11-19-98

MEMORANDUM

DATE: 11/19/98

SUBJECT: EXTENSION OF TIME LIMITED TOLERANCES OF **PROPICONAZOLE** ON **CORN, PINEAPPLES** (PP#8F3674) AND **PEANUTS** (PP#8F3654)

DP Barcode: D250861	PRAT Case#: 280695
Submission #: S551227	Caswell#: 323EE
Chemical#: 122101	Class: Fungicide
Trade Name: Tilt 45W, Tilt 428C	40 CFR: 180.434
EPA Reg#: 100 - 780, 100-737	

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INTRODUCTION

The time limited tolerances for propiconazole on corn, peanuts and pineapples will expire 12/31/98. A permament tolerance cannot be established at this time due a toxicology data gap (pending review of cancer study). Based on conversations with the Registration Division (RD), the Health Effects Division (HED) has been asked to extend these tolerances for two years. This memo will provide justification for a two year extension of these tolerances.

Furthermore, it should be noted that RD forwarded a Notice of Pesticide Registration for propiconazole to HED. The notice states that this product (TILT 45W, EPA Reg No 100-780) is conditionally registered provided that the restricted entry interval (REI) be changed to 12-hours because this is the appropriate time period for products bearing the signal word "Caution". Acute toxicity information is available for the technical. The Worker Protection Standard (WPS) requires a **24-hour** REI if the technical material has acute dermal, eye, or skin irritation toxicity designated in Toxicity Category II. Since the technical has an acute toxicity category of II, **RD should insure that the appropriate 24-hour REI, as required by the WPS, appears on the label.**

SUMMARY

The acute dietary risk estimates (food only) do not exceed HED's level of concern. Using Theoretical Maximum Residue Contribution (TMRC), HED concludes that the high-end exposure estimate is 0.01 mg/kg/day, which utilizes 3.3% of the dietary (food only) acute RfD for females 13+ years (the only population subgroup of concern), and should be viewed as a conservative risk estimate. Refinement using anticipated residue values and percent crop-treated data in conjunction with Monte Carlo analysis, would result in a lower acute dietary exposure estimate. The drinking water level of comparison (DWLOC) for acute exposure estimates for females 13 years and older is 8,700 ug/L. Environmental Fate and Effects Division's (EFED's) peak Expected Environmental Concentration (EEC) (acute) value of 0.11 ug/L is lower than this acute DWLOC. Therefore, HED concludes, with reasonable certainty, that the acute aggregate risk from propiconazole is less than our level of concern .

The short- and intermediate-term aggregate risk estimates, which include a residential use (adults applying wood preservative), do not exceed HED's level of concern for females 13 years and older, the population of concern. The short- and intermediate term Margins of Exposure (MOE) is 200 for residential exposure, for females 13 years and older. The DWLOC for short and intermediate term exposure estimates for females 13 years and older is 4,500 ug/L. EFED's 56-day EEC value of 0.09 ug/L is lower than this short- and intermediate term DWLOC. Therefore, HED concludes, with reasonable certainty, that the short- and intermediate term aggregate risk from propiconazole is less than our level of concern.

Chronic dietary risk estimates (food only) do not exceed HED's level of concern. In conducting this chronic dietary risk assessment, HED has made partially refined assumptions. Corn, peanuts and pineapples, the subject Raw Agricultural Commodities (RACs), will contain tolerance level residues. Corn is 6% crop treated, pineapple is 100% crop treated and peanuts are 1% crop treated. Some of the other commodities in this analysis contain tolerance level residues, and some contain anticipated residue estimates. In addition, some of the commodities in this analysis containing propiconazole residues are 100% crop treated and some are not. HED has calculated that dietary exposure to propiconazole from food will utilize 7% of the RfD for the U.S.

population, 6% of the RfD for males 13 years and older, 7% of the RfD for females 13 years and older (nursing) and 20% of the RfD for infants (non-nursing infants < 1 year old) and children. HED generally has no concern for exposures below 100 percent of the RfD because the RfD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. HED's DWLOCs are as follows: 420 ug/L for the US Population, 430 ug/L for males 13 years, 360 ug/L for females 13 years and older, and 100 ug/L for infants and children. EFED's chronic EEC [Generic Expected Environmental Concentration (GENEEC) 56-day value] of 0.09 ug/L is lower than these chronic DWLOCs. Therefore, HED concludes, with reasonable certainty that chronic aggregrate risk from propiconazole is less than our level of concern.

Under current HED criteria, the registered non-dietary uses of propiconazole do not constitute a chronic exposure scenario. Therefore, HED concludes that there is a reasonable certainty that no harm will result from chronic aggregate exposure to propiconazole residues.

Occupational exposure estimates do not exceed HED's level of concern.

