RISK ASSESSMENT FOR
SECTION 3 USE OF
PENDIMETHALIN PRODUCT PROWL 3.3 EC
IN CALIFORNIA
FOR THE CONTROL OF BROADLEAF WEEDS AND GRASSES ON
BEARING CITRUS CROPS

California Environmental Protection Agency
Department of Pesticide Regulation
830 K Street
Sacramento, CA 95814

February 17, 1999

I. INTRODUCTION

American Cyanamid Company requested a label amendment to Prowl 3.3 EC herbicide product for the control of broadleaf weeds and grasses on bearing citrus crops. Prowl 3.3 EC contains 37.4% active ingredient (a.i.) pendimethalin, N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzeneamine. The proposed use on bearing citrus is 5.94 lbs a.i. per acre per year with a 1-day pre-harvest interval (PHI). Based in the residue field trial data, DPR proposed a tolerance of 0.1 ppm for pendimethalin and its metabolites in and on citrus fruits.

A Reregistration Eligibility Decision (RED) document for pendimethalin was completed by USEPA in 1997 (USEPA, 1997). The health risk of pendimethalin was evaluated in accordance with the 1996 Food Quality Protection Act (FQPA). It concluded that all uses would "not cause unreasonable risks to humans or the environment and therefore, all products were eligible for reregistration". However, mitigation measures for occupational/ residential handlers and children were required. USEPA required a reduction in the maximum application rate for residential and recreation area turf (down from 3 to 2 lbs a.i. per acre), the use of personal protective equipment (added chemical resistant gloves), and longer restricted-entry intervals (extended from 12 to 24 hours) (USEPA, 1997). Additional data for product chemistry, residue chemistry, environmental fate, and occupational/residential exposures were also required before the reregistration of all products (USEPA, 1997).

In 1997, USEPA established time-limited tolerances for pendimethalin residues in or on fresh mint hay (0.1 ppm) and mint oil (5.0 ppm) in connection with granting an emergency exemption under Section 18 of the Federal Insecticide, Fungicide, and Rodenticide Act (Fed Reg, 1997). This authorized the use of pendimethalin on mint in Idaho, Oregon, South Dakota, and Washington. These mint time-limited tolerances were subsequently extended to May 31, 1999 (Fed Reg, 1998).

This document contains a health risk assessment of the proposed pendimethalin use on citrus. For consistency, this assessment relies mainly on the toxicological profile, and as an addition to the current use, as presented in the 1997 RED and includes the use on mint. It should be noted that USEPA did not evaluate the risk from acute exposures as it was determined that there were "no acute toxicological endpoints of concern". An assessment of the acute exposure is included in this assessment.

II. CHEMICAL PROFILE

Common Name: PENDIMETHALIN
CAS Number(s): 40487-42-1
EPA PC Code(s): 108501
Synonym(s)
3,4-DIMETHYL-2,6-DINITRO-N-(1-ETHYLPROPYL)-BENZENAMINE;
2,6-DINITRO-N-(1-ETHYL PROPYL)-3,4-XYLIDINE;
N-(1-ETHYLPROPYL)-3,4-DIMETHYL-2,6-DINITRO-BENZENAMINE;
N-(1-ETHYLPROPYL)-2,6-DINITRO-3,4-XYLIDINE; PROWL; STOMP;
3,4-DIMETHYL-2,6-DINITRO-N-(1-ETHYLPROPYL)ANILINE
Chemical Formula: $C_{13}H_{19}N_3O_4$
Molecular weight: 281.3

II.A. Physical and Chemical Properties (DPR database; American Cyanamid Company)

Physical appearance:	orange-yellow crystalline solid
Solubility (@25°C):	2.75×10^{-5} g/100 ml water
	6.1 g/100 ml propanol
	11.2 g/100 ml n-heptane
	161.0 g/100 ml acetone
Vapor pressure (mm Hg):	9.40×10^{-6} (@25°C)
Henry's Law constant:	34.18 atm $m^3 g.mol^{-1}$
Octanol-water partition coefficient (K_{ow}):	1.52×10^5
Hydrolysis ½ life:	28 days
Aqueous photolysis ½ life:	60 days

II.B. Use

Pendimethalin is a herbicide used on many food, feed, and non-food crops. It is also used in aquatic rice culture and in nonagricultural, residential outdoor weed controls, such as grounds plantings, ornamentals, and turf grass (e.g., residential, golf course, landscape, sod farms). According to the most recent published data on pesticide use in California, approximately 431,000 pounds was used during 1995 (DPR, 1996). The uses on cotton, landscape maintenance, garlic, and almond were above 10,000 pounds. These uses respectively constituted approximately 67%, 9%, 6%, and 4% of the total statewide use in 1995.

