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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

28/OCT/2003

MEMORANDUM

Subject:	Name of Pesticide Product:	MEP 42 Plant Growth Regulator
	EPA Reg. No. /File Symbol:	75095-E
	DP Barcode:	D293202
	Decision No:	331614
	PC Code:	109101
From:	Eugenia McAndrew, Biologist Technical Review Branch Registration Division (7505C)	
To:	Dennis McNeilly, PM Team 22 Fungicide Branch Registration Division (7505C)	
Applicant:	Hide, LLC 500A Highway 51 South Batesville, MS 38606	

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
109101	Mepiquat Chloride	4.2
	Inert Ingredient(s):	95.8
	Total:	100.0%

ACTION REQUESTED: PM requests review of acute toxicity data for MEP 42 Plant Growth Regulator, EPA File Symbol 75095-E.

BACKGROUND: Hide, LLC has submitted a six pack of acute toxicity studies in support of registration of MEP 42 Plant Growth Regulator, EPA File Symbol 75095-E. The studies were assigned MRID numbers 460406-03 to -08. The studies were conducted at Product Safety Labs, Dayton, New Jersey.

RECOMMENDATIONS: The six studies have been reviewed and are classified as acceptable.

The acute toxicity profile for MEP 42 Plant Growth Regulator, EPA File Symbol 75095-E, is as follows:

acute oral toxicity	IV	Acceptable	MRID 46040603
acute dermal toxicity	IV	Acceptable	MRID 46040604
acute inhalation toxicity	IV	Acceptable	MRID 46040605
primary eye irritation	IV	Acceptable	MRID 46040606
primary skin irritation	IV	Acceptable	MRID 46040607
dermal sensitization	Negative	Acceptable	MRID 46040608

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System.

PRODUCT ID #: 075095-00002

PRODUCT NAME: MEP 42 Plant Growth Regulator

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: CAUTION (optional)

Wear: Long-sleeved shirt and long pants, socks, shoes, and gloves.

First Aid: No statements are required. Registrant may use Category III statements.

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DATA EVALUATION RECORD

STUDY TYPE: ACUTE ORAL TOXICITY TESTING (870.1100 formerly §81-1)

Product Manager: 22 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid)

CITATION: Merkel, D. (2003) Hide, LLC-MEP 42; acute oral toxicity in rats- limit test. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 12909. June 13, 2003. MRID 46040603. Unpublished.

SPONSOR: Hide, LLC, 500A Highway 51 South, Batesville, MS 38606

EXECUTIVE SUMMARY: In an acute oral toxicity study, five young adult Sprague-Dawley derived albino rats/sex (Weight: 265-290 g males; 174-190 g females; Source: Ace Animals, Inc., Boyertown, PA) were given a single oral dose of Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid) at 5000 mg/kg (limit dose). Individual body weights were recorded just prior to dosing and on days 7 and 14. Animals were observed for clinical signs of toxicity and mortality for 14 days post dosing. Gross necropsies were performed on all animals.

Oral LD_{50} Males is > 5000 mg/kg (observed)
Oral LD_{50} Females is > 5000 mg/kg (observed)

Hide, LLC-MEP 42 is classified as Toxicity Category IV based on the observed value in both sexes.

All animals survived the exposure to the test substance and gained weight during the study. "There were no signs of gross toxicity, adverse pharmacologic effects or abnormal behavior." No gross abnormalities were noted at necropsy.

This study is classified as Acceptable (870.1100) and satisfies the guideline requirement for an acute oral study in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

OBSERVATIONS: All animals survived the exposure to the test substance and gained weight during the study. "There were no signs of gross toxicity, adverse pharmacologic effects or abnormal behavior."

GROSS NECROPSY: No gross abnormalities were noted at necropsy.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE DERMAL TOXICITY TESTING (870.1200 formerly §81-2)

Product Manager: 22 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid)

CITATION: Merkel, D. (2003) Hide, LLC-MEP 42; acute dermal toxicity in rats- limit test. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 12910. June 13, 2003. MRID 46040604. Unpublished.