Propiconazole has been classified as a Group C, possible human carcinogen, chemical by the HED Carcinogenicity Peer Review Committee (9/11/92). The Committee recommended using the RfD approach for quantification of human risk. Since the RfD approach is identical to the chronic assessment, a quantitative risk assessment using a cancer endpoint will not be done. HED's drinking water level of comparison for cancer is 420 ug/L for the US Population. EFED's chronic EEC, GENEEC 56-day, value of 0.09 ug/L is lower than this DWLOC. Therefore, HED concludes, with reasonable certainty, that exposure to propiconazole in drinking water is less than our level of concern.

The pre- and post-natal toxicology data base for propiconazole is complete with respect to current FQPA-relevant toxicological data requirements. An ad-hoc Food Quality Protection Act (FQPA) committee met and determined that the FQPA factor be removed for propiconazole be removed for purposes of these time limited tolerances (Ray Kent and Richard Keigwin 5/18/98).

Therefore, HED has no objection to the two-year extension of tolerances for corn, peanuts and pineapples. The time-limited tolerances for residues of propiconazole should remain at 12 ppm for corn fodder and forage; 0.1 ppm for sweet corn and corn grain; 0.2 ppm for peanuts; 20 ppm for peanuts, hay; and 0.1 ppm for pineapple and pineapple fodder.

TOXICOLOGICAL ENDPOINTS

DIETARY

1) ***Acute Toxicity.*** (Acute RfD = 0.3 mg/kg/day) [NOAEL = 30 mg/kg/day and an uncertainty factor (UF) of 100]. For acute dietary risk assessment, the Ad Hoc Toxicology Endpoint Selection Committee (TES; PIRAT toxicologist, TBII Section Head, SAB Chief [ID#97TX0017, DP Barcode: D235371, PIRAT, 6/9/97]) recommended use of the developmental NOAEL of 30 mg/kg/day from a developmental toxicity study (MRID# 40425001) in rats. The developmental LOAEL of 90 mg/kg/day was based on the increased incidence of unossified sternebrae, rudimentary ribs, and shortened or absent renal papillae. The population subgroup of concern is females 13+ years.

2) ***Chronic Toxicity.*** Chronic RfD = 0.013 mg/kg/day. The RfD was established by HED's RfD Committee based on a one-year feeding study (MRID# 00073928) in dogs with a NOAEL of 1.25 mg/kg/day and an uncertainty factor (UF) of 100. The LOAEL of 6.25 mg/kg/day was based on mild irritation of the gastric mucosa.

NON-DIETARY

1) ***Short- and Intermediate-Term Dermal Toxicity.*** For short- and intermediate-term dermal MOE calculations, the Ad Hoc Toxicology Endpoint Selection (TES) Committee (PIRAT toxicologist, TBII Section Head, SAB Chief) recommended use of the developmental NOAEL of 30 mg/kg/day from the developmental toxicity study (MRID# 40425001) in rats. At the developmental LOAEL of 90 mg/kg/day, there were increased incidence of unossified sternebrae, rudimentary ribs, and shortened or absent renal papillae.

2) ***Short- and Intermediate-Term Inhalation Toxicity.*** For short- and intermediate-term inhalation MOE calculations, the Ad Hoc TES Committee recommended use of the NOAEL of 92.8 mg/kg/day (0.5 mg/L), the highest dose tested (HDT), from the 5-day inhalation toxicity study (MRID# 42055333) in rats.

3) ***Chronic Toxicity.*** Chronic endpoints were not identified; therefore, a risk assessment is not required.

4) ***Dermal Penetration.*** Dermal penetration of 40% has been determined in a dermal penetration study (MRID# 00265795) in rats.

CANCER

1) ***Cancer Risk.*** Propiconazole has been classified as a Group C, "possible human carcinogen", chemical by the Cancer Peer Review Committee (CPRC) (9/11/92). The CPRC recommended using the RfD approach for quantification of human risk.

FQPA CONSIDERATIONS

1. FQPA Safety Factor. The pre- and post-natal toxicology data base for propiconazole is complete with respect to current FQPA-relevant toxicological data requirements. Propiconazole was reviewed by an ad-hoc FQPA Committee (Ray Kent and Richard Keigwin, 5/18/98). The Committee recommended that, based on the available toxicity information, the FQPA factor be removed for purposes of these time-limited tolerances.

Propiconazole is not developmentally toxic in the rabbit. There is evidence from a 2- generation study that propiconazole is developmentally toxic in the rat; however, toxicity in offspring occurred at doses that were toxic to the parents. In the rat developmental toxicity study, doses of 90 mg/kg/day and above were developmentally toxic at maternally toxic doses. At the maternal LOAEL of 90 mg/kg/day there was minimal maternal toxicity consisting of rales (1/24) and decreased weight gain on gestation days 6-8. Developmental toxicity at 90 mg/kg/day consisted of a statistically increased significance of unossified sternebrae and increased (not statistically significant) incidences of rudimentary ribs and shortened or absent renal papillae. At the highest dose of 300/360 mg/kg, fetotoxic and maternally toxic effects were more severe.