II.C. Metabolites

USEPA (1997) identified two significant metabolites in plants: 1) 3,5 -Dinitrobenzyl alcohol (or, 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dimitrobenzyl alcohol), and 2) 2,4-Dinotrobenzyl alcohol (or, 3-[(1-ethylpropyl)amino]-6-methyl-2,4-dinitrobenzyl alcohol). The tolerance for pendimethalin in agricultural commodities included both the parent compound and these two metabolites.

USEPA (1997) determined that there was no reasonable expectation of finite residue of concern in animals. Therefore, tolerances in livestock commodities were not needed.

III. TOXICOLOGICAL PROFILE

III.A. Acute Toxicity

The acute toxicity categories as determined by DPR for the various products of pendimethalin are presented in Table 1.

Table 1. Acute toxicity categories of pendimethalin - DPR database.

Products[a]	Oral Toxicity		Dermal Toxicity		Inhalation Toxicity	
	LD_{50}	Category	LD_{50}	Category	LD_{50}	Category
Stomp WDG	>5000 mg/kg	IV	>2000 mg/kg	III	N.S.[b]	
Stomp 3.3 EC	3956 mg/kg	III	>2000 mg/kg	III	>5.35 mg/l	IV
Pendulum 2G	>5000 mg/kg	IV	>2000 mg/kg	III	N.S.[b]	

a/ Stomp WDG is an alternate name of Prowl 60% DG

b/ Data not submitted.

In either the 1997 RED or assessing the time-limited tolerance for mint, USEPA determined that there were no toxicological endpoints of concern. Therefore, no risk assessment for acute toxicities was conducted by USEPA.

In a rabbit teratology study (Wolfe, 1982) submitted to DPR for the fulfillment of data requirements for pesticide registration, increased incidences of anorexia and adipsia were noted in the dams at 30 mg/kg/day during the treatment period (day 5 through 18 of gestation). In addition, during the treatment periods, three rabbits died at 30 mg/kg/day and one rabbit died at 60 mg/kg/day (highest dose tested) while no death occurred at the control and 15 mg/kg/day (lowest dose tested). Unfortunately, the day or time at which clinical signs and death first occurred was not specified in the report. The NOEL based on these maternal toxicities was 15 mg/kg/day. This NOEL was comparable to the NOEL of 10 mg/kg/day for short- and intermediate- term toxicity determined by USEPA (see next section). The NOEL of 15 mg/kg/day was used to assess the risk of acute exposures.

III.B. Short- and Intermediate-term Toxicity

USEPA (USEPA, 1997; Fed Reg, 1997) established a NOEL of 100 ppm in the diet (10 mg/kg/day) based on a 56-day thyroid function study (Fischer, 1993) and a 14-day intrathyroidal metabolism study (DeVito and Braverman, 1993) in rats. At the end of a 28-day exposure to the LOEL of 500 ppm (31 mg/kg/day), the statistically significant ($p<0.05$) changes in serum chemistry included: decreases in total serum T4 (38%), reverse T3 (25%) and total free T4 (28%), and an increase in the percent free T3 (13%). Histopathological observations included increased follicular cell height (40%) and decreased colloid areas (37%). Some of these effects were detected at 3 days of exposure, the earliest point of measurement in this time course study.

III.C. Chronic Toxicity

The predominant target of pendimethalin toxicity is the thyroid gland. USEPA (USEPA, 1997; Fed Reg, 1997) established a NOEL of 100 ppm in the diet (10 mg/kg/day) based on the aforementioned 56-day thyroid function study (Fischer, 1993), the aforementioned the 14-day intrathyroidal metabolism study (DeVito and Braverman, 1993), and a 92-day thyroid function study (Fischer, 1991). As mentioned in the previous section, the endpoints for thyroid toxicities at the LOEL of 500 ppm (31 mg/kg/day) included changes in serum chemistry measurements and histopathology.

