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OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: The HED Chapter of the Reregistration Eligibility Decision Document (RED) for Pendimethalin (Chemical number 108501; Case 0187)

FROM: Mary R.A. Clock, Biologist
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THRU: Michael Metzger, Acting Chief
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Health Effects Division (7509C)
and
Stephanie Irene, Acting Director
Health Effects Division (7509C)
3/15/96

TO: Sherry Sterling, Acting Chief
Reregistration Branch
Special Review and Reregistration Division (7508W)

Please find attached the Human Health Assessment for the Pendimethalin Reregistration Eligibility Decision Document (RED). This chapter includes the Hazard Assessment from William Greear in Toxicology Branch I (Attachment 1), the Product and Residue Chemistry Assessments from Bonnie Cropp-Kohlligian in the Chemistry Branch/Reregistration Support (Attachment 2), the Dietary Exposure Analysis from Mary Clock in the Risk Characterization and Analysis Branch (Attachment 3), and the Occupational and Residential Exposure Assessment from John Leahy in the Occupational and Residential Exposure Branch (Attachment 4).

CC: W.Greear/TOX 1 B.Cropp-Kohlligian/CBRS E.Doyle/SAB
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HED Chapter

PENDIMETHALIN

In this document, which is for use in EPA's development of the pendimethalin Reregistration Eligibility Decision Document (RED), HED presents the results of its risk characterization of the potential human health effects of dietary, and occupational and residential exposure to pendimethalin. Included is a discussion of the product chemistry, toxicology, and residue chemistry data that have been submitted as well as HED's recommendations for risk reduction and mitigation. At the present time, there are no Office of Water drinking water regulations or Health Advisories for pendimethalin; thus, this risk characterization does not include ingestion of pendimethalin contaminated drinking water or any exposures to pendimethalin contaminated ground or surface water. However, if upon completion of the Ecological Fate and Effects Division Chapter for the RED a concern is apparent, this may change.

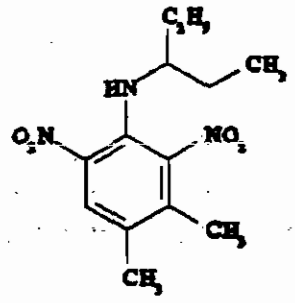
I. SCIENCE ASSESSMENT

A. PHYSICAL AND CHEMICAL PROPERTIES ASSESSMENT

All pertinent data requirements are satisfied for the 90% T and the pendimethalin TGAI; however additional product-specific data (physical/chemical properties) are outstanding for the 86.8% and 60% FIs. Provided that the Registrant submits the data required in the attached data summary tables for the 86.8% and the 60% FIs (Appendix 1, Product Chemistry Data Summary), and either certifies that the suppliers of beginning materials and the manufacturing processes for the pendimethalin technical product and MPs have not changed since the last comprehensive product chemistry review or submits complete updated product chemistry data packages, HED has no objections to the reregistration of pendimethalin with respect to product chemistry data requirements.

1. Description of Chemical

Pendimethalin [N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine] is a selective herbicide registered for control of broadleaf weeds and grassy weed species.



Empirical Formula:	$C_{13}H_{19}N_3O_4$
Molecular Weight:	281.3
CAS Registry No.:	40487-42-1
Shaughnessy No.:	108501

2. Identification of Active Ingredient

Pendimethalin is an orange-yellow crystalline solid with a melting point of 54-58 C. It is soluble in chlorinated hydrocarbons and aromatic solvents such as methylene chloride, acetone, and xylene, but only soluble in water at <0.5 ppm at 20 C. Pendimethalin is stable under acidic and alkaline conditions.

3. Manufacturing-Use Products

A search of the Reference Files System (REFS) conducted 9/14/95 identified three pendimethalin manufacturing-use products (MPs) registered to American Cyanamid Company under Shaughnessy No. 108501: the 90% technical (T; EPA Reg. No. 241-245), and the 86.8% and 60% formulation intermediates (FIs; EPA Reg. Nos. 241-291 and 241-281, respectively). Only the American Cyanamid 90% T, and 86.8% and 60% FIs are subject to a reregistration eligibility decision.

4. Regulatory Background

The Pendimethalin Reregistration Standard dated 7/20/84 and Guidance Document dated 3/85 required additional data for the American Cyanamid 90% T. The Pendimethalin

Reregistration Standard Update dated 3/19/90 required additional data concerning GLNs 62-2 and 62-3 for the 90% T. As was Agency policy at that time, data pertaining to the 86.8% and 60% FIs were not reviewed in the Update because the products were registered after the Guidance Document was issued. Data concerning the FIs have since been evaluated by either the HED's Chemistry Branch or Registration Division (RD).

In addition because pendimethalin contains dinitroanilines, a discussion of the potential for formation of nitrosamines and analysis of the 90% T for the presence of nitrosamines formed during manufacture and storage of the product was required. Submitted data indicate that no volatile nitrosamines are present (<0.5 ppm) and that total nonvolatile nitrosamines are present at less than 100 ppm. The Agency had previously determined that concentrations of N-nitroso-pendimethalin below 135 ppm were required to maintain the associated upper risk below $1x10^{-6}$ (45 FR 49600).

The current status of the product chemistry data requirements for American Cyanamid pendimethalin products is presented in the attached data summary tables (Appendix 1, Product Chemistry Data Summary). Refer to these tables for a listing of the outstanding product chemistry data requirements.

B. HUMAN HEALTH ASSESSMENT

1. Hazard/Dose-Response Assessment

The toxicology data base for pendimethalin is adequate and will support reregistration eligibility. There are not data gaps at this time.

a. Acute Toxicity

The table below summarizes the results of acute toxicity studies on Pendimethalin and the toxicity categories for the different routes of administration:

Table 1. Acute Toxicity Values of Technical Pendimethalin

TEST	RESULT	CATEGORY
Oral LD_{50} in rat (MRID 00026657)	LD_{50}(M) = 1250 mg/kg LD_{50}(F) = 1050 mg/kg	III
Dermal LD_{50} in rabbit (MRID 00026657)	LD_{50} > 5000 mg/kg	IV
Inhalation LC_{50} in rat (MRID 00073342)	LC_{50} > 320 mg/L (nominal concentration)	IV

Eye irritation in rabbit[a] (MRID 00026657)	Slight conjunctival irritation	III
Dermal irritation in rabbit[a] (MRID 00026657)	No irritation	IV
Dermal sensitization[a] (MRID 00153767)	Nonsensitizing	N/A

a Not required for the Technical Grade Active Ingredient; presented for informational purposes.

b. Subchronic Toxicity

Feeding Studies in Rats: In a 30-day feeding study in rats (MRID 000106754), pendimethalin technical (98.7%) was administered to groups of 10 males and 10 females RH Wistar rats in the diet at levels of 0, 800, 1,600 or 3,200 ppm (corresponding to 0, 80, 160, or 320 mg/kg/day). Urine was darker than controls in the 1,600 and 3,200 ppm groups. At 3,200 ppm there appeared to be increased liver weight. **The LOEL is 3,200 ppm (320 mg/kg/day) based on increased liver weight. The NOEL is 1,600 ppm (160 mg/kg/day).** Although this study is classified as Supplementary it provides useful information.

In a 13-week feeding study in rats (MRID 00156081), AC 92,553 (pendimethalin, 92.1%, Lot #AC3528-129-1) was administered to groups of 30 male and 30 female Charles River CD(SD)BR rats in the diet at levels of 0, 100, 500, or 5,000 ppm (corresponding to 0, 10, 50, or 500 mg/kg/day). At 5,000 ppm, rats displayed a dark yellow discoloration of the urine and yellow discoloration of abdominal fat. Body weight gain and food consumption were decreased. The hematocrit and hemoglobin levels were decreased and the number of platelets slightly increased in males. There was an increase in pale or mottled livers in males and dark red thyroids in both sexes at 5,000 ppm. The absolute weight of the liver was increased in males and females. Diffuse hypertrophy of the liver was also observed. **The LOEL is 5,000 ppm (500 mg/kg/day) based on decreased body weight gain and food consumption, decreased hematocrit and hemoglobin with an increase in platelets in males, increased liver weight, red thyroids, and hypertrophy of the liver. The NOEL is 500 ppm (mg/kg/day).**

In a second 13-week feeding study in rats (MRID 00059468), AC 92,553 technical (pendimethalin) was administered to groups of 25 male Long-Evans rats in the diet at levels of 0, 25, 50, 100, 500, or 2,500 ppm (corresponding to 0, 2.5, 5.0, 10.0, 50.0, or 250 mg/kg/day). The 2,500 ppm group was raised to 5,000 ppm (500 mg/kg/day) from week 8-13. There were no adverse effects noted with respect to mortality, body weight and gross and microscopic examination of mammary glands. **The LOEL was not determined. The**

NOEL was greater than 2,500 ppm (250 mg/kg/day). Although this study is classified as Supplementary it provides useful information.