Although there is some suggestion that fetotoxic effects may be more severe in developing rats than maternally toxic effects at the LOAEL of 90 mg/kg/day, the concern is not great enough to warrant departing from past decisions to remove the FQPA factor. Earlier FQPA Section 18 decisions to remove the factor were made for use of propiconazole on a variety of commodities.

Therefore, based on the above, HED concludes that the standard 100-fold uncertainty factor remain as is and that the FQPA factor of 10 be removed.

2. Endocrine Disrupter Effects. EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disrupter effects.

3. Cumulative Exposure. Propiconazole is a member of the triazole class of fungicides (G. Ware, The Pesticide Book, 4th Ed., 1994). Other members of this class include bitertanol, triadimenol, hexaconazole, penconazole, tebuconazole, diclobutrazol, myclobutanil, diniconazole, fenbuconazole, tetraconazole, cyproconazole and flusilazole.

HED does not have, at this time, available data to determine whether propiconazole has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of these tolerance actions, therefore, HED has not assumed that propiconazole has a common mechanism of toxicity with other substances.

EXPOSURES AND RISKS

In examining aggregate exposure, FQPA directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency looks at include drinking water (whether from groundwater or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor and/or outdoor uses). In evaluating food exposures, EPA takes into account varying consumption patterns of major identifiable subgroups of consumers, including infants and children.

1. From Food and Feed Uses:

Tolerances have been established (40 CFR 180.434) for the residues of propiconazole, (1-[[2-(2,*4*-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1*H*-1,2,4-triazole) and its metabolite determined as 2,4-dichlorobenzoic acid and expressed as parent compound, in or on a variety of raw agricultural and animal commodities at levels ranging from 0.05 ppm in milk to 60 ppm in grass, seed screenings.

Acute Risk (Acute RfD= 0.3 mg/kg/day)

The acute dietary risk (food only) does not exceed HED's level of concern. The HED DRES system was used for calculating acute dietary exposure. The analysis evaluates individual food consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS), and accumulates exposure to the chemical for each commodity. The acute dietary (food only) risk assessment used the Theoretical Maximum Residue Contribution (TMRC). The high-end exposure estimate is 0.01 mg/kg bwt/day. This exposure level utilizes 3.3% of the dietary (food only) acute RfD for females 13+ years (the only population subgroup of concern), and should be viewed as a conservative risk estimate. Refinement using anticipated residue values and percent crop-treated data in conjunction with Monte Carlo analysis, would result in a lower acute dietary exposure estimate.

Chronic Risk (Chronic RfD= 0.013 mg/kg/day)

The chronic dietary risk (food only) does not exceed HED's level of concern. The HED DRES system was used for calculating chronic dietary exposure. The analysis evaluates individual food consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS), and accumulates exposure to the chemical for each commodity. In conducting this chronic dietary risk assessment, HED has made partially refined assumptions. Corn, pineapples and peanuts, the subject RACs, will contain tolerance level residues. Corn is 6% crop treated, pineapple is 100% crop treated and peanuts is 1% crop treated. Some of the other commodities in this analysis contain tolerance level residues, and some contain anticipated residue estimates. In addition, some of the commodities in this analysis containing propiconazole residues are 100% crop treated and some are not.

The existing propiconazole tolerances (published, pending, and including the necessary Section 18 tolerance(s)) result in an Anticipated Residue Contribution (ARC) that is equivalent to the following percentages of the RfD:

Population Subgroup	ARC(mg/kg/day)	%RfD
U.S. Population (48 States)	0.0009	7%
Females 13+ Years, Nursing	0.0009	7%
Males 13+	0.00073	6%
Nursing Infants (<1 year old)	**0.00110**	**8%**
Non-Nursing Infants (<1 year old)	**0.0026**	**20%**
Children (1-6 years old)	**0.0017**	**13%**
Children (7-12 years old)	**0.0012**	**9%**
Western Region	0.00109	8%
Hispanics	0.0011	9%
Non-Hispanic Others	0.001	8%

The subgroups listed above are: (1) the U.S. population (48 states); (2) those for infants and children; (3) the other subgroups for which the percentage of the RfD occupied is greater than that occupied by the subgroup U.S. population (48 states) and (4) those groups of concern for drinking water assessment.

Cancer Risk:

Propiconazole has been classified as a Group C, possible human carcinogen, chemical by the HED Carcinogenicity Peer Review Committee (9/11/92). The committee recommended using the RfD approach for quantification of human risk. However, the RfD approach is identical to the chronic assessment. Therefore, a quantitative risk assessment using a cancer endpoint will not be done. Rather, the chronic risk assessment will be adequately protective for cancer risk as well as other chronic effects.