The RfD of 0.1 mg/kg/day was established based on the NOEL of 10 mg/kg/day and applying an uncertainty factor of 100 to account for the potential of a 10-fold higher human sensitivity than laboratory animals on a per body weight basis, and a 10-fold inter-individual variation of sensitivity within human populations.

III.D. Oncogenicity

Increased incidences of thyroid follicular cell adenomas occurred in male and female rats that received a lifetime exposure to pendimethalin in the diet. No evidence of oncogenicity was noted in two 18-month oncogenicity studies in mice. No evidence of mutagenicity was indicated in mammalian somatic and germ cells (USEPA, 1997). USEPA classified pendimethalin as a Group C carcinogen, "possible human carcinogen". The Office of Pesticide Program (OPP) determined that the lack of mammalian mutagenicity and the available mechanistic studies for thyroid tumors supported a non-linear approach to cancer risk assessment. Thus, risks for both non-oncogenic and oncogenic endpoints were assessed using the RfD approach based on thyroid hormonal endpoints established for the subchronic and chronic NOEL of 10 mg/kg/day.

III.E. Developmental Toxicity

USEPA concluded that no developmental effects occurred in both teratology studies in CD rats (Wolfe, 1979) and in rabbits (Wolfe, 1982) (USEPA, 1997). Thus, there was no developmental toxicity at dose levels lower than that which resulted in maternal toxicities.

III.F. Reproductive Toxicity

Based on a 2-generation reproductive toxicity study in rats (Irvine and Boughton, 1990), USEPA determined that the reproductive toxicity NOEL was 2,500 ppm in the diet (172 and 216 mg/kg/day in males and females, respectively). This was based on a statistically significant decrease in pup weight during lactation at the LOEL of 5,000 ppm (346 and 436 mg/kg/day in males and females, respectively). USEPA concluded that "a parental NOEL could not be definitely determined" (USEPA, 1997).

IV. EXPOSURE ASSESSMENT

IV.A. Dietary Exposures

Two sets of dietary exposure were presented in this section. The first set (Set I) was an assessment of the proposed tolerance of 0.1 ppm in citrus crops. Citrus crops included in the dietary analysis were: grapefruit, kumquat, lemon, lime, orange, tangelo, and tangerine. The second set (Set II) included not only the proposed tolerance for citrus, but also all the commodities for which tolerances currently exist, and the time-limited tolerance in fresh mint hay (0.1 ppm) and mint oil (5.0 ppm) under FIFRA Section 18 registration. Except for the tolerance of 0.05 ppm in rice, all other existing tolerances are at 0.1 ppm. However, conforming to the analysis presented in the RED (USEPA, 1997), the following assessment assumed the residue of 0.1 ppm for rice as well as using the onion (dry bulb) tolerance for shallots (dry bulb only).

The dietary exposure assessments presented in this document differed from the assessment presented in the RED (USEPA, 1997) and for evaluating the time-limited tolerance for mint on three key aspects. Firstly, instead of the DRES program used by USEPA, the Technical Assessment Systems (TAS) software programs were used in this dietary exposure assessment. Secondly, instead of the 1977-78 dietary consumption used by USEPA, the three year combined data (1989-90, 1990-91, 1991-92) from the USDA Continuing Surveys of Food Intakes by Individuals (CSFII) were used in this assessment. Lastly, this assessment included an acute exposure which was not conducted by USEPA.

Acute and chronic dietary exposures were estimated for 27 population subgroups based on geographic locations (i.e., 5 U.S. regions), seasons, age (i.e., infants, children, teens, adults, child-bearing age, seniors), gender, and physiological statuses (i.e., nursing, pregnant). Data for 17 representative groups were presented in Table 2. The acute exposure represented the 95th percentile of exposure among the "users" (surveyed individuals who consumed at least one of the listed commodities). For the citrus crops alone, the number of "users" for nursing and non-nursing infants (<1 yr) in the survey database was low, consisting only 2 and 13% of the total surveyed individuals in each respective population subgroup. The "users" for the remaining population subgroups ranged between 37% and 55% of the surveyed population subgroups. When all label-approved commodities were included in the analysis, the "users" were generally above 99% of the surveyed individuals in each population subgroup, with the exception of 55% for the nursing infants. Chronic exposure represented the average value, instead of the high end, of all surveyed individuals in each population subgroup.