In a third 13-week study in rats (MRID 00059469), AC 92,553 technical pendimethalin was administered to Sprague-Dawley rats in the diet at 0 or 2,500 ppm (corresponding to 0 or 250 mg/kg/day). There were no adverse effects noted with respect to mortality, body weight and gross and microscopic examination of the mammary gland. **The LOEL was not determined. The NOEL was greater than 2,500 ppm (250 mg/kg/day).** Although this study is classified as Supplementary it provides useful information.

In a special 92-day thyroid function feeding study (MRID 42054601), AC 92,553 (pendimethalin, 92.6%, Lot #AC5213-72A) was administered to groups of 80 male CD[Crl:CD(SD)] rats at dose levels of 0, 100, or 5,000 ppm (corresponding to 0, 4.98, or 245.4 mg/kg/day) for 28 days. Groups of 20 male rats were sacrificed at 15, 29, 57 and 92 days. At 100 ppm there was decreased total T_4, rT_3, total free T_4 and increased percent T_3, increased follicular cell height and decreased area occupied by colloid. At 5,000 ppm there were decreased body weight and food consumption compared to controls, increased thyroid weight, decreased total T_4, total T_3, rT_3, total free T_4 and [^{125}I]-T_4 to transthyretin bonding, increased percent free T_4, percent free T_3 and [^{125}I]-T_4 to albumin binding, increased follicular cell height and decreased area occupied by colloid and ultrastructural thyroid changes. Most parameters were reversible after treatment subsided except for decreased body weight. **The LOEL was 100 ppm (4.98 mg/kg/day) based on thyroid effects. The NOEL was less than 100 ppm (4.98 mg/kg/day).**

In a special 56-day feeding study to determine thyroid function (MRID 43135001), groups of 65-70 (5-15 per sacrifice time) male Crl:CD(SD) rats were treated at dose levels of 0, 500 or 5000 ppm (0, 31 or 292 mg/kg/day) of AC 92,553 (pendimethalin, 92.6%, Lot #AC5213-72A) in the diet for 28 days. A recovery period of up to 28 days was employed. There were no deaths or clinical signs of toxicity during or after the treatment period at either dose. At 500 ppm there was decreased total T_4 (38%), rT_3 (25%) and total free T_4 (28%) and increased percent free T_3 (13%), increased follicular cell height (40%) and decreased area occupied by colloid (51%) during treatment. At 5000 ppm, body weight (8%), body weight gain (29%) and food consumption (15%) were decreased compared to controls during the treatment period. Thyroid changes during treatment with 5000 ppm included: increased absolute (15%) and relative (23%) thyroid weight; decreased total T_4 (74%), total T_3 (25%), rT_3 (36%), total free T_4 (40%), and [^{125}I]-T_4 to transthyretrin binding; increased percent free T_4 (117%), percent free T_3 (26%) and [^{125}I]-T_4 to albumin binding; increased follicular cell height (75%) and decreased area occupied by colloid (45%); ultrastructural thyroid changes were consistent with mild to moderate TSH stimulation except for the accumulation of dense-bodies in the cytoplasm which may be reaction products of AC 92,553. Most parameters were reversible after treatment subsided except for a slight decreased body weight compared to controls (7%) at 5000 ppm. There were no changes in TSH, total free T_3 or diameter of

follicular cells. **The LOEL was 500 ppm (31 mg/kg/day) based on thyroid effects. The NOEL could not be determined.**

In a special 14-day feeding study to determine thyroid function (MRID 43135003), AC 92,553 (pendimethalin, 92.6%, Lot #AC5213-72A) was administered in the diet to groups of 10 male Crl:CD(SD) rats at dose levels of 0, 100 or 5,000 ppm (corresponding to 0, 10 or 500 mg/kg/day). At 5000 ppm AC 92, 533 for 14 days, TSH was increased and T_4 and T_3 were decreased. No treatment related effects were observed for rT_3 levels, thyroid weight, ^{131}I uptake in MIT, DIT or T_4. There was a significant increase of ^{131}I uptake by the thyroid of rats in the 5000 ppm group and an increase in incorporation of ^{131}I in T_3. Total T_3 and T_4 levels in the thyroid were not affected by treatment at 5,000 ppm. **The LOEL is 5,000 ppm (500 mg/kg/day) based on thyroid effects. The NOEL is 100 ppm (10 mg/kg/day).**

In a second special 14-day feeding study to determine biliary excretion and hepatic metabolism, AC 92,553 (pendimethalin, 92.98%, Lot #AC6539-77A) was administered to groups of 10 male Crl:CD(SD) rats at dose levels of 1, 100, or 5,000 ppm (corresponding to 0, 10, or 500 mg/kg/day). Ingestion of 5,000 ppm produced decreases in serum T_3 and T_4 with a compensatory increase in TSH. Also increased were liver weight, bile flow and cumulative biliary excretion of ^{125} I-T_4 with a slight increase in T_4-glucuronytransferase activity detected by generation of ^{125} I-T_4 glucuronide from ^{125} I-T_4 in vitro by hepatic microsomes. The increase in enzyme activity was also demonstrated in vivo by a significant increase in biliary excretion of ^{125} I-T_4-glucuronide. **The LOEL is 5,000 ppm (500 mg/kg/day) based on thyroid effects. The NOEL is 100 ppm (10 mg/kg/day).**

Feeding Studies in Dogs: In a 90-day feeding study (MRID 00026672), pendimethalin was administered to groups of 8 dogs at dose levels of 0, 62.5, 250 or 1,000 mg/kg/day. Body weight loss was apparent at 250 and 1,000 mg/kg/day. **The LOEL is 250 mg/kg/day based on body weight loss. The NOEL is 62.5 mg/kg/day.** Although this study is classified as Supplementary it provides useful information.

In a 30-day feeding study in dogs (MRID 000106754) AC 92,553 technical (pendimethalin, 98.7%) was administered to groups of 2 male and 2 female beagles in the diet at dose levels of 0, 0.625% or 1.25% (corresponding to 0, 125 or 250 mg/kg/day). A third test group received 5% in the diet (corresponding to 1,000 mg/kg/day) for 30 days. The protocol was changed so that dogs received the compound by gelatin capsule from days 17 to 30. Food consumption and body weight were decreased in all treated groups compared to controls. **The LOEL was 125mg/kg/day based on decreases in body weight and food consumption. The NOEL could not be determined.** Although this study is classified as Supplementary it provides useful information.

Feeding Study in Mice: In a 30-day feeding study in mice (MRID 000106754), pendimethalin technical (98.7%) was administered to groups of 10 male and 10 female CF-1 mice in the

diet at levels of 0, 500, 1,000 or 2,000 ppm (corresponding to 0, 75, 150 or 300 mg/kg/day). There were no adverse effects with respect to mortality, body weight, food consumption and organ weight. **The LOEL was not determined. The NOEL is greater than 2,000 ppm (300 mg/kg/day).** Although this study is classified as Supplementary it provides useful information.