2. *From Drinking Water:*

Propiconazole is moderately persistent and moderately mobile to immobile in soil and aqueous environments. It has the potential to be transported with water, particularly in coarse-textured soils low in organic matter. Propiconazole's persistence indicates the potential to reach surface water with run-off or adsorbed to soil particles. There is no established Maximum Contaminant Level for residues of propiconazole in drinking water. No health advisory levels for propiconazole in drinking water have been established (EPA Clean Water Hotline, 11/2/98).

EFED used the SCI-GROW and Generic Expected Environmental Concentration (GENEEC) models to determine concentrations of pesticides in ground and surface water. EFED calculated the following Tier 1 Estimated EEC's for propiconazole.

TABLE 1: EEC CONCENTRATIONS FOR PROPICONAZOLE

Application Method	SCI-GROW (ug/L)	GENEEC Acute Peak EEC (ug/L)	GENEEC Chronic 56-day EEC (ug/L)
Ground/Aerial Application	0.0014	0.11	0.09

Notes:
These calculations are based on annual application rates from the Banner (EC), Banner GL, and Banner MAXX labels at a maximum single application rate of propiconazole at 0.885 lb ai/A at 14 day application intervals. The maximum annual application rate cannot exceed 7.08 lbs ai/A/year

3. *From Non-Dietary Uses:*

a. **Turfgrass and Ornamentals** -

In HED' *North Dakota, and Minnesota, and on Wheat in Kansas and by the USDA* (W. Cutchin et al. dated 7/2/97) it was stated that the Registration Division (RD) reported that there was no use of products containing propiconazole by homeowners. RD also stated that two sources reported usage by lawn care operators and landscapers. Based on information regarding acres-treated, between 3850 to 6725 households are estimated to be potentially treated with propiconazole. This represents between 0.004% to 0.007% of all households nationally. It should also be noted that according to the HED's Reference File System, formulations for lawns/turf and ornamental plants containing propiconazole are not registered for residential indoor or outdoor use. Therefore a risk assessment for turfgrass and ornamentals was not performed. Note that previous Section 18 assessments (Propiconazole on Blueberries in Maine, ID# 98ME01, 5/29/98) included risk assessments for turf use.

b. **Wood Preservation**

Propiconazole is currently registered for residential use as a wood preservative. Under current HED guidelines, these uses do not present a chronic exposure scenario, but may constitute a short- and/or intermediate-term exposure scenario.

Applicators

An exposure estimate and risk assessment was conducted for the application of Woodlife-P Wood Preservative (EPA Reg No 1409-65) using the DRAFT SOPs for Residential Exposure Assessments (12/18/97) and is summarized in **Table 2.** The following considerations and assumptions were used:

* Average daily dose (ADD) is based on the amount of active ingredient (ai) handled per day and not the exposure duration (i.e., a single painting event per day).

* The amount of the product handled per day is assumed to be 2 gallons.

* The density of formulation is not given on the label. Therefore, the density of water was assumed for converting volume in oz. to lb ai. One gallon of paint weighs approximately 10 lbs.

* Application Rates (ARs) used were derived from the label for Woodlife-P Wood Preservative as follows: **AR** = 0.005 (% ai) x 1 gallon (vol of can) x 10 lbs /1 gallon = **0.05 lb ai/can**

* Homeowner applicators are assumed to be wearing short pants, short sleeved shirt, and no gloves.

* The SOPs for Residential Exposure Assessments rely on high-end scenarios and should be considered conservative estimates. They are intended to represent Tier 1 assessments. If a Tier 1 assessment indicates a potential concern, a more detailed exposure assessment is warranted, possibly including chemical-specific or site-specific data.

* One of the variables used for assessing residential handlers exposure comes from the Pesticide Handlers Exposure Database (PHED). These units of exposure are considered to be central tendency values. When these PHED values are combined with the upper percentile of amount of the product handled per day and a bounding estimate of max application rate, the resulting estimates are considered to be central tendency to high-end estimates.

Short-term dermal and inhalation MOEs are 200 and 20,000, respectively. MOEs less than 100 exceed HED's level of concern.

Table 2. Residential Exposure and Risk Assessment for Application of Wood Preservation
DERMAL

Table 2. Residential Exposure and Risk Assessment for Application of Wood Preservation							
[1]AR (lb ai/can)	[1]N (cans/day)	[1]UE (mg/lb ai)	[2]AF	[2]BW (kg)	[3]ADD (mg/kg/day)	[4]NOAEL (mg/kg/day)	[5] Short- and Intermediate-term MOE
0.05	2	230	0.4	60	0.15	30	200
INHALATION							
[1]AR (lb ai/can)	[1]N (cans/day)	[1]UE (mg/lb ai)	[2]AF	[2]BW (kg)	[3]ADD (mg/kg/day)	[4]NOAEL (mg/kg/day)	[5] Short- and Intermediate-term MOE
0.05	2	0.284	1.0	60	0.00047	92.8	200,000