As shown in Table 2, the exposure on a body weight basis is generally higher for infants and children (1-6 years old) than for other population subgroups. Since the acute exposure represented the high end (95th percentile) of distribution for users only, the difference between Set I and Set II for the acute exposure was not as distinct as for the chronic exposures. The highest acute exposure was 1.56 ug/kg/day (non-nursing infants) for the citrus crops at the proposed tolerance, and 2.08 ug/kg/day (children 1-6 yrs) for all commodities combined. These values were nearly 50% higher than the highest short- and intermediate-term exposure of 1.4 ug/kg/day (non-nursing infants) presented in the RED. The exposures from citrus commodities contributed to approximately 11-33% of the chronic exposures from all commodities. The respective highest chronic exposures for Set I (citrus only) and Set II (all commodities) were 0.17 and 0.87 ug/kg/day (children 1-6 years old).

The acute exposure levels were also used for assessing the risk of short- and intermediate-term exposures (defined by USEPA as more than 1 day) especially since changes in some of the thyroid toxicity endpoints at the NOEL of 10 mg/kg/day occurred at the earliest measurement of 3 days after the exposure.

The use of tolerances in this Theoretical Maximum Residue Contribution (TMRC) assessment for all commodities was an initial tier of exposure estimation. Since the probability for all commodities all at the tolerance is extremely unlikely, the TMRC approach tends to overestimate the exposures. Nevertheless, a more time-consuming refinement assessment based on the anticipated residues was not conducted since the TMRC analysis did not show significant risk (e.g., exceeding 100% RfD).

VI.B. Drinking Water Exposures

No maximum concentration level (MCL) or Health Advisories (HAs) were established for pendimethalin and/or its significant degradation products in the drinking water. Because of the high soil adsorption and low water solubility, the potential for surface water runoff and groundwater leaching is low. USEPA's limited monitoring database showed that the highest detected residue was 0.9 ppb in the ground water and 17.6 ppb (USEPA, 1997; Fed Reg, 1997) in the surface water (USEPA, 1997). Using the highest detected level of 17.6 ppb and the default water consumption of 1 liter per day for a 10 kg child, the estimated exposure from drinking water was 1.8 ug/kg/day. It is unlikely that the use on citrus will substantially increase the levels detected in the drinking water. It was recognized that future monitoring of drinking water sources was needed to ascertain the levels of risk from drinking water (USEPA, 1997).

Table 2. Acute and chronic dietary exposures to pendimethalin

Population Subgroups[a]	Acute Exposure[b] (ug/kg/day)		Chronic Exposure[c] (ug/kg/day)	
	Set I[d] (citrus)	Set II[e] (all)	Set I[d] (citrus)	Set II[e] (all)
U.S. Pop., all seasons	0.64	1.13	0.071	0.41
Hispanics	0.82	1.24	0.083	0.42
Non-Hispanic Whites	0.59	1.07	0.067	0.40
Non-Hispanic Blacks	0.77	1.31	0.080	0.45
Non-Hispanic others	0.70	1.25	0.093	0.45
Infants (<1 yr), nursing	1.36	0.72	0.083	0.25
Infants (<1 yr), non-nursing	1.56	1.80	0.083	0.76
Children; 1-6 yrs	1.42	2.08	0.170	0.87
Children; 7-12 yrs	0.77	1.43	0.099	0.63
Females 13-19 yrs, NP, NN	0.50	0.92	0.054	0.37
Females 20+ yrs, NP, NN	0.46	0.75	0.060	0.30
Females 13+ yrs, P, NN	0.60	0.72	0.060	0.30
Females 13+ yrs; N	0.47	0.89	0.074	0.38
Females 13-50 yrs	0.48	0.80	0.055	0.31
Males 13-19 yrs	0.56	1.18	0.061	0.45
Males 20+ yrs	0.40	0.78	0.049	0.32
Seniors; 55+ yrs	0.43	0.73	0.069	0.31

a/ "Non-Hispanic others": Non Hispanic who are not white or black. "NP": not pregnant. "NN": not nursing. "P": pregnant. "N": nursing. "Females 13-50 yrs": women of child-bearing age.
b/ The exposures represented the 95th percentile of the "users" (those who reported to consume at least one commodity included in the analysis).
c/ The exposure represented the average exposure of all surveyed individuals.
d/ Set I: The exposure from citrus crops at the proposed tolerance of 0.1 ppm.
e/ Set II: The exposure from all label-allowed commodities at the tolerance.