Dermal Study in Rabbits: In a 21-day dermal toxicity study (MRID 00026663), AC 92,553 (pendimethalin) was dermally applied to the back of 3 or 4 New Zealand white rabbits/group at dose levels of 0, 250, 500 or 1000 mg/kg/day. There were no adverse effects with respect to mortality, food and water intake, hematology, urinalysis and gross and microscopic pathology. **The systemic LOEL was not determined. The systemic NOEL is greater than 1000 mg/kg/day.**

c. Chronic Toxicity/Carcinogenicity

Feeding Studies in Rats: In a 2-year study in rats (MRID 40174401), AC 92,533 (pendimethalin, 91.9%, Lot #AC3528-129-1), was administered to groups of 55 male and 55 female Crl:CD(SD)BR rats in the diet at levels of 0, 100, 500 or 5,000 ppm (corresponding to 0, 5, 25, or 250 mg/kg/day). Ten rats/sex/group were interim sacrificed as 12 months. At 5,000 ppm, survival in males was slightly decreased and body weight gain was decreased. There was decreased food consumption, increased gamma glutamyl transferase and cholesterol, increase in liver weight and/or liver body and/or brain weight ratios, generalized icterus, dark adipose tissue in females, diffusely dark thyroids, follicular cell hyperplasia of the thyroid and thyroid follicular cell adenoma. **The LOEL is 5000 ppm (250 mg/kg/day) based on decreased survival, body weight gain and decreased food consumption, increased gamma glutamyl transferase, cholesterol and liver wieghts, and thyroid effects. The NOEL is 500 ppm (25 mg/kg/day).**

In a second 2-year feeding study in rats (MRID 42027802), AC 92,533 (pendimethalin, 92.6%, Lot #AC5213-72A) was administered to groups of 125 male Sprague-Dawley (Crl:CD(SD)BR) at dose levels of 0, 1250, 2500, 3750, or 5000 ppm (corresponding to 0, 51, 103, 154, and 213 mg/kg/day). Fifteen rats/group were interim sacrificed at 1, 13, 26, 39 and 52 days. There was decreased colloid and increased cysts of the thyroid follicular cells and an increase in liver weight at 1250 ppm and above. At 2500 ppm and above there was increased pigment and hypertrophy of follicular cells, increased thyroid weight and an increase in eosinophilic and basophilic foci of cellular alteration, hepatocellular enlargement and hepatocellular intracytoplasmic inclusions. There was a decrease in body weight gain at 3750 ppm and above and hyperplasia of follicular cells. At 5000 ppm GGT and total cholesterol were increased and there was an increase in thyroid follicular adenomas. The LOEL is less than or equal to 1250 ppm ($\leq$51 mg/kg/day) based on non-neoplastic thyroid follicular cell changes. The NOEL was not determined.

Feeding Study in Mice: In an 18-month feeding study in mice (MRID 40909901), AC 92,533 (pendimethalin, 92.6%, Lot #AC5218-72A) was administered to groups of 65 male and 65 female Charles River CD-1 mice at dose levels of 100, 500, or 5,000 ppm (corresponding to 12.3, 62.3 and 622.1 mg/kg/day in males and 15.6, 78.3 and 806.9 mg/kg/day in females). There were 2 control groups consisting of 65 mice/sex each. Ten mice/sex were sacrificed at 12 months in 1 control and all treated groups. (One control group only consisted of 55 mice/sex.) At 5,000 ppm there was increased mortality in females, decreased body weight in females, increased absolute thyroid, liver and gall bladder weights and/or relative body and brain weight ratios in males and females and amyloidosis in males. **The LOEL is 5,000 ppm (622.1 mg/kg/day [M]; 806.99 mg/kg/day [F]) based on mortality, body weight decrease, organ weight changes and amyloidosis. The NOEL is 500 ppm (62.3 mg/kg/day [M]; 78.3 mg/kg/day [F]).**

Oral Study in Dogs: In a 2-year oral study in dogs (MRID 00058657), AC 92,533 (pendimethalin, 91.4%, Lot #77-02) was administered via capsule to groups of 4/sex beagle dogs at dose levels of 0, 12.5, 50 or 200 mg/kg/day. Serum alkaline phosphatase (SAP), liver weight and inflammation and hemosiderosis of the liver were increased at 50 mg/kg/day and above. Yellow color of the hair was observed in all treated dogs. **The LOEL is 50 mg/kg/day based on increased SAP, liver weights and liver pathology. The NOEL is 12.5 mg/kg/day.**

d. Developmental Toxicity

Oral Study in Rats: Pendimethalin (94.2% a.i.) was administered in corn oil to groups of 30 mated Sprague-Dawley CD strain rats by gavage at daily dose levels of 0, 125, 250, or 500 mg/kg/day from gestation day 6 through 15 (MRID 00025752). Females were observed for signs of toxicity, and body weights were measured during gestation. Animals were sacrificed on gestation day 21 and reproductive observations were made and uteri were examined for live fetuses and intra-uterine deaths. Fetuses were weighed, sexed, and examined for external, visceral and skeletal alterations. There were no maternal or developmental effects noted at any dose level tested, and based on these results, **the NOELs for developmental and maternal toxicity are ≥500 mg/kg/day (highest dose tested).** Although this study is classified as Supplementary, when considered in conjunction with the rabbit developmental toxicity study (MRID 00117444) it will satisfy guideline requirement §83-3. It is not upgradable because an adequate dose range may not have been tested.

Oral Study in Rabbits: Pendimethalin was administered in corn oil to groups of 20 artificially inseminated New Zealand White strain rabbits by gavage at dose levels of 0, 15, 30, or 60 mg/kg/day from gestation day 6 through 18 (MRID 00117444). Females were observed for signs of toxicity, and body weights were measured during gestation. Animals were sacrificed on gestation day 29 and reproductive observations were made and uteri were examined for live fetuses and intra-uterine deaths. Fetuses were weighed, sexed, and examined for

external, visceral and skeletal alterations. **No maternal toxicity was reported at doses ≤60 mg/kg/day (highest dose tested). However, the range-finding study indicated that doses ≥ 125 mg/kg/day were associated with increased mortality** (3/5, 5/5 and 4/5 in the 125, 250, and 500 mg/kg/day, respectively compared with 0/5 in the control group). A slight increase in the mean incidence of skeletal anomalies in the mid- and high-dose groups which consisted of findings of less than twelve pairs of ribs (0/111, 1/118 and 4/107 fetuses in the control, mid-, and high-dose groups, respectively, not statistically significant) and/or missing or incompletely ossified vertebrae (0/111, 1/118 and 7/107 fetuses in the control, mid and high dose groups, respectively). No individual litter data or historical control data were available in the report to support a conclusion regarding the significance of these alterations. **A developmental toxicity NOEL could not be determined from this study.** Although this study is Supplementary and does not satisfy §83-3 guideline requirements for a rabbit developmental toxicity study, it is upgradable pending receipt of individual litter data (fetal alterations) and historical control data. **If, however, the additional data indicates the lack of any developmental or maternal effects at any dose, an additional developmental study (species to be determined) may be required.**

e. Reproductive Toxicity

Feeding Studies in Rats: In a 2-generation reproduction study (MRID 417252203), AC 92,533 (pendimethalin, 92.6%, Lot #AC5213-72A) was administered to groups of 25 male and 25 female Sprague-Dawley derived OFA-SD (IOPS-CAW) rats at dose levels of 0, 500, 2500 or 5000 ppm (corresponding to 0, 34, 172 and 346 mg/kg/day) in males and 0, 43, 216, 436 mg/kg/day in females). **There were no clinical signs or changes in organ weight data. There was a minimal (5%) decrease in body weight gain and food consumption (possibly due to palatability) at 2500 ppm. At 5000 ppm the decrease in body weight gain was as high as 20 %. The LOEL for parental effects is 5000 ppm (346 and 436 mg/kg/day, in males and females) based on weight gain and food consumption depression. The NOEL for parental effects is 2500 ppm (172 and 216 mg/kg/day, in males and females, respectively). There were decreased pup weights during much of lactation at 5000 ppm. The LOEL for reproductive effects is 5000 ppm (346 and 436 mg/kg/day in males and female, respectively). The NOEL for reproductive effects is 2500 ppm (172 and 216 mg/kg/day, in males and females, respectively).**

In a 3-generation reproduction study (MRIDs 00026671, 0040304, 00059470) AC 92,533 technical (pendimethalin) was administered to groups of 10 male and 20 female Long-Evans rats at dose levels of 0, 500 or 5000 ppm (corresponding to 0, 25 and 250 mg/kg/day). At 5000 ppm there was a decrease in body weights in male and female parental animals. **The LOEL for parental toxicity is 5000 ppm (250 mg/kg/day) based on decreased body weights. The NOEL for parental toxicity is 500 ppm (25 mg/kg/day).** Pup body weight gain was decreased during lactation. There were possible decreases in pups born alive and pup survival. **The LOEL for reproductive toxicity is 5000 ppm (250 mg/kg/day) based**

on pup body weight gain and possible decreased pups born alive and pup survival . The NOEL for reproductive toxicity is 500 ppm (25 mg/kg/day).

f. Mutagenicity

There are acceptable studies to satisfy the initial mutagenicity testing requirements for all three categories (gene mutations, structural chromosomal aberrations, and other genotoxic effects). The positive Salmonella results in one study indicated that pendimethalin may have potential genotoxic activity. Subsequent assays for germ cell effects (Chinese hamster ovary cells and rat testicular cells) and additional Salmonella assays, submitted to address this concern, were all negative. No other mutagenicity studies are required at this time.