[1]AR = application rate, N = number of cans paint used per day, UE = PHED unit exposure ,
[2]AF = Absorption Factor , BW=body weight
[3]ADD = average daily dose (mg/kg/day) = [UE * AR * N* AF]/ BW
[4]NOAEL = Short- and Intermediate-Term No Observable Adverse Effect Level
[5]MOE = NOAEL/ADD

Postapplication

According to the Environmental Fate and Effects Division's Pesticide Fate One Line Summary Program, propiconazole has a vapor pressure of 4.2E-7 torr. Pesticides having vapor pressures less than 1E-4 torr are considered to be non-volatile and not readily aerosolized (DRAFT North America Free Trade Agreement Inhalation Exposure Waivers for Pesticides Guidance Document). Furthermore, exposure from contact with treated wood via dermal and oral routes are expected to be minimal . Therefore, HED determined that neither a quantitative exposure estimate or a risk assessment for postapplication exposure is needed.

DETERMINATION OF SAFETY FOR U.S. ADULT POPULATION AND INFANTS AND CHILDREN

1. Acute Aggregate Risk

The subpopulation of concern for acute risk is females 13 years and older only. The acute dietary (food only) risk does not exceed HED's level of concern. Using TMRC, HED concluded that the high-end exposure estimate is 0.01 mg/kg/day. This exposure level utilizes 3.3% of the dietary (food only) acute RfD for females 13 years and older. Acute drinking water levels of comparison (DWLOC) are summarized in **Table 3.** The acute DWLOC for females 13+ is 8,700 µg/L, which is substantially higher than the peak EEC of 0.11 µg/L provided by EFED. Therefore, the risk from acute aggregate exposure to propiconazole does not exceed HED's level of concern.

Table 3: Acute Drinking Water Levels of Comparison				
Population[1]	**Acute RfD (mg/kg/day)[2]**	**TMRC (food exposure mg/kg/day)**	**Max Water Exposure (mg/kg/day) [3]**	**DWLOC (ug/L)[4,5]**
Females 13+,nursing	0.3	0.01	0.29	8700

Notes:
1. Within each of these categories, the subgroup with the highest TMRC was selected.
2. Acute RfD = NOAEL/MOE = 30/100
3. Max water exposure = Acute RfD - Acute dietary food (from the DRES analysis).
4 .DWLOC = Max Water Exposure (mg/kg/day) *(kg body weight) ÷ (10^{-3} mg/μg)* (water consumed(L)/day)
5. HED Default body weight is 60 kg for Females 13+
6. HED Default Daily Drinking Rates are: 2L/day for Adults

2. Short-and intermediate-term aggregate risk

a. Short-and intermediate-term aggregate exposure takes into account chronic dietary food and water (considered to be a background exposure level) plus short- and intermediate-term residential uses. For propiconazole, the short and intermediate-term dermal NOAEL and acute dietary NOAEL were selected from the same developmental study.

When endpoints from multiple studies are selected from risk assessment, risks should only be aggregated if the endpoints (toxic effects) are the same and the multiple residential exposure scenarios have a reasonable chance of occurring together. In this case the dermal and inhalation endpoints do not have the same toxic effects. Therefore the MOE_{dermal} and $MOE_{inhalation}$ cannot be aggregated together. Furthermore, because the dermal exposure is the driving factor when considering exposure from residential uses (adults applying wood preservative), exposure via inhalation was not considered in the calculation for risk from short-and intermediate-term aggregate exposure (residential dermal exposure = 0.15 mg/kg /day and MOE of 200; inhalation exposure of 0.00047 with an MOE of 200,000). Therefore, using the HED Aggregate Risk Assessment Interim Guidance (presented to HED on 4/28/98 by M. Metzger) short- and intermediate term aggregate MOEs can be calculated as follows:

$$\text{Aggregate MOE} = \frac{1}{\frac{1}{MOE_{FOOD}} + \frac{1}{MOE_{WATER}} + \frac{1}{MOE_{\text{Residential DERMAL}}}}$$

b. MOEs can be calculated for dietary as well as residential exposures. However, there are no drinking water estimates (only estimates of EEC provided by EEFD). Assuming a minimum Aggregate MOE of 100, short- and intermediate term drinking water levels of comparison (DWLOC) were estimated by solving the following equations:

*Assuming that **Aggregate MOE = 100**, the previous equation was solved for the term "**MOE_{WATER}**" as follows:

$$\frac{1}{\frac{1}{MOE_{FOOD}} + \frac{1}{MOE_{WATER}} + \frac{1}{MOE_{DERMAL}}} = 100$$

$$\frac{1}{33{,}333} + \frac{1}{200} + \frac{1}{MOE_{WATER}} = \frac{1}{100}$$

$$\left[\frac{1}{33{,}333} + \frac{1}{200}\right] + \frac{1}{MOE_{WATER}} = \frac{1}{100}$$

$$\frac{1}{100} - \left[\frac{1}{33{,}333} + \frac{1}{200}\right] = \frac{1}{MOE_{WATER}}$$

$$\frac{1}{\frac{1}{100} - \left[\frac{1}{33{,}333} + \frac{1}{200}\right]} = 200 = MOE_{water}$$

