}$$

Table 6. Occupational Postapplication Exposure and Risk

Postapplication Activities (highest exposure crop)	Transfer Coefficient (cm^2/hr)	Short-Term Daily Dermal Absorbed Dose (mg/kg/day)	Intermediate-Term Dermal Absorbed Dose (mg/kg/day)	Short-Term Day '0' MOE (day of treatment)	Intermediate-Term Day '0' MOE	Days to Reach Target MOE of at least 100
Irrigation, scouting, weeding mature/high foliage plants (sunflowers)	1000[1]	0.020	0.0017	5,000	14,000	0
Irrigation, scouting, thinning, weeding immature/low foliage plants (canola)	1500[2]	0.030	0.026	3,300	960	0
Hand Harvesting (beets)	2500[3]	0.050	0.043	2,000	580	0

1. Transfer Coefficient is the high-end value taken from Agriculture reentry Task Force study ARF009.
2. Transfer Coefficient is the high-end value taken from Agriculture reentry Task Force study ARF021.
3. Transfer Coefficient is the high-end value taken from Agriculture reentry Task Force study ARF021.

Table 6 shows the dermal MOEs calculated on the day of application which represent the highest day of exposure. MOE's are above the target of 100 for all occupational activities on day zero.

Draft copies of Select® and Select® 2EC labels have a 24-hour restricted entry interval (REI). The 24-hour REI does not comply with the Worker Protection Standard: as shown in Table 1, clethodim is categorized in Category I for primary dermal irritation. The appropriate REI that should be stated on the labels is **48 hours**.

5.0 Non-Occupational/Residential Exposure

Based on clethodim labels, Select® and Select® 2EC, are both intended for weed control use in residential and/or public areas. However, the registrant has indicated that the product is not for use by homeowners (personal communication with D. Kenny, 08/30/00). Therefore, a non-occupational handler exposure assessment was not performed. **RD must ensure that a statement prohibiting use by homeowners will be added to all clethodim labels.**

The clethodim labels permit application to commercial and residential sites and on other non-crop or non-planted areas including rights of way such as railroads, highways, roads,

dividers, medians, pipelines, public utility lines, pumping stations, transformer stations and substations, around airports, electric utilities, commercial buildings, manufacturing plants, storage yards, rail yards, fence lines, parkways, ornamental gardens, walkways, patios, greenhouse benches, along driveways and around golf courses. It is possible that the public could be exposed to clethodim residues in areas such as patios, along drive ways and around golf courses and fence lines. However, in these areas, weed control with clethodim is typically done to kill unwanted weeds of all types (grass and broadleaf) through spot treatment, typically resulting in a small treated area. It is unlikely that adults and children would be exposed to these treated areas. Further, occupational postapplication exposure to clethodim is likely to exceed that from residential postapplication, and, as can be seen in Table 5 above, occupational postapplication exposure and risk do not exceed HED's level of concern. Therefore, a non-occupational postapplication exposure assessment was not performed.

Attachments:

1. Clethodim: Report of the Hazard Identification Assessment Review Committee. October 24, 1997.
2. Clethodim: Report of the FQPA Safety Factor Committee. August 31, 2000.

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