In a reverse gene mutation assay in bacteria (MRID 00153768), strains (TA1535, TA1537, TA1538, TA98, TA100) of S. typhimurium were exposed to AC 92,533 (pendimethalin, 92.2%, Lot #AC3528-129-1) at concentrations of 50, 158, 500, 1581 or 5000 μg/plate in the presence and absence of mammalian hamster S9. Subsequent tests with TA98, TA1538 and TA100 used dose levels of 250, 500, 1000, 3000 or 5000 μg/plate. AC 92,533 was tested up to the limit dose of 5000 μg/plate. A precipitate was formed at 5000 μg/plate. The positive controls did induce the appropriate responses in the corresponding strains. **This study was considered positive since there was evidence of a 2-fold dose-related increase in the number of induced mutant colonies over background at all doses from 50 to 5000 μg/plate.**

In a *Salmonella*/microsome plate incorporation assay and in an *Escherichia coli* WP2(uvrA) reverse mutation assay (MRID 43177801), strains TA98, TA100, TA1535, TA1537, TA1538 and WP2(uvrA) were exposed to pendimethalin at concentrations of 25, 50, 100 250, 500 and 750 μg/plate, with and without exogenous metabolic activation. Preparations for metabolic activation were made from Aroclor 1254 induced male Sprague-Dawley rat livers. The test material was delivered in DMSO. No cytotoxicity was seen at any concentration of pendimethalin tested. The upper concentration was limited by test material solubility (a precipitate was observed at concentrations of 750 μg/plate and above). Positive and vehicle control values were appropriate. **There was no evidence of an increase number of mutant colonies over solvent control values at any concentration of pendimethalin tested, either with or without S9 mix.**

In a Salmonella/microsome plate incorporation and disk assay and in an Escherichia coli WP2(uvrA) reserve mutation assay (MRID 43135005), strains TA98, TA100, TA1535, TA1537, and WP2(uvrA) were exposed to pendimethalin (90.7% , Lot #AC8088-149) at 50, 158, 500, 1581 and 5000 μg/plate or 1000 μg/paper disk/plate, with and without exogenous metabolic activation. Preparations for metabolic activation were made from Aroclor 1254 induced male rat livers. The test material was delivered in DMSO. Cytogenetic determinations were not made or discussed in this study. The highest concentration was

limited by solubility (a precipitate was seen at 1581 and 5000 μg/plate). Positive and vehicle controls were appropriate. **There was no evidence of induced mutant colonies over background vehicle control values at any concentration of pendimethalin tested in any strain with or without S9 mix.**

In a *Salmonella*/microsome plate incorporation and disk assay and in an *Escherichia coli* WP2(uvrA) reverse mutation assay (MRID 43135006), strains TA98, TA100, TA1535, TA1537, TA1538, and WP2(uvrA) were exposed to pendimethalin (99.5%, Lot #AC5042-52F) at concentrations of 50, 100, 250, 500, and 750 μg/plate without exogenous metabolic activation and to the same concentrations plus an additional concentration of 25 μg/plate with exogenous metabolic activation. A confirmatory assay tested concentrations of 25, 50, 100, 250, 500 and 750 μg/plate both with and without S9 mix. Preparations for metabolic activation were made from Aroclor 1254 induced male rat livers. The test material was delivered in DMSO. No cytogenicity was seen at any concentration tested up to 5000 μg/plate. The upper concentration tested was limited by solubility of the test material. Positive and vehicle control values were appropriate. **No evidence of a mutagenic response was seen at any dose in any strain with or without S9 mix in either assay.**

In a forward mutation study (MRID 43177802) at the HGPRT locus in Chinese hamster ovary CHO-K1-BH4 cells in culture, cells were exposed to pendimethalin (90.9%, Lot #AC5042-37D) at concentrations of 1, 5, 7.5, 10, 20, 30, 40, and 50 μg/ml in the absence of an exogenous metabolic activation system and to 10, 25, 50, 75, 100, 125, 150, and 175 μg/ml in the presence of an exogenous metabolic activation system (S9-mix). Preparations for metabolic activation were made from Aroclor 1254 induced male Sprague-Dawley rat liver. The test material was delivered in DMSO. Cytotoxicity was unacceptably high at 30, 40 and 50 μg/ml in the absence of S9 mix and at 150, 150, and 175 μg/ml with S9 mix; therefore, mutagenicity was not evaluated at these concentrations. A yellow precipitate was seen at concentrations $\geq$50 μg/ml. Positive, negative, and vehicle control values were appropriate. **There was no evidence of induced mutant colonies over background either with or without S9 mix at any concentration evaluated in this study.**

In a chromosomal aberration study (MRID 00153770), Chinese hamster ovary (CHO) cells were exposed to AC 92,533 (pendimethalin, 92.2%, Lot #AC3528-129-1) at dose levels ranging from 5 to 25 μg/plate with or without rat liver S9 and at 12.5 to 100 μg/ml with rat liver S9. **There was no induction of chromosomal aberrations in CHO cells at dose levels of up to 25 μg/plate without S9 and up to 100 μg/ml with S9.**

In a mouse micronucleus study (MRID 42027801), AC 92,533 (pendimethalin, 92.98%, Lot #AC6539-77A) was administered to 5 male and 5 female ICR mice by gavage at dose levels of 313,625 or 1250 mg/kg. Administration of AC 92,533 did not cause a significant increase in the frequency of micronucleated polychromatic erythrocytes (MPEs) in bone marrow cells harvested 24, 48, or 72 hours posttreatment. Deaths and other signs of compound toxicity

were seen in high-dose males and females. although there was no evidence of a cytotoxic effect on the target organ (bone marrow cells), the findings of overt toxicity at 1250 mg/kg (80% of the LD_{50}) clearly indicated that the maximum tolerated dose was achieved. Therefore, **AC 92,533 was adequately tested and found to be nonclastogenic in the mouse micronucleus assay.**

In an alkaline elution assay (MRID 43135007), three rats per dose per sacrifice time were given single i.p. doses of pendimethalin (90.7%, Lot #AC8088-149) at 1250, 2500 or 5000 mg/kg/body weight. (The alkaline elution assay detects DNA single strand breaks and DNA/DNA and DNA/protein crosslinks). The test compound was delivered in corn oil. Testicular cells were harvested 2, 6 and 24 hours after treatment. At the 6 hr sacrifice time, all rats receiving 2500 or 5000 mg/kg were lethargic while those receiving 1250 mg/kg appeared normal. At 24 hr, rats receiving 5000 mg/kg appeared lethargic and ungroomed with dehydrated intestinal tissue while all other rats at lower doses appeared normal. No testicular cell cytotoxicity as measured by trypan blue exclusion was evident at any test material dost or sacrifice time. All positive and vehicle control rats appeared normal at all sacrifice times and no testicular cytotoxicity was seen. **There was no evidence of DNA single strand break induction or DNA/DNA or DNA/protein crosslink formation at any dose or sacrifice time.**

g. Metabolism

In a metabolism study (MRID 00046275), when [^{14}C]pendimethalin was administered to rats, about 70% of the radioactivity was excreted in the feces and 20% in the urine within 24 hours. The excretion of radioactivity in the urine peaked at 6 to 12 hours wherein 11.2% of the dose was excreted. The maximum residual radioactivity in the tissues was found in the 6-hour samples (except for fat at 12 hours). The levels of radioactivity detected in liver, kidney, muscle, fat, and blood at 6 hours were 29.8, 16.9, 1.3, 12.2, and 5.4 ppm, respectively. Within 96 hours, the radioactivity found in the tissues was 0.3 ppm or less, except for fat which was 0.9 ppm. The major portion of the radioactivity that was excreted in the feces was identified as the parent compound. Pendimethalin is metabolized in rats mainly through oxidation of the 4-methyl group attached to the benzene ring as well as oxidation of the alkyl side chain of the N-substituted dinitroaniline compound. Pendimethalin is rapidly eliminated from the body with 70% being excreted in the feces primarily unchanged as parent compound and 20% in the urine within 24 hours. It is mainly metabolized through oxidation of the 4-methyl group on the benzene ring and the alkyl side chain.

h. Toxicological Endpoints of Concern Identified for Use in Risk Assessment

The Health Effects Division's Toxicological Endpoint Selection Committee (TESC), Cancer Peer Review Committee (CPRC) and Reference Dose Committee (RfD Committee)

considered the toxicity data available for pendimethalin. Based upon a review of the toxicology database for pendimethalin, toxicology endpoints and dose levels of concern have been identified for use in risk assessments corresponding to the categories below (TES report date 1/17/96, CPRC report date 7/24/92, RfD report date 2/6/96).