** After calculating the value for the term "MOE_{WATER}", **the short-term water exposure** was " back-calculated" as follows:

$$MOE_{WATER} = \frac{\text{ACUTE Dietary NOAEL}}{\text{Short- and Intermediate Term Water Exposure}}$$

$$\text{Short-Term Water Exposure} = \frac{30 \text{ mg/kg/day}}{200} = 0.15 \text{ mg/kg/day}$$

*** Using the **Short-and Intermediate-Term Water Exposure** value from the equation above, the Short-term DWLOC was calculated as follows:

$$\text{DWLOC}(\mu g/L) = \frac{\text{Short-Term Water Exposure (mg/kg/day) x Body Wt (kg)}}{\text{(1E-3 mg/}\mu g\text{) x Daily Drinking Rate (L/day)}}$$

c. MOEs for dietary, dermal residential exposures, as well as short-and intermediate-term aggregate drinking water DWLOCs, are summarized in **Table 4**. The short-and intermediate-term DWLOC is 4,500 ug/L which is higher than average surface water EEC (0.09 ug/L) provided by EFED. Therefore, short- and intermediate-term aggregate risk does not exceed HED's level of concern.

TABLE 4: DWLOCs based on Short- and Intermediate-Term Aggregate Risk			
		Children[1]	US Population[2]
	Acceptable Short-Term Aggregate MOE	N/A	100
FOOD ONLY	ACUTE Dietary NOAEL (mg/kg/day)		30
	CHRONIC Food Exposure (mg/kg/day)		0.0009
	Food MOE		**33,000**
RESIDENTIAL DERMAL	Short- and Intermediate-Term Dermal NOAEL (mg/kg/day)		30
	ADD Dermal Exposure (mg/kg/day)		0.15
	Dermal MOE		**200**
DRINKING WATER ONLY	ACUTE Dietary NOAEL (mg/kg/day)		30
	Short- and Intermediate-Term Water Exposure (mg/kg/day)		0.15
	Short-term Aggregate DWLOC (ug/L)		**4,500**
	Average Surface Water EEC (ug/L)	0.09	

[1]Acute Dietary NOAEL applies to females 13+ only. Estimates of residential exposures include adults only. Therefore, the short- and intermediate aggregate risk does not apply to children

[2]Values are for Females 13+

3. Chronic Aggregate Risk

The chronic dietary (food only) risk does not exceed HED's level of concern. HED has calculated that dietary exposure to propiconazole from food will utilize 7% of the RfD for the U.S. population, 20 percent of the RfD for non-nursing infants less than one year old, 8 percent for nursing infants less than one year old, and 9 percent for children 7-12 years old. HED generally has no concern for exposures below 100 percent of the RfD because the RfD represents the level at or below which daily aggregate exposure over a lifetime will not pose appreciable risks to human health.

Chronic drinking water levels of comparison (DWLOC) are summarized in **Table 5.** The subgroup with the lowest chronic DWLOC is non nursing infants (< 1 year) at 100 µg/L which is substantially higher than the GENEEC 56-day EEC of 0.09 µg/L provided by EFED. Therefore, HED concludes with reasonable certainty that exposure to propiconazole in drinking water is less than our level of concern.

Table 5. Chronic Drinking Water Levels of Comparison

Population[2]	RfD (mg/kg/day)[3]	ARC (food exposure mg/kg/day)	Max Water Exposure (mg/kg/day) [4]	DWLOC (ug/L)[5,6]
US Population	0.013	0.000888	0.012112	420
Males 13+	0.013	0.00073	0.01227	430
Females 13+,nursing	0.013	0.000913	0.012087	360
non-nursing infants < 1 yr	0.013	0.002654	0.010346	100

Notes:
2. Within each of these categories, the subgroup with the highest ARC was selected.
3. RfD = 1.25 mg/kg/day ÷100
4. Max water exposure = RfD - Chronic dietary food (from the DRES analysis) - RfD.
5. DWLOC = Max Water Exposure (mg/kg/day) * (kg body weight)÷ (10^{-3} mg/μg)* (water consumed(L)/day)
6. HED Default body weights are: General US Population = 70 kg; Females 13+ = 60 kg; Infants/children = 10 kg
7. HED Default Daily Drinking Rates are: 2L/day for Adults and 1L/day for infants/children

Under current HED criteria, the registered non-dietary uses of propiconazole do not constitute a chronic exposure scenario. Therefore, HED concludes that there is a reasonable certainty that no harm will result from chronic aggregate exposure to propiconazole residues.