IV.C. Residential Exposures (USEPA, 1997; Table 6 and 7)

USEPA determined that there was no chronic residential exposure. The RED presented the Daily Absorbed Dose (DAD) for short- and intermediate-term exposures for homeowner applications (mixing/loading/application) based on a 10% dermal absorption factor. The DADs were 0.0003 mg/kg/day for using backpack sprayer and 0.013 mg/kg/day for using low pressure handwand (RED, Table 6). The DADs for post-application exposures to residential turf were estimated for various time after lawn treatment (2 hours to 3 days) and two application rates (2 and 3 lbs per acre), using the default body weight of 17 kg for a 3-6 years old child. The highest DAD was 0.14 mg/kg/day 2 hours after lawn treatment at 3 lbs per acre (RED, Table 7).

DPR determined that the use of citrus would not increase the residential exposure.

VI.D. Occupational Exposures (USEPA, 1997; RED Table 6, 8 and 9)

USEPA (1997) identified 13 major occupational exposure scenarios for mixing/loading, and applying products containing pendimethalin. The exposure for post-application workers (e.g., cultivating, irrigating, other re-entry tasks) was also assessed. The Daily Absorbed Dose (DAD) for short- and intermediate-term exposures presented in the RED included the absorbed dose from inhalation exposure (assuming 50% inhalation absorption) when it is greater than 5% of the dermal DAD. The default body weight was 70 kg for an adult. Various assumptions were made in the exposure calculations, such as: areas of application per day, application conditions (e.g., enclosed cockpits for aerial applications), frequency of (e.g., days per week), and patterns (e.g., days of continuous exposure, application settings per year). It was concluded that no chronic occupational exposures exist. Therefore, only the risk of intermediate-term exposure was evaluated.

The exposures of handlers were estimated based on the Pesticide Handler's Exposure Database (PHED), Version 1.1. Baseline exposures represented long pants, long sleeve shirts, no gloves, open mixing/loading, enclosed cockpit, and open cab tractor. The DADs for all classes of handlers ranged from 0.003 mg/kg/day (loading granulars and for solid broadcast application and the spreader) to as high as 6.56 mg/kg/day (mixing/loading liquid for aerial applications and irrigation systems) (RED Table 6, USEPA, 1997).

The DADs for the post-application exposure were estimated based on a published study for 5 different chemicals (USEPA, 1997). The two occupational scenarios included in the RED were: golf course turf maintenance and sod farm turfgrass harvesting. The estimated DAD for golf course maintenance was 0.003 mg/kg/day (2 hours after treatment) (RED Table 8). The highest DAD for sod farm workers was 0.069 mg/kg/day (2 hours after treatment) (RED Table 9). USEPA recognized that these two scenarios may not represent all conditions under which post-application exposures occurred.

DPR estimated the Absorbed Daily Dose (ADD) for mixer/loader and applicators for the new use on citrus, using the PHED, Version 1.1 (PHED, 1998). The estimates were based on an application rate of 5.94 lbs per acre, 80 acres of application per day, a 76 kg worker wearing long pants, long sleeve shirts, shoes, socks and gloves, and using the same 10% dermal absorption factor. The ADD was 0.014 mg/kg/day for a mixer/loader and 0.009 mg/kg/day for an applicator. These ADDs were used to evaluate the risk of acute exposures. The Seasonal Absorbed Daily Dose (SADD), comparable to the DAD in the RED (USEPA, 1997), was subsequently estimated by a factor of 5/7 (5 days per week of exposure). The estimated SADD was 0.01 mg/kg/day for a mixer/loader and 0.064 mg/kg/day for an applicator. The SADDs were used to assess the risk of intermediate-term exposures.

DPR determined that there was no harvester's exposure associated with the proposed use on citrus because pendimethalin would be incorporated into the soil after application.

