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

MAR 14 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT Exposure Assessment Branch (EAB) Deferral on Petitions for Temporary Tolerances for Paclobutrazol on Peaches and Nectarines (Petition No. 6G3394) and on Apples (Petition No. 7G3524 Tox. Chem. No. 628C: Tox. Proj. No. 8-0416)

TO Robert J. Taylor
Product Manager 25
Registration Division (TS-767C)

THRU: Judith Hauswirth, Ph. D., Section Head Judith W. Hauswirth 3/8/88
Review Section 6
Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: Roger Gardner, Toxicologist
Review Section 6 Roger Gardner 2-24-88
Toxicology Branch
Hazard Evaluation Division (TS-769) 3/10/88

Actions Requested

EAB has evaluated an exposure assessment for the use of CULTAR™ 2SC which was submitted to the Agency by the Registrant (ICI). Because of computational errors and unsupported assumptions in the submitted assessment, EAB conducted its own exposure assessment and stated:

> EAB...estimates the daily dermal exposure to a 60 kg individual mixing, loading and applying paclobutrazol to be 1.8 mg/kg/day. EAB defers to the Toxicology Branch the evaluation of data and calculation of the MOSs.

Recommendations and Conclusions

1. Margins of Safety calculated from the 10 mg/kg/day NOEL for developmental toxicity and dermal exposure estimates for applicators and mixer/loaders are unacceptable (43 for mixer/loaders, 6 for applicators, and 6 for individuals doing mixing/loading and application; see Section II. below for discussion).

3. Dermal penetration data are needed to more appropriately assess the significance of the exposure estimates provided (see Section I. C. 6. below).

2. The requested Experimental Use Permit is not toxicologically supported because of the unacceptably low MOS values.

I. Background

A. Formulations and Uses

Paclobutrazol is a plant growth regulator with the chemical name (2RS, 3RS)-1-(4-chlorophenyl)-4, 4-dimethyl-(1,2,4-triazol-1-yl) pentan-3-ol. The formulation proposed for use on apples, nectarines, and peaches (CULTAR™ 2SC) contains 22.3% active ingredient, and the Confidential Statement of Formulation indicates CULTAR™ 2SC contains inert ingredients which are cleared under 40 CFR §180.1000 for use on food crops.

B. Dermal absorption data

The Exposure Assessment provided by the Registrant and that of EAB assumes 100% dermal penetration for paclobutrazol (see Appendices I. and II. below). Other assumptions regarding dermal penetration and the effect of protective clothing are also discussed in the Appendices. The Registrant's assessment referred to an in vitro dermal penetration study (Scott, R. C. and S. J. Madsley, 1984) which was used to adjust the exposure estimates for dermal penetration. However, the Toxicology Branch has no record of submission or review of that study.

In a letter dated April 9, 1987, the Registrant submitted two protocols for dermal absorption studies of paclobutrazol in rats. Comments on the protocols were requested from the Toxicology Branch (see Gardner, 1987), but a final report on dermal absorption has not been received for review.

C. Toxicology Data

1. Acute Toxicity

Technical grade paclobutrazol and CULTAR™ 2SC formulations are classified into Toxicity Category III for acute oral and dermal toxicity. The technical grade is also classified into Category III for primary dermal and eye irritation; CULTAR™ 2SC is classified into Category IV with respect to inhalation toxicity and primary dermal and eye irritation. Neither of the materials are skin sensitizers.

2. Subchronic and Chronic Toxicity

A one-year study in dogs established a NOEL of 15 mg/kg/day. The effects included elevated serum alkaline phosphatase and triglyceride levels, hepatocellular hypertrophy, increased liver weights, and increased hepatic aminopyrine N-demethylase, and the LEL was 75 mg/kg/day. The highest dose tested was 300 mg/kg/day.

The NOEL for rats given paclobutrazol in the diet for 90 days is 250 ppm (12.5 mg/kg/day), and the LEL is 1250 ppm (62.5 mg/kg/day). The effects included increased liver weights and aminopyrine-N-demethylase activity.

3. Developmental Toxicity

The NOEL in a rat teratology study for maternal toxicity (decreased body weight gain during dosing) was 40 mg/kg/day (lowest dose tested). The LEL

was 100 mg/kg/day. The 200 mg/kg/day dose (highest dose tested) caused mortality (5/24 animals in the group) as well as grossly observable liver effects (pallor and enlargement). An increase in the incidence of cleft palate was observed in fetuses from dams given maternally toxic doses, but a NOEL for fetal toxicity (delayed ossification) was not established.