SPONSOR: Hide, LLC, 500A Highway 51 South, Batesville, MS 38606

EXECUTIVE SUMMARY: In an acute dermal toxicity study, five young adult Sprague-Dawley derived albino rats/sex (Weight: 260-302 g males; 218-253 g females; Source: Ace Animals, Inc., Boyertown, PA) were topically exposed to a single application of Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid) at 5000 mg/kg (limit dose). The test substance was applied to a dose area of 2 inches by 3 inches (approximately 10% of the total body surface of each animal), covered with a gauze pad and wrapped with tape for a 24 hour exposure. Individual body weights were recorded just prior to dosing and on days 7 and 14. Animals were observed for clinical signs of toxicity and mortality at several hours after application and once daily for 14 days. Gross necropsies were performed on all animals.

Dermal LD_{50} Males is > 5000 mg/kg (observed)
Dermal LD_{50} Females is > 5000 mg/kg (observed)

Hide, LLC-MEP 42 is classified as Toxicity Category IV based on the observed LD_{50} values in both sexes.

"All animals survived, gained weight and appeared active and healthy. There were no signs of gross toxicity, dermal irritation, adverse pharmacologic effects or abnormal behavior." No gross abnormalities were noted at necropsy.

This study is classified as Acceptable (870.1200) and satisfies the guideline requirement for an acute dermal study in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

OBSERVATIONS: "All animals survived, gained weight and appeared active and healthy. There were no signs of gross toxicity, dermal irritation, adverse pharmacologic effects or abnormal behavior."

GROSS NECROPSY: No gross abnormalities were noted at necropsy.

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DATA EVALUATION RECORD

STUDY TYPE: ACUTE INHALATION TOXICITY TESTING (870.1300 formerly §81-3)

Product Manager: 22 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid)

CITATION: Merkel, D. (2003) Hide, LLC-MEP 42; acute inhalation toxicity in rats- limit test. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 12911. June 13, 2003. MRID 46040605. Unpublished.

SPONSOR: Hide, LLC, 500A Highway 51 South, Batesville, MS 38606

EXECUTIVE SUMMARY: In an acute inhalation toxicity study, five young adult Sprague-Dawley derived albino rats/sex (Weight: 302-321 g males; 205-222 g females; Source: Ace Animals, Inc., Boyertown, PA) were exposed by whole body inhalation to Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid) at 2.04 mg/L for a 4 hour exposure. Individual body weights were recorded just prior to dosing and on days 7 and 14. All animals were observed for clinical signs of toxicity and mortality during the exposure and for 14 days post exposure. Gross necropsies were performed on all animals.

Inhalation LC_{50} Males is > 2.04 mg/L (observed)
Inhalation LC_{50} Females is > 2.04 mg/L (observed)

Hide, LLC-MEP 42 is classified as Toxicity Category IV based on the observed LC_{50} values in both sexes.

All animals survived and gained weight during the study. In chamber observations included ocular and nasal discharge, hunched posture and hypoactivity. The animals recovered from these symptoms after removal from the exposure chamber. No gross abnormalities were noted at necropsy. The gravimetric chamber concentration was 2.04 mg/L. The mass median aerodynamic diameter was estimated to be 2.8 µm with a geometric standard deviation of 2.11-2.15.

This study is classified as Acceptable (870.1300) and satisfies the guideline requirement for an acute inhalation study in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

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RESULTS:

Exposure Concentration mg/L (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
2.04	0/5	0/5	0/10

Chamber Atmosphere		
Gravimetric conc.	MMAD	GSD
2.04 mg/L	2.8 µm	2.11-2.15

Chamber Environment[a]	
Chamber Volume	150 L
Airflow	45.8 LPM
Temperature	21 °C
Relative Humidity	45-90 %

[a] whole body

OBSERVATIONS: All animals survived and gained weight during the study. In chamber observations included ocular and nasal discharge, hunched posture and hypoactivity. The animals recovered from these symptoms after removal from the exposure chamber.