RfD: HED RfD/Peer Review Committee established the RfD for pendimethalin at 0.13 mg/kg/day (HED RfD Report, 2/6/96). An uncertainty factor (UF) of 100 was used to account for both the interspecies and intraspecies variability. The NOEL from the chronic toxicity study in dogs is 12.5 mg/kg/day. The LOEL of 50 mg/kg/day, was based on increased alkaline phosphatase activity in the blood, increased liver weight and hepatic pathology including inflammation and hemosiderosis.

Cancer Classification and Basis: The chemical has been classified as a "Group C", possible human carcinogen, "based on statistically significant increased trend and pairwise comparison between the high dose group and controls for thyroid follicular cell adenomas in male and female rats". For the purpose of risk assessment, the RfD approach will be used for quantification of chronic human risk (HED report dated July 24, 1992). The RfD committee (meetings dated 11/20/95 and 1/5/96) determined that the hypothesis that thyroid tumors associated with pendimethalin are due to a thyroid-pituitary imbalance can be supported.

Acute Dietary: There are no toxicologic endpoints of concern for acute dietary risk. Therefore, this risk assessment is not required.

Short Term Occupational and Residential (one to seven days): In a 21-day dermal toxicity study (MRID 00026663), in rabbits, AC92,553 (pendimethalin) was dermally applied to the back of 3 or 4 New Zealand white rabbits/group at dose levels of 0, 250, 500 or 1000 mg/kg/day. There were no adverse effects with respect to mortality, food and water intake, hematology, urinalysis and gross and microscopic pathology. The systemic LOEL was not determined. The systemic NOEL is greater than 1000 mg/kg/day.

This risk assessment is not required.

Intermediate Term Occupational and Residential (one week to several months): In a 2-year oral study in dogs (MRID 00058657), pendimethalin (AC 92,533, 91.4%, Lot 77-02) was administered via capsule to groups of 4/sex beagle dogs at dose levels of 0, 12.5, 50 or 200 mg/kg/day.

Serum alkaline phosphatase (SAP), liver weight and inflammation and hemosiderosis of the liver were increased at 50 mg/kg/day and above. Yellow color of the hair was observed in all treated dogs. The LOEL is 50 mg/kg/day based on increased SAP, liver weights and liver pathology. The NOEL is 12.5 mg/kg/day.

Although this is a chronic dog study it is felt that the study is appropriate for intermediate term exposures since some effects relating to thyroid endocrine disruption occur in other studies at 31 mg/kg/day and progress in severity at 51 mg/kg/day and are observed as early as 15 to 28 days.

Endpoint and dose for use in risk assessment: 12.5 mg/kg/day (to be used with 10 % dermal absorption rate) from the chronic dog study is the NOEL. An MOE of 100 is considered adequate. The effects observed at 50 mg/kg/day and higher include increased alkaline phosphatase activity in the blood, increased liver weight and hepatic pathology including inflammation and hemosiderosis. Effects observed at similar doses at earlier time points, in special hormonal rat studies, included thyroid endocrine changes and increased liver weight as described above.

This risk assessment is required.

Chronic Occupational or Residential Exposure (90 Days or more): Endpoint and dose for use in risk assessment: The same endpoint will be used as was used for the Intermediate Term Endpoint (see above). This is the same NOEL used for the RfD.

This risk assessment is required.

Inhalation Occupational or Residential Exposure: There are no inhalation endpoints of concern. Therefore, this risk assessment is not required.

Dermal Absorption: There were no dermal absorption studies and no appropriate toxicity studies available to allow an estimation of the dermal absorption by a route to route comparison of toxicity. However, structurally related chemicals: oryzalin, trifluralin and ethalfluralin have dermal absorption studies (in monkeys) indicating that absorption is 2.3%, ~1%, and 2.8% percent, respectively. The solubilities (water) for pendimethalin and related chemicals, oryzalin, ethalflualin and trifluralin are similar: 0.5 ppm, 2.5 ppm, 0.3 ppm and < 1 ppm, respectively. Therefore, for risk characterization purposes, it is estimated that absorption for pendimethalin will be no greater than 10%.

i. Incidence Reports

A search in the Office of Pesticide Programs' Incident Data System (2/28/96) indicated 12 reports with 3 of these involving 5 humans (the remainder concern fish, wildlife or domestic animals). The symptoms included signs of systemic illness: vomiting, diarrhea, chills and shakiness. Three people were hospitalized when they were exposed to a mixture of pesticides including pendimethalin and nitrogen. The data base does not indicate the associated use patterns or activities in which the poisoned individuals were involved.

The California Pesticide Illness Surveillance Program for 1982-1992 contained six reports. In three the effects were systemic (vomiting, diarrhea, etc.), two had skin effects, and one involved eye effects.

Pendimethalin ranked 41st on a list of the top 200 active ingredients for which the National Pesticide Telecommunications Network (NPTN) received calls during 1982-1991. There were 682 calls, with 91 concerning human poisoning due to pendimethalin. HED has requested more details on the NPTN reports for review.

2. Exposure Assessment

a. Registered Uses

i. Agricultural food/feed

Pendimethalin [N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine] is a herbicide registered for use on numerous food/feed crops. Pendimethalin is manufactured by American Cyanamid Co. under the trade names Pentagon®, Prowl®, Pursuit®, and Squadron®. Formulations registered for food/feed uses include emulsifiable concentrates (EC), soluble concentrates/liquid (SC/L), Granulars (G) and water dispersable granules (WDG) or dry flowables (DF). Pendimethalin is applied to soil as preplant, preemergence, and postemergence applications, including at layby, with ground or aerial equipment.

A REFs search conducted 9/14/95 indicated that there are eight pendimethalin end-use products (EPs) with food/feed uses registered to American Cyanamid Co. These EPs are presented in Table 2 below.

Table 2. End-Use Products Registered to American Cyanamid Co.

EPA Reg. No.	Acceptance Date	Formulation Class	Product Name
241-243	7/95	4 lb/gal EC	Prowl® Herbicide
241-244	2/87	3 lb/gal EC	Prowl® 3E Herbicide
241-268	7/95	60% WDG	Pentagon® DG Herbicide
241-297	2/91	2 lb/gal SC/L	Squadron® Herbicide
241-315	1/93	2.7 lb/gal EC	Pursuit® Plus Herbicide
241-327	2/95	2 lb/gal SC/L	Squadron® Herbicide
241-331	10/95	3 lb/gal EC	Pursuit® Plus EC Herbicide
241-337*	5/95	3.3 lb/gal EC	Prowl® 3.3 EC Herbicide

* Including SLN Nos. ID930012, MT930003, NV920004, NY940003, OR930001, OR930002, UT920004, WA920015, WA920034, WY920005.

ii. Agricultural and Residential non-food

Products containing pendimethalin are intended for both occupational and homeowner uses. Pendimethalin is used on landscape and grounds plantings, ornamentals, turfgrass (residential, golf-course, landscape, and sod-farms). Homeowners use pendimethalin to control weeds on lawns, including spot treatment. Treatments are also made to homeowner lawns, landscape and grounds and golf courses by commercial applicators/sprayers. Large scale applications of pendimethalin are made to ornamental crops. Other ways of applying pendimethalin include backpack sprayer, low pressure hand wand (spot treatment), ground boom, or broadcast spreader.

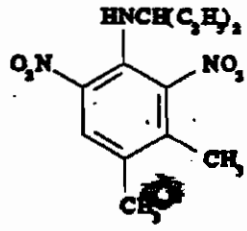
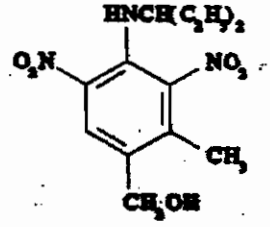
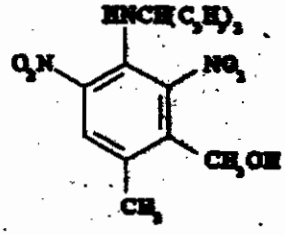
b. Dietary Exposure

i. Residue Chemistry Regulatory Background

The Pendimethalin Guidance Document was issued 3/85. Pendimethalin was the subject of a Reregistration Standard Update issued 4/13/90. These documents summarized regulatory conclusions regarding the available residue chemistry data. The 1990 Update specified that additional data were required for reregistration purposes. Several submissions of data have been received since the Update. The information contained in this document outlines the current Residue Chemistry Science Assessments with respect to the reregistration of pendimethalin.