A second rat study suggested that a NOEL for maternal toxicity was greater than 100 mg/kg/day (highest dose tested). Dose-related fetal effects (renal dilatation, hydroureter, and minor skeletal defects or variations) were observed at 40 and 100 mg/kg/day dose levels, and a NOEL of 10 mg/kg/day was established for fetal effects.

These results suggested an adult-to developmental toxicity ratio (A:D ratio) for rats of 2.5 based on LEL's for maternal and developmental toxicity or 4 based on the NOEL's for the two types of toxicity.

In a rabbit teratology study fertility of the animals was low. Only the low and mid-dose groups contained the recommended minimum number of litters at the end of the study. Within those limitations the NOEL for maternal toxicity (as indicated by decreased body weight gain during the dosing period) was 25 mg/kg/day and the LEL was 75 mg/kg/day. There were no effects on the fetuses of low and mid dose groups that could be attributed to paclobutrazol, nor in the fetuses of the limited number of litters in the high dose group and the NOEL was set at 125 mg/kg/day (highest dose tested). These results suggest that the rat is the most sensitive species tested.

Based on these considerations, a NOEL for developmental toxicity was established at 10 mg/kg/day.

4. Mutagenicity

No effects were seen in a battery of mutagenicity studies that included point mutation tests in Salmonella and mouse lymphoma cells in vitro, a micronucleus test in mice, cytogenetic effects in rats, and a dominant lethal assay in mice.

5. Metabolism

Rats and dogs readily absorb low and high oral doses of paclobutrazol, and excretion is rapid. The major route of excretion is the urine. Metabolites include free or conjugated diol and carboxylic acid forms of paclobutrazol with the halogenated phenyl and triazol groups remaining unchanged in rats.

6. Data Gaps

Although there are no data gaps for the proposed Experimental Use Permits and temporary tolerances, the teratology studies in rats suggested a potential for developmental toxicity associated with paclobutrazol. Information on applicator exposure (see below) suggested low Margins of Safety based on the assumption of 100% dermal penetration. Dermal penetration data are needed to fully assess the significance of the exposure estimates since MOS values for the proposed uses are too low to be acceptable.

5. Provisional Acceptable Daily Intake (PADI)

Subchronic and chronic toxicity studies indicated that the liver is the target organ. The lowest NOEL in a feeding study was found in a 90-day rat study (250 ppm or 12.5 mg/kg/day), and the NOEL is used with a 1000-fold Safety Factor in the absence of chronic feeding studies to determine the PADI level.

Using the Safety Factor and NOEL, the PADI is calculated as follows:

$$\frac{12.5 \text{ mg/kg/day}}{1000} = 0.0125 \text{ mg/kg/day}$$

D. Dermal Exposure Estimates

The Registrant's dermal exposure estimates were:

$$\text{Mixer/loader} = 8.27 \times 10^{-2} \text{ mg/kg/day}$$
$$\text{Applicator} = 9.31 \times 10^{-1} \text{ mg/kg/day}$$

EAB's estimates were:

$$\text{Mixer/loader} = 2.3 \times 10^{-1} \text{ mg/kg/day}$$
$$\text{Applicator} = 1.6 \text{ mg/kg/day}$$

II. Discussion

Dividing the 10 mg/kg/day NOEL for developmental toxicity (see Section I. C. above) by the exposure estimates mentioned above, the following Margins of Safety are calculated:

	Margins of Safety	
Individual	Registrant estimate	EAB estimate
Mixer/loader	121	43
Applicator	10	6
Total	9	6

These MOS values are unacceptable, and in view of the absence of dermal penetration data they are subject to change.

III. References

Gardner, R. Memorandum dated June 30, 1987. Subject: Dermal Absorption Study Protocols Proposed for Paclobutrazol Tox. Chem. No. 628C; Tox. Proj. No. 7-0600. To: R. J. Taylor, Product Manager 25, Registration Division.

Scott, R. C. and S. J. Madsley. 1984. The In Vitro Absorption of Paclobutrazol (PP333) Through Human Epidermal Membranes: Technical Grade and From Formulations Designated JF7844, JF9082, JF9121, and JF9136. ICI Americas. Inc. CTL Report No.: CTL/P/991.