V. RISK CHARACTERIZATION

Risks to pendimethalin exposure were characterized in terms of Margin Of Exposure (MOE). MOE is calculated as the ratio of the NOEL to the exposure.

V.A. Dietary

The MOEs for acute dietary exposure were calculated based on the acute NOEL of 15 mg/kg/day (maternal toxicities of clinical signs and death in pregnant rabbits at the LOEL of 30 mg/kg/day). The MOE at the highest acute exposure of 2.08 ug/kg/day (Table 2, Acute Exposure, Set II, children 1-6 years) was >7,000.

The MOEs for short- and intermediate-term exposure were calculated based on the NOEL of 10 mg/kg/day (effects on thyroid functions in rats at the LOEL of 31 mg/kg/day). Since the thyroid effects occurred in rats at the earliest measurement time of 3 days after the treatment, the acute dietary exposures were used as a conservative estimate for this exposure scenario. The MOE at the highest exposure of 2.08 ug/k/day was >4,900. This exposure level was 2% of the RfD of 0.1 mg/kg/day.

The MOEs for chronic dietary exposure were calculated based on the NOEL of 10 mg/kg/day (effects on thyroid functions in rats at the LOEL of 31 mg/kg/day). As presented in Table 2, the chronic exposure of 0.85 ug/kg/day for children 1-6 years old was the highest among all population subgroups (Table 2, Chronic Exposure, Set II, including all commodities). The MOE at this exposure was >11,700. The exposure level was less than 1% of the RfD of 0.1 mg/kg/day.

These initial tier of exposure estimates assumed that all commodities having a current tolerance contain residues at the tolerance. The assessment included the consumption of citrus commodities at the proposed tolerance of 0.1 ppm. The acute MOE far exceeds the benchmark

MOE of 100 generally needed to accommodate the potential of a 10-fold higher human sensitivity than laboratory animals on a per body weight basis, and a 10-fold inter-individual variation of sensitivity within human populations. The short- and intermediate-term and chronic exposures also represented only as much as 2% of the RfD. These levels of risk did not present health risks of concern and therefore, no further refinement of the exposures to reflect a more realistic residue profile is needed.

V.B. Drinking Water

Using the highest detected level of 17.6 ppb and the default water consumption of 1 liter per day for a 10 kg child, the estimated exposure from drinking water was 1.8 ug/kg/day. This represented less than 2% of the RfD of 0.1 mg/kg/day (USEPA, 1997).

V.C. Residential Exposures

Using the short- and intermediate-term NOEL of 10 mg/kg/day for thyroid effects, and the DADs estimated by USEPA for the two homeowner application scenarios (0.0003 mg/kg/day for backpack sprayer and 0.013 mg/kg/day for low pressure handwand application), the MOEs were at least 770 (RED, Table 6). The MOEs for these two scenarios were above the benchmark MOE of 100 and did not present health risks of concern.

Based on the DAD of 0.14 mg/kg/day for children that received post-application exposure to residential turfgrass 2 hours after a 3 lbs per acre treatment, the MOE was 71. This is less than the benchmark MOE of 100 generally needed for health protection. When the application rate was reduced to 2 lbs per acre, the exposure was proportionally reduced to 0.09 mg/kg/day, and the MOE increased to 111 (RED, Table 7). An agreement between the registrant and USEPA was reached to reduce the maximum application rate from 3 to 2 lbs per acre for residential and recreation area turf grass (USEPA, 1997).

V.D. Occupational Exposures

Of the 13 exposure scenarios, not only mixing/loading liquid for aerial applications and irrigation systems had low MOE (MOE of 1.5 based on the DAD of 6.56 mg/kg/day), the following 3 work tasks also showed MOEs below 100: mixing/loading liquid for rights-of-way spraying (MOE of 59) and groundboom application (MOE of 15), and mixing/loading/applying for low pressure handwand (MOE of 17) (RED, Table 6). As a mitigation measure, USEPA added chemical-resistant gloves to the baseline attire for workers as represented by these scenarios.

Based on the exposure of 0.003 mg/kg/day, the MOE for maintaining golf course turf 2 hours after the treatment was 2,900 (RED, Table 8). Based on the exposure of 0.069 mg/kg/day (2 hours after treatment), the MOE for harvesting turf at the sod farm was 144 (RED, Table 9).