Tolerances of 0.1 ppm (except 0.05 ppm for rice grain) are established for the combined residues of pendimethalin [N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine] and its metabolite 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol in/on beans, corn (field and fresh), cottonseed, onions (dry bulb), peanuts, potatoes, grain sorghum, soybeans, sugarcane, and sunflower seeds [40 CFR §180.361(a)]. A tolerance of 0.25 ppm has been established for the combined residues of pendimethalin and its metabolites 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol and 3-[(1-ethylpropyl)amino]-6-methyl-2,4-dinitrobenzyl alcohol in/on peanut hulls [40 CFR §180.361(b)]. A tolerance with regional registration of 0.1 ppm has been established for the combined residues of pendimethalin and its metabolite 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol in/on garlic [40 CFR §180.361(c)]. The molecular structures of pendimethalin and currently regulated metabolites are depicted in Table 3 below.

Table 3. Chemical names and structures of pendimethalin and its metabolites.

Common/Chemical Names	Structures
Pendimethalin N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine	
3,5-Dinitrobenzyl alcohol metabolite 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol	
2,4-Dinitrobenzyl alcohol metabolite 3-[(1-ethylpropyl)amino]-6-methyl-2,4-dinitrobenzyl alcohol	

The Agency has recently updated the Livestock Feeds Table [Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Table II (September, 1995)]. Additional residue data are now required for some commodities as a result of changes in Table II; these data requirements have been incorporated into this document. These new data requirements will be imposed at the issuance of the Pendimethalin RED but should not impinge on the reregistration eligibility decision for pendimethalin. The need for additional tolerances and for revisions to exposure/risk assessments will be determined upon receipt of the required residue chemistry data.

ii. Summary of Science Findings

GLN 171-4 (a): Plant Metabolism

The qualitative nature of the residue in plants is understood based on adequate studies conducted with [^{14}C]pendimethalin on potatoes and sweet corn. The results of these studies are supported by additional corn, cotton, dry bean, lima bean, peanut, potato, red table beet, rice, snapbean, soybean, sugarcane, and wheat metabolism data. Pendimethalin *per se* and its 3,5-dinitrobenzyl alcohol metabolite are the residues of concern.

The current tolerance expressions specify the combined residues of pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite and, for peanut hulls, the 2,4-dinitrobenzyl alcohol metabolite as well.

GLN 171-4 (b): Animal Metabolism

Adequate goat and poultry metabolism studies are available. The Agency has determined that there is no reasonable expectation of finite pendimethalin residues of concern in animal commodities (40 CFR §180.6(a)(3)). No additional animal metabolism, analytical methods, storage stability, and magnitude of the residue data are required. Tolerances for pendimethalin residues of concern in livestock commodities are not needed.

GLN 171-4 (c) and (d): Residue Analytical Methods-Plants and Animals

Adequate methods are available for data collection and tolerance enforcement. Methods I through IV in PAM Vol. II are gas chromatography/electron capture (GC/ECD) methods. Methods used for data collection are essentially the same as the PAM Vol. II methods.

Radiovalidation data using samples from the potato metabolism study remain outstanding and are considered confirmatory.

The FDA PESTDATA database dated 1/94 (PAM Volume I, Appendix I) indicates that pendimethalin is completely recovered (>80%) by Multiresidue Methods Section 302 (Luke method; Protocol D) and 303 (Mills, Onley, Gaither method; Protocol E, nonfatty), and partially recovered (50-80%) by Multiresidue Method Section 304 (Mills fatty food method; Protocol E, fatty).

GLN 171-4 (e): Storage Stability

HED concludes that available storage stability data on almonds (representative of oilseeds), alfalfa seed (representative of non-oily seeds), onions, potatoes, soybean forage and hay,

wheat straw, and alfalfa forage and hay adequately support the plant magnitude of the residue data. No additional storage stability data are required.

GLN 171-4 (k): Magnitude of the Residue in Plants

The reregistration requirements for magnitude of the residue in/on beans (succulent and dry); bean forage; bean fodder; corn stover (fodder); corn forage; field corn; pop corn; sweet corn (K+CWHR); cottonseed; garlic; onions (dry bulb); peanuts; peanut hay; potatoes; rice grain; rice straw; sorghum stover (fodder); sorghum forage; grain sorghum; soybeans; soybean forage; soybean hay; sugarcane; and sunflower seeds have been satisfied. Tobacco magnitude of the residue remain outstanding and are considered confirmatory.

Pendimethalin residue data requirements for cotton gin byproducts which result from changes in the Livestock Feeds Table (Table II (September, 1995)) should be imposed at this time. However, this requirement should not impinge on the reregistration eligibility decision for pendimethalin. The need for additional tolerances and revisions to the exposure/risk assessments will be made upon receipt and evaluation of required data.

GLN 171-4 (l): Magnitude of the Residue in Processed Food/Feed

Adequate data are available to demonstrate that pendimethalin residues of concern do not concentrate in commodities derived from corn, cottonseed, peanuts, potatoes, soybeans, sugarcane, and sunflower seeds. Rice processing data remain outstanding and are considered confirmatory.

GLN 171-4 (j): Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

The Agency has determined that there is no reasonable expectation of finite pendimethalin residues of concern in animal commodities (40 CFR §180.6(a)(3)). Therefore, livestock feeding studies and tolerances on livestock commodities are not required.

GLNs 165-1 and 165-2: Confined/Field Rotational Crops

The available confined rotational crop study is not adequate. A new confined rotational crop study is required. This, however, will not preclude the reregistration of pendimethalin.

c. Occupational and Residential Exposure

An occupational and/or residential exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete.

Handler (Mixer/Loader/Applicator) Exposures and Assumptions

HED has determined that there is potential exposure to persons handling pendimethalin. Handler exposures may occur to:

- Occupational handlers involved in food, feed, fiber, ornamental, turf, rights-of-way and other noncrop treatments, and
- Homeowner handlers making applications to residential turf.

No handler exposure studies were conducted by the Registrant for pendimethalin.

HED has determined that there is potential exposure to mixers, loaders, applicators, or other handlers during usual use-patterns associated with pendimethalin. Based on the use patterns and potential exposures described above, thirteen major exposure scenarios were identified for pendimethalin: (1a) mixing/loading water-dispersible granulars (dry flowables) for rights-of-way sprayers; (1b) mixing/loading water-dispersible granulars (dry flowables) for groundboom applications; (2) mixing/loading wettable powders for groundboom application (Note: all currently registered wettable powder end-use products are packaged in water soluble packets); (3) loading granulars for solid-broadcast applications; (4a) mixing/loading liquid for aerial applications and irrigation systems (the mixer/loader scenario for aerial and irrigation applications were combined since they use the same mixing/loading techniques and similar acres treated and application rates); (4b) mixing/loading liquid formulations for rights-of-way spraying; (4c) mixing/loading liquid formulations for groundboom applications or to impregnate dry bulk fertilizer. (Note: impregnating dry bulk fertilizer is included in this scenario since the daily amount of liquid formulation handled would be approximately the same as the amount handled to support groundboom applications); (5) applying as a spray with aerial (fixed wing) equipment; (6) applying as a spray with rights-of-way equipment; (7) applying as a spray with groundboom equipment; (8) applying granulars with a tractor-drawn broadcast spreader; (9) flagging during aerial spray application; (10) mixing/loading/applying as a spray with backpack sprayer; (11) mixing/loading/applying with a low-pressure handwand sprayer; (12) mixing/loading/applying with a push-type granular broadcast spreader; and (13) mixing/loading/applying using a high-volume turf sprayer (similar to those used for turfgrass applications by commercial handlers).

Daily dermal exposure is calculated using the following formula:

Daily Exposure (mg ai/day) =

Unit Exposure (mg ai/lb ai) x Use Rate (lb ai/A or lb ai/gallon) x Daily Area Treated (A/day)

The dermal absorption value (10%) was applied to the Daily Dermal Exposure to find the Daily Dermal Dose.

Daily Systemic Dose Due to Dermal Exposure is calculated using the following formula:

Daily Systemic Dermal Dose (mg ai/kg bw/day) =

*Unit Exposure (mg ai/lb ai) x Use (lb ai/A) x Daily Acres Treated (A/day) / Body Wt (kg) * .10 (dermal absorption rate)*

The following assumptions were made regarding the area treated:

For aerial applications: 800 acres per day (upper-end estimate for field corn, soybeans, and grain sorghum);

For groundboom applications: 80 acres per day;

For rights-of-way applications: 10 acres per day;

For spot treatments using backpack and low-pressure handwand sprayers: 1,000 square feet per day by homeowner applicators and one acre per day by commercial applicators; and

For residential turf applications: one acre per day by homeowner applicators using a broadcast spreader and eight acres per day by commercial applicators using high-volume turf sprayers.