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APPENDIX I

The Exposure Assessment Branch's
Assessment of the Proposed Use of Paclobutrazol on Apples

Shaughnessy No: 125601

Date Out of EAB: 1/27/88

To: R. Taylor
Product Manager #25
Registration Division (TS-767C)

From: Michael P. Firestone, Chief
Special Review Section
Exposure Assessment Branch/HED (TS-769C)

Thru: Paul F. Schuda, Chief
Exposure Assessment Branch/HED (TS-769C)

Attached, please find the EAB review of:

Reg./File # : 212190

Chemical Name : Paclobutrazol

Type Product : Growth Regulator

Product Name :

Company Name : ICI

Purpose : Exposure assessment

Date Received : 1/15/88 Action Code: 350

Date Completed: 1/26/88 EAB #(s): 80285

Monitoring study requested: ____ Total Reviewing Time: 2 days

Monitoring study voluntarily: ____

Deferrals to: ____ Ecological Effects Branch

____ Residue Chemistry Branch

X Toxicology Branch

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1.0 INTRODUCTION

ICI Americas, Inc., has submitted an exposure assessment to support registration and EUP requests for the use of Cultar 2SC on peaches, nectarines, and apples. Cultar 2SC is a plant growth regulator that contains paclobutrazol as the active ingredient. It is intended that Cultar 2SC will be applied by air-blast equipment at 0.1 to 0.5 lbs ai/acre. The Toxicology Branch has determined that paclobutrazol is a developmental toxicant.

2.0 ICI EXPOSURE ASSESSMENT

ICI prepared an exposure assessment for the airblast application of paclobutrazol to apples at 0.5 lbs ai/acre. The exposure assessment assumed a 70 kg individual and that exposure is reduced 90% for a mixer/loader by wearing impermeable gloves, and 61% for an applicator wearing long-sleeved shirts instead of short-sleeved shirts. It is assumed that the workers will wear hats, long-sleeved shirts, long pants, shoes, and socks; and in addition, impermeable gloves during mixing/loading. No adjustment was made for dermal absorption and ICI assumed that inhalation exposure is negligible compared to dermal exposure.

The use assumptions were the airblast application of paclobutrazol at 0.5 lbs ai/acre in 100 gallons of spray to 30 acres of apples daily. The application to 30 acres will require six hours of spray time and 70 minutes of mixing/loading time.

To estimate mixer/loader exposure, a 1983 Spray Operator Safety Study by the British Agrochemicals Association, Limited, was used. This study, now published by Abbott, I.M., et al [Worker Exposure to a Herbicide Applied with Ground Sprayers in the United Kingdom, Am. Ind. Hyg. Assoc. J. 48(2):167-175 (1987)] has been previously reviewed by EAB and is acceptable for use in appropriate exposure assessments. ICI used the total potential dermal exposure for six hydraulic sprayer, tractor-drawn mixer/loader replicates. The mean exposure for the six replicates was 102 mg which was divided by the approximately 12 kg ai (26.46 lb ai) handled and a 70 kg body weight to yield a potential dermal exposure of 0.055 mg/kg/lb ai. The mixer/loader exposure estimate was adjusted by the 15 lb ai/day that would be handled to yield an exposure estimate of "0.083 mg/kg/day." ICI compared their daily exposure estimate to a NOEL of 10 mg/kg/day to estimate a MOS of 121.

Applicator exposure was estimated using EAB's airblast exposure regression equation. Based on the application rate of 0.5 lbs ai/acre, the hourly exposure is 18.4 mg/hr or 0.26 mg/kg/hr for a 70 kg individual. This estimate, based on the applicator wearing a short-sleeved shirt, was multiplied by"0.39"to estimate

exposure with a long-sleeved shirt. The daily exposure of 0.93 mg/kg/day was estimated based on a six-hour spray day. ICI calculated a MOS of 11 for the airblast applicator, assuming 100% dermal absorption.

Applicator MOSs were also calculated based on ICI's estimate of a dermal absorption flux rate of 14.76 ug/cm^2/hr. By assuming 3000 cm^2 of exposed skin and six hours of exposure per day, an internal dose estimate of 266 mg/day was derived. This was reduced 400-fold, which is the ratio of the concentration of paclobutrazol in Cultar 2SC to paclobutrazol in the spray solution. For a 70 kg individual, the daily dosages were estimated to be 9.5 ug/kg/day in a short-sleeved shirt which yielded a MOS of 1054. The MOS of 1054 was divided by "59%" to yield a MOS of 1786 for applicators in long-sleeved shirts.