USEPA had further concerns for other possible exposure scenarios associated with the use of pendimethalin. Pending further studies on the post-application exposures specific to pendimethalin, USEPA requires that the 12-hour Restricted Entry Interval (REI) be increased to 24 hours for all uses within the Workers Protection Standard (WPS). For noncrop areas, USEPA required a reduction of the maximum application rate from 3 to 2 lbs per acre.

The estimated ADD for the proposed use on citrus was 0.014 mg/kg/day for a mixer/loader and 0.009 mg/kg/day for an applicator. Based on the acute NOEL of 15 mg/kg/day, the corresponding acute MOEs were > 1,000. The estimated SADD was 0.01 mg/kg/day for a mixer/loader and 0.064 mg/kg/day for an applicator. Based on the subchronic NOEL of 10 mg/kg/day, the corresponding subchronic MOEs were ≥ 1,000. Thus, the proposed use on citrus does not pose a significant health risk for mixer/loader and applicators.

V.E. <u>Aggregate Exposures</u>

The potential pathways of exposure to pendimethalin included dietary, drinking water, and residential contact. As presented in the previous sections, the highest acute exposure from the diet was 2.08 ug/kg/day for children 1-6 years old. Using the highest monitored level of 17.6 ppb detected in the surface water, and assuming 1 liter drinking water consumption for a 10 kg child, the potential drinking water exposure was 1.8 ug/kg/day (USEPA, 1997). The sum of exposure from these two pathways was 3.88 ug/kg/day. The corresponding MOE was > 3,800, based on the acute NOEL of 15 mg/kg/day (maternal toxicities of clinical signs and death in pregnant rabbits at the LOEL of 30 mg/kg/day). Based on the RED, the post-application exposure to residues on residential turfgrass appeared to be the predominant pathway of exposure which is not impacted by the proposed use on citrus. The exposure was 0.09 mg/kg/day (90 ug/kg/day) at the reduced application rate of 2 lbs per acre. The acute MOE for the total exposures of 93.88 ug/kg/day from all three pathways was 160.

The same exposure estimate could be used for calculating the MOE using the USEPA NOEL of 10 mg/kg/day (effects on thyroid functions in rats at the LOEL of 31 mg/kg/day) for short- and intermediate-term exposures. The corresponding MOE was 107.

V.F. <u>Cumulative Exposures</u>

The 1996 Food Quality Protection Act (FQPA) required that the cumulative effects from "other substances that have a common mechanism of toxicity" be addressed (FIFRA Section 408(b)(2)(d)(v)). USEPA determined that "pendimethalin does not appear to produce a toxic metabolite produced by other substances" (USEPA, 1997, Fed Reg, 1997). Therefore, for the purpose of the two evaluations, USEPA did not assume that pendimethalin has a common mechanism of toxicity with other substances (USEPA, 1997; Fed Reg, 1997).

V.G. <u>Safety Determination for Infants and Children</u>

The 1996 FQPA required the application of an additional 10-fold uncertainty (safety) factor "unless reliable data demonstrate that the additional factor is unnecessary to protect infants and children" (USEPA, 1997). The submission of the pre- and post-natal toxicity data as required for the pesticide registration has been met. Based on these data, USEPA determined that an additional factor of 10 is not needed for the protection of infants and children (USEPA, 1997, Fed Reg, 1997).

VI. CONCLUSIONS

In evaluating the reregistration of products containing pendimethalin, USEPA concluded that pending further required submissions (i.e., product-specific data, revised confidential statements of formula, and revised labeling), "pendimethalin products will be reregistered" (USEPA, 1997). In approving the time-limited tolerance for mint under the Emergency Exemption registration (Section 18), USEPA's also included all uses of pendimethalin in the risk evaluation (Fed Reg, 1997, 1998). Both of these evaluations took into consideration the issues specifically required by the 1996 FQPA; namely, the risk of aggregate exposures, the cumulative risk of exposures to chemicals with a common mechanism of toxicity, and the need for an additional uncertainty factor for protecting infants and children.