Other assumptions regarding worker exposure include the following:

- Some commercial mixers, loaders, flaggers, and applicators are exposed more than 7 days in a three-month (ninety-day) period (reasonable worse-case estimate). Therefore, the exposure/risk assessment for commercial handlers includes a calculation of intermediate-term exposure (7 or more days per year).

- Aerial applicators are in enclosed cockpits.

- Wettable powder formulations are contained in water-soluble packaging (all currently registered wettable powder products are in water soluble packaging).

- Homeowner handlers would be exposed fewer than 7 days in a three-month (ninety-day) period. Therefore, no exposure/risk assessment for homeowner handlers uses was calculated calculated using the intermediate-term toxicological endpoint.

Table 4. Exposure Scenario Descriptions for Uses of Pendimethalin

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Mixer/Loader Exposure			
Mixing Water Dispersible Granulars (Dry Flowables) (1a and 1b)	PHED V1.1	80 acres groundboom, and 10 acres rights-of-way	Baseline: "Best Available" grades: Hands grades A,B,C, dermal acceptable grades. Hands = 7 replicates; Dermal = 16 to 26 replicates. Low confidence in dermal data. PHED data used for baseline, no protection factors (PFs) were necessary.
Mixing Wettable Powders (Water Soluble Packets) (2)	PHED V1.1	80 acres groundboom	Baseline: "Best Available" grades: Hands, dermal all grades. Hands = 5 replicates; Dermal = 6 to 15 replicates. Low confidence in dermal data. PHED data used for baseline, no PFs were necessary.
Loading Granulars (3)	PHED V1.1	80 acres solid broadcast	Baseline: "Best Available" grades: Hands all grades and dermal acceptable grades. Hands = 10 replicates; Dermal = 29 to 36 replicates. Low confidence in dermal data. PHED data used for baseline, no PFs were necessary.
Mixing Liquid (E.C.) (4a, b, and c)	PHED V1.1	80 acres groundboom, 800 acres aerial, and 10 acres rights-of-way	Baseline: "Best Available" grades: Hands, dermal acceptable grades. Hands = 53 replicates; Dermal = 25 to 122 replicates. High confidence in dermal data. PPE: "Best Available" grades: Hands and dermal acceptable grades. Hands = 59 replicates; Dermal = 25 to 122 replicates. High confidence in dermal data. PHED data used for baseline and PPE, no PFs were necessary.
Applicator Exposure			
Aerial equipment--enclosed cockpit (liquids) (5)	PHED V1.1	800 acres for fixed-wing	Baseline: "Best Available" grades: Hands acceptable grades, dermal grades A,B,C. Hands = 34 replicates; Dermal = 24 to 48 replicates. Medium confidence in dermal data. PHED data used for baseline, no PFs were necessary.
Rights-of-Way (6)	PHED V1.1	10 acres	Baseline: "Best Available" grades: Hands, dermal, acceptable grades. Hands = 16 replicates; Dermal = 16 (no head data) replicates. Low (only because of no head data) confidence in dermal data. PHED data used for baseline, no PFs were necessary.
Groundboom (7)	PHED V1.1	80 acres	Baseline: "Best Available" grades: Hands, dermal acceptable grades. Hands = 29 replicates; Dermal = 32 to 42 replicates. High confidence in dermal data. PHED data used for baseline, no PFs were necessary.
Solid Broadcast Spreader (tractor drawn) (8)	PHED V1.1	80 acres	Baseline: "Best Available" grades: Hands, dermal acceptable grades. Hands = 5 replicates; Dermal = 4 to 5 replicates. Low confidence in dermal data. PHED data used for baseline, no PFs were necessary.
Flagger			
Liquids (9)	PHED V1.1	800 acres	Baseline: "Best Available" grades: Hands, dermal acceptable grades. Hands = 16 replicates; Dermal = 16 to 18 replicates. High confidence in dermal data. PHED data used for baseline, no PFs were necessary.
Mixer/Loader Applicator			
Backpack Sprayer (spot treatment) (10)	PHED V1.1	Homeowner: 1,000ft^2; Occupational: 1 acre	Baseline: "Best Available" grades: Hands and dermal grades A,B,C. Hands = 11 replicates; Dermal = 9 to 11 replicates. Low confidence in dermal data. PHED data used for baseline was derived from single layer clothing and chemical resistant gloves; a 90% PF was used to remove the chemical resistant gloves to simulate a no glove scenario.

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Low Pressure Handwand (11)	PHED V1.1	Homeowner: 1,000ft²; Occupational: 1 acre	Baseline: "Best Available" grades: Hands, dermal all grades. Hands = 70 replicates; Dermal = 25 to 96 replicates. Low confidence in both dermal data. PPE: "Best Available" grades: Hands acceptable grades, dermal all grades. Hands = 15 replicates; Dermal = 25 to 96 replicates. Low confidence in dermal data. PHED data used for baseline and PPE values, no PFs were necessary.
Residential Broadcast Spreader (12)	PHED V1.1	1 acre	Baseline: "Best Available" grades: Hands and dermal grades A,B,C. Hands = 15 replicates; Dermal = 15 (no head data) replicates. Low (no head data) confidence in dermal data. PHED data used for baseline, no PF were necessary.
High Volume Turf Sprayer (13)	PHED V1.1	8 acres	Baseline: "Best Available" grades: Hands and dermal all grades. Hands = 14 replicates; Dermal = 14 (no head data) replicates. Low confidence in dermal data. PHED data used for baseline was derived from single layer clothing and chemical resistant gloves; a 90% PF was used to remove the chemical resistant gloves to simulate a no glove scenario.

a Standard Assumptions based on an 8-hour work day as estimated by HED. BEAD data were not available.

b "Best Available" grades are defined by HED SOP for meeting Subdivision U Guidelines. Best available grades are assigned as follows: matrices with grades A and B data and a minimum of 15 replicates; if not available, then grades A, B, and C data and a minimum of 15 replicates; if not available, then all data regardless of the quality and number of replicates. Data confidence are assigned as follows:

High = grades A and B and 15 or more replicates per body part
Medium = grades A, B, and C and 15 or more replicates per body part
Low = grades A, B, C, D, and E or any combination of grades with less than 15 replicates

Postapplication Exposures and Assumptions

HED has determined that there is potential exposure to persons entering treated sites after application is complete. Post-application exposures may occur to:

- Agricultural workers following applications to commercial or research food, feed, fiber, ornamental, and turf crops during routine crop-production tasks, such as planting, transplanting, incorporation, cultivation, hoeing, scouting, thinning, and harvesting;

- Mowers and other golf-course maintenance workers following applications to turfgrass on golf courses;

- Landscape and grounds maintenance workers following applications to commercial landscape plantings;

- Workers following applications in rights-of-way and other noncrop areas; and

- Persons, including children, following applications to residential turf or ornamental plantings.

No postapplication studies have been conducted by the Registrant for pendimethalin.

3. Risk Characterization

a. Dietary Risk

Food uses evaluated in the Dietary Risk Evaluation System (DRES) analysis were the published uses of pendimethalin listed in 40 CFR § 180.361 and the Tolerance Index System (TIS). The analysis used tolerance level residues for commodities with registered pendimethalin tolerances.

Reassessed Tolerances:

In the Product and Residue Chemistry Chapter of the Reregistration Eligibility Document (B. Cropp-Kohlligian, 12/12/95), HED recommended that tolerances for residues of pendimethalin on rice be increased from 0.05 ppm to 0.1 ppm due to the analytical method's limit of quantification for the combined residues of pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite. In the same memo, HED recommended that the tolerance for onions (dry bulb) be applied to shallots (dry bulb only).

In the DRES analysis, both rice and dry bulb shallots were included at these recommended tolerance levels. See Table 1 within Attachment 3, Dietary Risk Assessment, for all the commodities and tolerances included in this analysis.

Results

In order to estimate a worst case chronic dietary risk from uses being supported in reregistration, tolerance level residues were used in the analysis to calculate a Theoretical Maximum Residue Contribution (TMRC). These exposure estimates were then compared to the RfD for pendimethalin for chronic dietary risk. See Tables 2 and 3 within Attachment 3, Dietary Risk Assessment, for a summary of the TMRCs and percentages of the RfD.

Chronic Exposure from Pendimethalin for Reregistration

The Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population from all currently published tolerances are listed below. See also Table 3 within Attachment 3, Dietary Risk Assessment.