3.0 EAB EVALUATION OF ICI'S ASSESSMENT

EAB does not concur with the exposure estimates presented by ICI for mixer/loaders and airblast applicators based on computational errors and disagreement over some assumptions. Specific reasons are as follows:

1. Assumption of average worker weight of 70 kg. EAB uses a weight of 60 kg rather than 70 kg when a developmental toxicity endpoint is involved.

2. Mixer/loader exposure is reduced 90% by the use of impermeable gloves. This assumption is valid only if the reduction is to the hands and not the entire mixer/loader. EAB is not certain as to the extent of the reduction since it does not appear to have been utilized in the exposure assessment.

3. Applicator exposure is reduced 61% by wearing a long-sleeved rather than a short-sleeved shirt. ICI referenced the August 1, 1985 EAB review of Clipper 50WP (EAB #5561) and the July 22, 1985 EAB review of Cymbush (EAB #5742) as the basis for this assumption. EAB has reread both reviews and cannot find any reference to long-sleeved shirts reducing dermal exposure 61% when compared to shirt-sleeved shirt exposure. The estimate of 61% seems overinflated. A study by Nigg, et al, (Dicofol Exposure to Florida Citrus Applications: Effects of Protective Clothing, Achr. Environ. Contam. Toxicol. 15:121-134, 1986) in which dicofol was applied by airblast showed that the forearms of the applicators received 9% of the total exposure.

4. The daily exposure to mixer/loaders was calculated incorrectly. The exposure estimate should be 0.827

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mg/kg/day and not 0.0827 mg/kg/day. This miscalculation was carried to the MOS calculation. The MOS should, therefore, be 12 and not 121.

5. The reduction of the hourly airblast applicator exposures from 0.26 mg/kg/hr to 0.16 mg/kg/hr to compensate for long-sleeved shirts is unjustified. As previously stated, EAB does not accept the assumption that the long-sleeved, rather than short-sleeved, shirt will reduce the exposure 61%. In addition, the 0.26 mg/kg/hr was multipled by 0.59. The relationship of 0.59 to a 61% reduction is unclear. Did ICI intend to use 0.39?

6. The calculation of MOSs based on the dermal absorption is unacceptable and bizarre. EAB defers to the Toxicology Branch for final evaluation of the dermal absorption data, but EAB believes the ICI calculations have no relationship to airblast applications. The airblast applicator MOSs are derived from a dermal absorption flux rate of 14.76 ug/cm^2/hr. Nowhere in the derivation is any exposure number related to airblast application. ICI has not presented data in its assessment to demonstrate that the dermal absorption flux rate of 14.76 ug/cm_2/hr occurs at deposition rates of paclobutrazol expected during airblast applications. As initially stated, EAB defers to the Toxicology Branch to evaluate the dermal absorption data.

4.0 EAB EXPOSURE ASSESSMENT

EAB has conducted an exposure assessment for the proposed use of paclobutrazol. The use assumptions presented by ICI will be used, as will the same surrogate studies used by ICI.

The Abbott study had a total of 18 replicates for mixing/loading that EAB considers valid for this assessment. The exposure estimates presented in Abbott are potential exposure for the dermal deposition of 2,4-D on the exposed skin or clothing. EAB has estimated dermal exposure for an individual wearing long-sleeved shirts and long pants that reduce exposure to covered areas by 50% and protective gloves that reduce hand exposure by 90%. Based on Abbott, the mean dermal exposure to the 18 replicates is 0.93 mg/lb ai. A 60 kg mixer/loader handling 15 lb ai/day (30 acres at 0.5 lbs ai/acre) will receive a daily dermal exposure of (0.93 mg/lb ai x 15 lb ai/day x 1/60 kg) 0.23 mg/kg/day.

The daily dermal exposure to the airblast applicator wearing long pants and shirt-sleeved shirt is [((4.6 x 0.5) + 16)mg/hr x 6 hr/day x 1/60 kg] 1.8 mg/kg/day. Based on Nigg's determination that the forearms of airblast applicators received 9% of the dermal exposure, the use of long-sleeved shirts could potentially reduce the airblast applicator exposure to 1.6 mg/kg/day, assuming elimination of forearm exposure. The orchard grower will be expected to do both mixing/loading and application which would yield a combined dermal exposure of 1.8 mg/kg/day.