Based on the two evaluations by the USEPA in 1997, the risk associated with the proposed use of Prowl 3.3 EC on citrus was assessed. For the general population, the use on citrus is expected only to impact the dietary pathway of exposure. In addition, the risk of occupational exposures associated with the pesticide application was also evaluated.

The proposed tolerance for citrus was 0.1 ppm. The following citrus crops were included in the dietary exposure analysis: grapefruit, kumquat, lemon, lime, orange, tangelo, and tangerine. The acute dietary exposure, not assessed by the USEPA, was nearly 50% higher than the short- and intermediate-term dietary exposure presented by USEPA. The acute MOE was >4,900, substantially above the benchmark MOE of 100 needed for the protection of human health. The short- and intermediate-term and chronic dietary exposures that included citrus remained to be within 2% of the RfD. Thus, the addition of citrus crops is not expected to result in significant risk.

As with the two previous USEPA analyses, the post-application dermal exposure to residues on residential turfgrass remained to be the predominant pathway of exposure. Based on the lawn application rate of 2 lbs per acre, the acute MOE for the aggregate exposure was 160. Assuming that the short- and intermediate-term aggregate exposure was at the same level as the acute exposure, but applying the NOEL of 10 mg/kg/day as used by USEPA, the MOE was 107. These MOEs were at or above the benchmark MOE of 100 for the protection of health. USEPA determined that an additional uncertainty factor of 10 is not needed for the protection of infants and children (USEPA, 1997, Fed Reg, 1997).

Based on the current available data, USEPA did not assume that pendimethalin has a common mechanism of toxicity with other substances (USEPA, 1997; Fed Reg, 1997).

Occupational exposures to pendimethalin for the use on citrus were assessed. The acute and subchronic/seasonal MOE for mixer/loader and applicators were >1,000, above the benchmark MOE of 100 needed for the protection of human health.

Taken the FQPA requirements into consideration, this assessment concluded that the proposed use of pendimethalin on citrus is not likely to result in significant risk to either the general population or workers.

VI. REFERENCES

American Cyanamid Company (submitted to DPR in 1985) Prowl and Stomp (pendimethalin) herbicides 4 EC formulation. Data in response to Pesticide Contamination Prevention Act. AB2021. CDPR Vol. 361-75.

California Department of Pesticide Regulation (CDPR) 1996 Pesticide Use Report. Cal/EPA. CDPR, Sacramento, CA.

DeVito, W. J. and L. E. Braverman. 1993 A 14-day intrathyroidal metabolism study in male rats with AC92,553. University of Massachusetts Medical School, Worcester, MS. DPR Vol. 361-126, 147610.

Federal Register (Fed Reg) 1998 Pendimethalin; Extension of tolerance for emergency exemptions. Fed Reg 63(42):10545-10547.

Federal Register (Fed Reg) 1997 Pendimethalin; Pesticide tolerance for emergency exemption. Fed Reg 62(100):28355-28361.

Fischer, J. E. 1991 92-Day thyroid function study in albino rats with AC92,553. American Cyanamid Company, NJ, study T-0270. DPR Vol. 361-109, #099135.

Fischer, J. E. 1993 56-Day thyroid function study in albino rats with AC92,553. American Cyanamid Company, NJ, study AX 93-1. DPR Vol. 361-125, #147605.

Irvine, L. F. H. and P. Boughton 1990 AC92,553. Dietary rat two-generation (two litters per generation) reproduction toxicity study. Toxicology Laboratories Limited, Ledbury, Herefordshire. Report CBG/2/90. DPR Vol. 361-103, #089055.

PHED, 1998. PHED Surrogate Exposure Guide. Estimates of worker exposure from the Pesticide Handler Exposure Daetabase (PHED). Version 1.1. August, 1998.

USEPA 1997 Reregistration eligibility decision (RED); Pendimethalin. USEPA, Prevention, Pesticides, and Toxic Substances (7508W), EPA 738-R-97-007, June 1997.

Wolfe, G. W. 1979 Oral teratology study in rats, AC 92,553. Hazleton Laboratories America, Inc. Final Report. DPR Vol. 361-042, #2911.

Wolfe, G. W. 1982 Teratology study in rabbits, AC 92,553 Technical. Final Report. Hazleton Laboratories America, Inc. DPR Vol. 361-066, #039915.