GROSS NECROPSY: No gross abnormalities were noted at necropsy.

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DATA EVALUATION RECORD

STUDY TYPE: PRIMARY EYE IRRITATION TESTING (870.2400 formerly §81-4)

Product Manager: 22 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid)

CITATION: Merkel, D. (2003) Hide, LLC-MEP 42; primary eye irritation in rabbits. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 12912. June 13, 2003. MRID 46040606. Unpublished.

SPONSOR: Hide, LLC, 500A Highway 51 South, Batesville, MS 38606

EXECUTIVE SUMMARY: In a primary eye irritation study, 0.1 mL of Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid) was placed into the conjunctival sac of the right eye of three young adult male New Zealand albino rabbits (Source: Davidson's Mill Farm, South Brunswick, NJ). All animals were observed for ocular irritation at 1, 24, 48 and 72 hours post-instillation.

Hide, LLC-MEP 42 is classified as Toxicity Category IV.

"All animals appeared active and healthy. There were no signs of gross toxicity, eye irritation, adverse pharmacologic effects or abnormal behavior."

This study is classified as Acceptable (870.2400) and satisfies the guideline requirement for a primary eye irritation study in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS:

Observations	Number "positive"/number tested			
	Hours			
	1	24	48	72
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae:				
Redness*	0/3	0/3	0/3	0/3
Chemosis*	0/3	0/3	0/3	0/3
Discharge*	0/3	0/3	0/3	0/3

*Score of 2 or more required to be considered "positive."

OBSERVATIONS: "All animals appeared active and healthy. There were no signs of gross toxicity, eye irritation, adverse pharmacologic effects or abnormal behavior."

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY DERMAL IRRITATION TESTING (870.2500 formerly §81-5)

Product Manager: 22 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid)

CITATION: Merkel, D. (2003) Hide, LLC-MEP 42; primary skin irritation in rabbits. Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 12913. June 13, 2003. MRID 46040607. Unpublished.

SPONSOR: Hide, LLC, 500A Highway 51 South, Batesville, MS 38606

EXECUTIVE SUMMARY: In a primary skin irritation study, three young adult New Zealand albino rabbits (1 male and 2 female; Source: Davidson's Mill Farms, South Brunswick, NJ) were topically exposed to Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid) . Five-tenths of a mL of test substance was applied to one 6 cm^2 intact dose site on each animal, covered with a gauze pad and wrapped with tape for a 4 hour exposure. Animals were observed 1, 24, 48 and 72 hours after patch removal.

Hide, LLC-MEP 42 is classified as Toxicity Category IV based on the observations in this study.

Primary Dermal Irritation Index (PDII) = 0.4 Very slight erythema was noted at all test sites and very slight edema at 2/3 sites one hour after patch removal. All sites were free of dermal irritation by 24 hours.

This study is classified as Acceptable (870.2500) and satisfies the guideline requirement for a primary skin irritation study in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS: Primary Dermal Irritation Index (PDII) = 0.4

OBSERVATIONS: Very slight erythema was noted at all test sites and very slight edema at 2/3 sites one hour after patch removal. All sites were free of dermal irritation by 24 hours.

DATA EVALUATION RECORD

STUDY TYPE: DERMAL SENSITIZATION TESTING (870.2600 formerly §81-6)

Product Manager: 22 **Reviewer:** Eugenia McAndrew

TEST MATERIAL PURITY: Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid)

CITATION: Merkel, D. (2003) Hide, LLC-MEP 42; dermal sensitization in guinea pigs (Buehler Method). Product Safety Labs, Dayton, New Jersey. Laboratory Report Number 12914. June 13, 2003. MRID 46040608. Unpublished.