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5.0 CONCLUSIONS

EAB has evaluated the ICI exposure assessment for the use of Cultar 2SC on apples and has concluded that it is unacceptable, based on computational errors and unsupported assumptions.

EAB has conducted an exposure assessment for the proposed use and estimates the daily dermal exposure to a 60 kg individual mixing, loading, and applying paclobutrazol to be 1.8 mg/kg/day. EAB defers to the Toxicology Branch the evaluation of dermal absorption data and calculations of the MOSs.

Curt Lunchick

Curt Lunchick, Chemist
Special Review Section
Exposure Assessment Branch/HED (TS-769C)

1.8 mg/kg/day

APPENDIX II

The Registrants Exposure Assessment
of the Proposed Use of Paclobutrazol on Apples

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Exposure Assessment for CULTAR™ 2SC

A worker exposure assessment has been prepared in response to toxicology review concerns about developmental toxicology potential of paclobutrazol.

CULTAR 2SC - Use Pattern

CULTAR 2SC is a plant growth regulator which will be applied by trailer-mounted air-blast sprayer equipment in apple orchards. CULTAR applications are made as a dilute spray in 100 to 200 gallons per acre. Most commercial equipment for this use has a tank capacity of 500 gallons or more. Mixing is done with the concentrate in a semi-closed mechanical system to give a final concentration of 0.1 to 0.5 lb ai/A according to the proposed label.

Assumptions

1. The average worker weighs 70 kg. 60 to be more realistic
2. Exposure is reduced by 90% for a mixer/loader by wearing impermeable gloves.

   Exposure is reduced 61% for an applicator by wearing a long-sleeved shirt instead of a short-sleeved shirt.
3. Workers will wear hats, long-sleeved shirt, long pants, socks and shoes. Mixer/loaders will also wear impermeable gloves.
4. There is no adjustment for dermal penetration. Assume 100% in this assessment.
5. Respiratory exposure is negligible compared to dermal exposure.

Application Apparatus

1. CULTAR will be applied at 0.5 lb ai/A in 100 gallons per acre (the most concentrated spray mix on the proposed label).
2. Most apple orchards are large enough to require a full day's work of spraying for both the mixer/loader and applicator.
   - At 100 gallons per acre an applicator can spray 5 acres per load (500 gallons); 6 loads per 6-hour day, for a total of 30 acres per day. reasonable
   - A full day's work for a mixer/loader would require mixing 6 loads taking about 70 minutes total per day.

15 lbs a.i./day = 30 acres x 0.5 lb a.i./acre

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Mixer/Loader Exposure

Surrogate Study - Spray Operator Safety Study (1983), British Agrochemicals Association Limited (2) provides data on mixer/loaders using similar concentrations of active ingredient and spray volume mixed per tank as would be used for CULTAR. Surrogate data was used from hydraulic sprayer tractor-drawn operators only since these data most closely match the CULTAR 2SC use pattern. The other types of equipment tested in the surrogate used low spray volumes per tank or low volume applications (CDA) and are inappropriate for comparison to CULTAR. There were six replications in the surrogate study.

Exposure was determined in the surrogate in terms of mg/kg/lb handled.

A. Mean exposure to 2,4-D: 102.1 mg/tank

$$\frac{102.1 \text{ mg}}{\text{Tank}} \times \frac{1 \text{ Man}}{70 \text{ kg}} \times \frac{1\text{-Tank}}{26.46 \text{ lb ai}} = 5.51 \times 10^{-2} \text{ mg/kg/lb}$$

B. Mixer/loader exposure to paclobutrazol:

$$\frac{5.51 \times 10^{-2} \text{ mg/kg}}{\text{lb ai}} \times \frac{0.5 \text{ lb ai}}{100 \text{ Gal}} \times \frac{500 \text{ Gal}}{\text{Tank}} \times \frac{6 \text{ Tanks}}{\text{Day}} = 8.27 \times 10^{-2} \text{ mg/kg bw/day}$$

Paclobutrazol NOEL Devel. Toxicity = 10 mg/kg/day

$$\frac{10}{8.27 \times 10^{-2}} = 120.92 \text{ MOS}$$

Applicator Exposure

Applicator exposure from air-blast application is discussed in Reinhert (1) and the following linear regression equation relating lb ai/A applied to exposure was developed. Using Reinhert as the surrogate, applicator exposure is calculated below.