DETERMINATION OF CANCER RISK

Propiconazole has been classified as a Group C, possible human carcinogen, chemical by the HED Carcinogenicity Peer Review Committee (9/11/92). The Committee recommended using the RfD approach for quantification of human risk. The RfD approach is identical to the chronic assessment. Therefore, a quantitative risk assessment using a cancer endpoint will not be done. Rather, the chronic risk assessment will be adequately protective for cancer risk as well as other chronic effects. **HED's drinking water level of comparison from cancer is 420 ug/L for the US Population.** EFED's chronic EEC, GENEEC 56-day, value of 0.09 ug/L is lower than the cancer DWLOC for the US population (420 ppb). Therefore, HED concludes with reasonable certainty that exposure to propiconazole in drinking water is less than our level of concern.

DETERMINATION OF SAFETY TO OCCUPATIONALLY EXPOSED WORKERS

1. ***Occupational Exposure***: Occupational exposure assumptions and estimates of exposure are summarized in **Tables 6 and 7**, respectively. Worker exposure estimates are based on surrogate data from the Pesticide Handlers Exposure Database (PHED), as presented in the PHED Surrogate Exposure Guide (PSEG, 5/97). Short-and intermediate-term dermal MOEs ranged from 5,000 for aerial mixer/loader (all liquid formulations) to 50,000 for ground mixer/loaders. Short and intermediate-term inhalation MOEs range from 120,000 for aerial mixer/loaders to 6,000,000 for mixer/loaders (water soluble bags). Therefore, MOEs calculated do not exceed HED's level of concern for occupationally exposed workers.

Table 6. Occupational Exposure Assumptions	
PARAMETER	**ASSUMPTION**
Pesticide Handlers Exposure Database (PHED), Version 1.1, (5/97)	Mixer/Loader [**all liquid formulations**, open mixing]: Dermal = **23** µg/lb ai handled **(high Confidence Data)** Inhalation = **1.2** µg/lb ai handled **(high Confidence Data)** PPE: single layer of clothes with gloves
	Mixer/Loader [**water soluble bags**]: Dermal = **9.8** µg/lb ai handled **(low confidence Data)** Inhalation = **0.106** µg/lb ai handled **(Low Confidence Data)** PPE: single layer of clothes with gloves
	Applicator - Ground [**Liquid , Ground Boom, Open Cab**]: Dermal = **14** µg/lb ai applied **(Medium Confidence Data)** Inhalation = **0.74** µg/lb ai handled **(High Confidence Data)** PPE: single layer of clothes with gloves
	Applicator - Air [**Fixed Wing, Liquid Formulations Enclosed Cab**]: Dermal = **5.0** µg/lb ai applied **(Medium Confidence Data)** Inhalation = **0.07** µg/lb ai handled **(Medium Confidence Data)** PPE: single layer of clothes without gloves
Percent Absorption	Dermal: **40** % (dermal study) Inhalation: **100%** (default)
Application Type	**ground and air**
Maximum Application Rate	**0.113** lb ai/A
Acres Treated/Day (HED Default)	Ground: **80** acres, Air: **350** acres

Table 7. Occupational Exposure and Risk Assessment

WORKER	DERMAL		INHALATION	
	ADD (mg/kg/day)	**SHORT & INTERMEDIATE-TERM MOE**	**ADD (mg/kg/day)**	**SHORT & INTERMEDIATE-TERM MOE**
MIXER/LOADERS				
Water Soluble Bags Ground Mixer/loader	0.0006	50,000	0.000015	6,000,000
All Liquid Formulations Ground Mixer/Loader	0.0014	21,000	0.00018	515,000
Water Soluble Bags Aerial Mixer/Loader	0.0026	12,000	0.000066	1,400,000

Table 7. Occupational Exposure and Risk Assessment				
All Liquid Formulations Aerial Mixer/loader	0.006	5,000	0.0008	120,000
APPLICATOR				
Ground Applicator	.00084	36,000	.00011	840,000
Aerial Applicator	.0013	23,000	.000046	2,000,000

Notes:
Application Rate = 0.113 lb/ai/A
Average Daily Dose (ADD) = [PHED unit exposure (mg/lb ai) x % absorption x application rate (lb ai/A) x acres treated/day] ÷ body weight (60 kg)
MOE = NOAEL/ADD
Short- and Intermediate Term Dermal NOAEL= 30 mg/kg/day
Short- and Intermediate Term Inhalation NOAEL= 92.8 mg/kg/day

2. ***Post-application***: Exposure during postapplication activities was estimated using the input parameters summarized in **Table 8.** The following considerations and assumptions were used when selecting these parameters:

- An initial dissipation rate of 20% (0.2) and 10% (0.1) each day after use. These are default values established by HED's Science Advisory Council for Exposure.

- Transfer coefficients (Tc) of 10,000 to 4,000 cm^2/hr for corn, 4,000 cm^2/hr for peanuts, and 2,500 to 1,000 cm^2/hr for pineapples were used. These are also default values established by HED's Science Advisory Council for Exposure.