SPONSOR: Hide, LLC, 500A Highway 51 South, Batesville, MS 38606

EXECUTIVE SUMMARY: In a dermal sensitization study conducted with Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid), 30 young adult male and female Hartley albino guinea pigs (Source: Elm Hill Breeding Labs, Chelmsford, MA) were tested using the Buehler method. Preliminary testing was conducted with four animals to determine the correct concentrations for induction and challenge. For the main study, twenty test animals were induced with three applications (six hours/exposure, once per week for three weeks) of 0.4 mL of undiluted test substance. Twenty-seven days after the first induction dose, 0.4 mL of a 50% w/w mixture of the test substance in distilled water (highest non-irritating concentration) was applied to a naive site on the twenty test guinea pigs and to ten naive control guinea pigs for a six-hour challenge exposure. Reactions were scored 24 and 48 hours after each induction and after the challenge. A positive control study using α-Hexylcinnamaldehyde, Technical, 85% (HCA), was conducted within six months of the main study to validate the test system.

Hide, LLC-MEP 42 is classified as a non-sensitizer based on the results of this study.

Very faint erythema (0.5) was noted at 6/20 test animal sites during the induction phase. Following the challenge, very faint erythema (0.5) was noted at 4/20 test animal sites at 24 hours only. In the naive control group, very faint erythema (0.5) was noted at 2/10 test sites at 24 hours only. No positive results were observed in either group. Based on these results, the test substance is not considered to be a contact sensitizer. The positive response observed in the HCA study validates the test system used in this study.

This study is classified as Acceptable (870.2600) and satisfies the guideline requirement for a dermal sensitization study in the guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

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PROCEDURE: In a dermal sensitization study conducted with Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid), 30 young adult male and female Hartley albino guinea pigs (Source: Elm Hill Breeding Labs, Chelmsford, MA) were tested using the Buehler method. Preliminary testing was conducted with four animals to determine the correct concentrations for induction and challenge. For the main study, twenty test animals were induced with three applications (six hours/exposure, once per week for three weeks) of 0.4 mL of undiluted test substance. Twenty-seven days after the first induction dose, 0.4 mL of a 50% w/w mixture of the test substance in distilled water (highest non-irritating concentration) was applied to a naive site on the twenty test guinea pigs and to ten naive control guinea pigs for a six-hour challenge exposure. Reactions were scored 24 and 48 hours after each induction and after the challenge. A positive control study using α-Hexylcinnamaldehyde, Technical, 85% (HCA), was conducted within six months of the main study to validate the test system.

RESULTS: Very faint erythema (0.5) was noted at 6/20 test animal sites during the induction phase. Following the challenge, very faint erythema (0.5) was noted at 4/20 test animal sites at 24 hours only. In the naive control group, very faint erythema (0.5) was noted at 2/10 test sites at 24 hours only. No positive results were observed in either group. Based on these results, the test substance is not considered to be a contact sensitizer. The positive response observed in the HCA study validates the test system used in this study.

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ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D293202
2. **PC CODES:** 109101
3. **CURRENT DATE:** 28/OCT/2003
4. **TEST MATERIAL:** Hide, LLC-MEP 42 (Lot # BC218209; 4.2% Mepiquat chloride; pink liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Product Safety Labs 12909/6-13-03	46040603	LD_{50} > 5000 mg/kg (males females combined)	IV	A
Acute dermal toxicity/rat Product Safety Labs 12910/6-13-03	46040603	LD_{50} > 5000 mg/kg (males females combined)	IV	A
Acute inhalation toxicity/rat Product Safety Labs 12911/6-13-03	46040603	LC_{50} > 2.04 mg/L (males females combined)	IV	A
Primary eye irritation/rabbit Product Safety Labs 12912/6-13-03	46040603	Non-irritant	IV	A
Primary dermal irritation/rabbit Product Safety Labs 12913/6-13-03	46040603	PDII = 0.4 Slight irritant	IV	A
Dermal sensitization/guinea pig Product Safety Labs 12914/6-13-03	46040603	Not a sensitizer	–	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated**

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