$Y = (4.8 \times 0.5 \text{ lb ai/A}) + 16 \text{ mg/hr} = 18.4 \text{ mg/hr}$

$$18.4 \text{ mg/hr} \times \frac{1 \text{ Man}}{70 \text{ kg}} = 2.63 \times 10^{-1} \text{ mg/kg/hr}$$

$$2.63 \times 10^{-1} \text{ mg/kg/hr} \times 0.59 \text{ (long sleeves)} = 1.55 \times 10^{-1} \text{ mg/kg/hr}$$

$$1.55 \times 10^{-1} \times \frac{6 \text{ Hr}}{\text{Day}} = 9.31 \times 10^{-1} \text{ mg/kg/day}$$

$$\frac{10 \text{ mg/kg/day NOEL}}{9.31 \times 10^{-1} \text{ mg/kg/day}} = 10.75 \text{ MOS}$$

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Hourly respiratory exposure for air-blast applicators is lower than hourly dermal exposure by 10^{-3}; therefore, respiratory exposure can be considered negligible (1).

Dermal Absorption of Paclobutrazol

Absorption of paclobutrazol is very slow; therefore, actual exposure to paclobutrazol will be much lower than the potential exposure previously calculated.

Absorption of paclobutrazol across human abdominal epidermis has been measured in-vitro (3). Percutaneous absorption of paclobutrazol following dermal application was very slow and ranged from <0.01 to 14.76 ug/cm^2/hr for four different formulations and technical material. Permeability constants for the four formulations ranged from 5.84×10^{-5} to 6.7×10^{-4} cm/hr.

Using 14.76 ug/cm^2/hr as the mean absorption rate:

3000 cm^2 of exposed skin (with short-sleeved shirt)

A worker exposed to formulation applied to exposed skin would absorb:

$$\frac{14.76 \text{ ug}}{\text{cm}^2 \text{ Hour}} \times 3000 \text{ cm}^2 \times \frac{6 \text{ Hr}}{\text{Day}} = 2.66 \times 10^5 \text{ ug/day}$$

$$\frac{\text{X Exposure}}{0.5 \text{ lb ai}/100 \text{ Gal}} = \frac{2.66 \times 10^2 \text{ mg/day}}{2 \text{ lb/Gal}}$$

Absorption is proportional to dilution of active ingredient according to Ficks Law of Diffusion; therefore, exposure = 6.64×10^{-1} mg/day.

$$\frac{6.64 \times 10^{-1} \text{ mg}}{\text{Day}} \times \frac{1 \text{ Man}}{70 \text{ kg}} = 9.49 \times 10^{-3} \text{ mg/kg/day}$$

$$\text{MOS w/Short Sleeves} = \frac{10 \text{ (NOEL)}}{9.49 \times 10^{-3}} = 1054$$

$$\text{MOS w/Long Sleeves} = \frac{10}{(9.49 \times 10^{-3})\ (0.59)} = 1786$$

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ATTACHMENT

Basis for Assumptions:

Assumption 1: This is a standard EPA assumption for male workers.

Assumption 2: Please see EAB Review of August 1, 1985 of Clipper 50 WP (EPA Reg. No. 10182-77). Please also see EAB Review of July 22, 1985 of CYMBUSH (pecans) (EPA Reg. No. 10182-65 (R)).

Assumption 3: The clothing listed are standard protective clothing.

Assumption 4: 100% penetration was assumed for lack of data that may be correlated with the surrogate data.

Assumption 5: Please see EAB review of August 1, 1985 of Clipper 50 WP (EPA Reg. No. 10182-77). Please also see the notice in the September 26, 1984 Federal Register regarding Linuron (page 37843 through 37847).

G6/122887CRF03

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References

1. Reinhert, J. C. and Severn, D. J., 1986. Dermal Exposure to Pesticides: The Environmental Protection Agency's Viewpoint. ACS Symposium Series.

2. British Agrochemicals Association Limited. 1983. Alembic House, 93 Albert Embankment, London SE1 7TU.

3. Scott, R. C. and S. J. Mawdsley. 1984. The In-Vitro Absorption of Paclobutrazol (PP333) Through Human Epidermal Membranes: Technical Grade and From Formulations Designated JF7844, JF9082, JF9121, and JF9136. ICI CTL Report No. : CTL/P/991.

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