Table 8: Input Parameters for Estimating Postapplication Exposure and Risk	
Application rate (lb ai/A)	0.113
Percent DFR after initial treatment	0.2
Percent dissipation per day	0.1
Transfer Coeffienct cm2/hr (high range)	10,000
Transfer Coefficient cm2/hr (low range)	1,000
Hours worked per day (hrs/day)	8
Body Weight (kg)	60
Dermal Absorption (ranges from 0 to 1.0)	.4
Years worked per lifetime	35
Years per lifetime	70

A summary of the estimated exposures during postapplication activities are summarized in **Table 9.** The short-term MOE for postapplication exposure activities for the worst case scenario (i.e. harvesting corn) is 220 immediately after application and 250 one day after application. The intermediate-term MOE immediately after application is 700 and 800 one day after application. Therefore these MOEs do not exceed HED's level of concern (MOE ≥ 100) for postapplication exposure and the 24-hour restrictive entry interval (REI) that appears on the label is adequate.

Table 9; Postapplication Exposure for Propiconazole

DAT	DFR (ug/cm2)	ADD (mg/kg/day)		SHORT- and INTERMEDIATE TERM MOE	
		low	high	low	high
0	.253	0.014	0.135	2,220	222
1	0.228	0.012	0.122	2,467	247

Notes:
DAT = Days after treatment
DFR = Dislodgeable Foliar Residue
ADD = Average Daily Dose
MOE = NOEL/ADD (short- and intermediate term NOEL = 30)

3. ***Restrictive Entry Interval (REI)***: RD forwarded a Notice of Pesticide Registration for propiconazole to HED. The notice states that this product (TILT 45W, EPA Reg No 100-780) is conditionally registered provided that the REI be changed to 12-hours because this is the appropriate time period for products bearing the signal word "Caution". Acute toxicity information is available for the technical. The Worker Protection Standard (WPS) requires a **24-hour** REI if the technical material has acute dermal, eye, or skin irritation toxicity designated in Toxicity Category II. Since the technical has an acute toxicity category of II, **RD should insure that the appropriate 24-hour REI, as required by the WPS, appears on the label.**

OTHER CONSIDERATIONS

Metabolism in Plants and Animals

1. The nature of the residue in plants and animals is adequately understood. The residues of concern are propiconazole and its metabolites determined as 2,4-dichlorobenzoic acid and expressed as parent compound (as specified in 40 CFR 180.434).

Analytical Enforcement Methodology

2. Adequate enforcement methodology (GC/ECD) is available to enforce the tolerance expression. Analytical methodologies for the determination of propiconazole and its metabolites in plant and animal commodities (Ciba-Geigy Analytical Methods AG-454, MRID# 434342-01 and AG-517, respectively) have been successfully validated by the Agency's Analytical Chemistry Laboratory, and have been approved for publication in PAM II for enforcement purposes (PP#4F4321, DP Barcode: D210252, W. Cutchin, 4/13/95).

Magnitude of the Residues

3. a. Corn: The currently established time-limited tolerances are appropriate for both plant and animal commodities (Memo, M. Flood, PP#8F3674, 5/6/93). [Note that according to the latest CFR (July 1998), the animal commodity tolerances are no longer time-limited.]

   b. Peanuts: Residue data support the time-limited tolerances of 20, 1, and 0.2 ppm for residues of propiconazole and metabolites in/on peanut hay, peanut hulls, and peanuts, respectively. The storage stability study which was submitted cast doubt on the validity of the analyses. The study was unacceptable and the registrant was required to repeat it (Memo, M. Flood, PP#8F3654, 11/8/93). The required storage stability study is outstanding.

   c. Pineapple: The currently established time-limited tolerances are appropriate (Memo, M. Flood, PP#8F3674, 5/6/93).

Rotational Crop Restrictions

4. Soybeans may be planted as a double crop following a cereal crop which has been treated with Tilt 45W. Do not rotate to any crop intended for food, grazing, or any component of animal feed or bedding within 105 days of Tilt application, unless the crop appears on the product label.

International Residue Limits

5. There are no CODEX, Canadian, or Mexican Maximum Residue Limits (MRL) for propiconazole on corn, peanuts, or pineapple. Thus, harmonization of tolerances is not an issue for these tolerancex extension requests.

ADDITIONAL INFORMATION

Reregistration Status. Propiconazole is a list C chemical for reregistration. The Reregistration Eligibility Document has not been scheduled for completion; however, it may be a candidate for the next fiscal year.

Attachments: DRES Runs: Acute/Chronic (Cancer): B. Steinwand, 3/11/98
Amendment Tier 1 Drinking Water Assessment for Propiconazole, James Hetrick, 11/19/98.
Ad-hoc FQPA - Ray Kent and Richard Kiegwin, 5/18/98
cc with Attachments: M. Collantes, Steve Weiss, D. Dotson, S.Williams, HED Reading file - B. Steinwand

cc without Attachments:

ATTACHMENTS