Subgroup	Exposure	% Reference Dose
U.S. population	0.000319	0.25
Children (1-6)	0.000693	0.53

The DRES analysis for the published uses and reassessed tolerances of pendimethalin indicate that the overall U.S. population would receive 0.25 percent of the RfD and the highest subgroup, children ages 1-6 years, would receive 0.53 percent of the RfD. Therefore, the chronic dietary risk posed from pendimethalin is not of concern for the reregistration scenario.

b. Occupational and Residential Risk

Table 5 below shows the estimated exposure and risks for individuals using pendimethalin in both residential and occupational settings. Estimated unit dermal exposure values (mg/kg/lb ai) for each task were obtained from the Pesticide Handler's Exposure Database (PHED), Version 1.1. The unit exposure value was used to find the absorbed daily dose and a corresponding margin of exposure (MOE) for each use, based on the intermediate-term (12.5 mg/kg/day) endpoint of concern (equations used to find daily exposures are presented in the previous section on occupational and residential exposure assessment). Risk from and intermediate-term (1 week to several months) is presented in terms of the Margin of Exposure (MOE), described below. The Toxicology Endpoint Selection document (TES) for pendimethalin (dated 1/17/96) specified that NO risk assessment was required for inhalation exposure nor for short-term exposure (1 to 7 days); therefore, these exposures were not calculated.

MOEs from intermediate-term exposures were calculated using the following formula:

MOE = NOEL / Total Daily Systemic Dose Due to Dermal Exposure

For pendimethalin, an MOE value of at least 100 is considered adequate.

Table 5. Intermediate-Term Exposure and Risk to Pendimethalin

Exposure Scenario (Scen. #)	Dermal Unit Exposure[a] (mg/lb ai)	Application Rate[b] (lb ai/acre)	Daily Acres Treated[c]	Daily Total Exposure[d] (mg/kg/day)	Intermediate-Term MOE[e]
Mixer/Loader Exposure					
Mixing/Loading Water Dispersible Granulars (Dry Flowables) for Rights-of-Way Spraying (1a)	0.07	3.96	10	0.04	3,125
Mixing/Loading Water Dispersible Granulars (Dry Flowables) for Groundboom Applications (1b)		3.96	80	0.32	347
Mixing/Loading Wettable Powders (water soluble packets) for Groundboom Applications(2)	0.02 (wtr. sol. pk.)	3.0	80	0.07	1,563
Loading Granulars for Solid Broadcast Applications (3)	0.005	3.0	80	0.02	1,563
Mixing/Loading Liquid (E.C.) for Aerial Applications and Irrigation Systems (4a)	2.9	1.98	800	65.66	1.9
Mixing/Loading Liquid (E.C.) for Rights-of-Way Spraying (4b)		4.0	10	1.66	73.5
Mixing/Loading Liquid (E.C.) for Groundboom Applications (4c)		1.98	80	6.56	18.9
Applicator Exposure					
Aerial-Fixed Wing - enclosed cockpit (liquid) (5)	0.005	1.98	800	0.11	962
Rights-of-Way (6)	1.2	4.0	10	0.69	176
Groundboom Tractor (7)	0.015	3.96	80	0.07	1,250
Solid Broadcast Spreader (tractor drawn) (8)	0.01	3.0	80	0.04	1,786
Flagger					
Flagging (liquid) (9)	0.01	1.98	800	0.23	417
Mixer/Loader/Applicator					
Backpack (spot treatment) (10)	2.6	3.96 or 0.09/1000ft²	(H) 1000ft² (O) 1.0	(H) 0.003 (O) 0.15	(O) 735
Low Pressure Handwand (spot treatment) (11)	103.8	3.96 or 0.09/1000ft²	(H) 1000ft² (O) 1.0	(H) 0.13 (O) 5.87	(O) 21
Residential Broadcast Spreader (12)	2.9	3.0	1.0	0.12	1,042
High Volume Turf Sprayer (13)	0.77	3.96	8	0.35	347

a Dermal unit exposures represent long pants, long sleeve shirts, no gloves, open mixing/loading, enclosed cockpit, open cab tractor.

b Application rates were derived from the following labels: EPA Reg. Nos. (E.C.) 241-337 and 241-305, (Granular) 538-188, (WDG) 10404-52, 241-340, and 241-268 (CA only), (WP) 538-195 (water soluble packets only).

c Values represent the area [(H) = homeowner, (O) = occupational] which can be used in a single day to complete treatments for each exposure scenario of concern.

d Daily Total exposure (mg/kg/day) = Daily dermal exposure / 70 kg body weight; where Daily dermal exposure (mg/day) = Exposure (mg/lb ai) * Max. Appl. Rate (lb ai/acre or lb ai/gal) * Max. Treated (acres o gallons of spray solution).

e Intermediate-Term MOE = NOEL (intermediate-term NOEL = 12.5 mg/kg/day) / daily total systemic dose due to dermal exposure (with dermal absorption rate of 10% applied to dermal exposure).

Handler Risk Summary

Exposure and risk for the intermediate-term uses of pendimethalin are summarized in Table 5. Intermediate-term risk was calculated using the 12.5 mg/kg/day endpoint. Intermediate-term use (continuous use for 1 week to several months) is not considered a likely scenario for homeowner uses of pendimethalin; therefore, no intermediate-term MOE was calculated for homeowner uses. Exposure estimates are based on the best available exposure data derived from the Pesticide Handlers Exposure Database (PHED), which varied in quality from high confidence data to low confidence data (see Table 4 for a description of the confidence level associated with exposure data).

Intermediate-term Risk

The calculations indicate that the MOEs for intermediate-term exposures for handlers wearing baseline protection (long-sleeve shirt, long pants, shoes, and socks) are over 100 for all but the following use scenarios: (4a, b, c) mixing/loading liquid formulations for aerial application and irrigation/chemigation systems (MOE=1.9), mixing/loading liquids for groundboom application (MOE=73.5), and mixing/loading liquids for rights-of-way application (MOE=18.9), and mixing, loading, and applying using low-pressure handwand equipment (spot treatment) (MOE=21). The risks to these workers for these scenarios are reduced to an adequate level (MOEs are all above 100) when workers wear additional PPE consisting of chemical-resistant gloves.

Risk From Postapplication Exposures

Exposures following applications to commercial or research food, feed, fiber, turf, and ornamental crops may be mitigated by restricted-entry intervals (REIs). REIs allow sufficient time to pass for field residues to dissipate to levels that result in adequate MOEs for entering workers who contact treated surfaces. However, restricted-entry intervals are generally not feasible as a mitigation measure for post-application homeowner exposures and occupational exposures in noncrop areas (such as rights-of-ways), or in turf- and ornamental-plant settings such as parks and landscape plantings.

Post Application Risk Summary

There are no pendimethalin-specific post-application exposure data available at this time. These chemical-specific data are necessary for HED to establish permanent restricted-entry intervals since an intermediate-term endpoint of concern has been identified. In the absence of available postapplication data for pendimethalin uses, HED has qualitatively analyzed potential post-application exposure and risk based on the nature of pendimethalin use.

HED has concluded that the following characteristics of pendimethalin use indicate a reduced level of concern.

- Pendimethalin use-directions indicate that most applications to food, feed, and fiber crops occur early in the season--preplant, at plant, or preemergent to the weeds. Applications to areas with established plants are usually layby or otherwise directed to avoid contacting crop foliage, thus minimizing worker risk from foliar contact in these crops;

- Most workers entering food, feed, and fiber crops would likely be performing non-hand-labor tasks such as scouting, mechanical incorporation, and mechanical cultivation, given the timing of applications (early season) and the crops involved. Non-hand labor results in much lower direct contact/exposure compared to hand labor tasks. Exceptions include hand-transplanting tobacco and hand-planting or hand-aligning mechanically-planted sugarcane seed pieces in recently treated areas;

- Workers entering rights-of-way and other noncrop areas would likely perform non-hand-labor tasks;

- Landscape and grounds maintenance workers performing tasks in commercial landscape plantings may perform hand-labor tasks, such as hoeing, thinning, or weeding, but exposures to treated surfaces are likely to be infrequent and short in duration;

- Golf course workers may be exposed while mowing, tending greens, or performing other maintenance tasks, but their exposures are likely to be limited and relatively short in duration;

- Persons, including children, may be exposed to treated ornamentals at residential sites, but their exposures are likely to be limited and of short duration.

HED has concluded that the following characteristics of other pendimethalin uses indicate an **increased level of concern.**

- Most applications to ornamentals and turf are to established plants and are often broadcast over the entire ornamental and turf foliage, thus increasing potential exposure risk from foliar contact with such treated foliage;

- Workers entering turf and ornamental production areas following pendimethalin applications may perform hand-labor tasks such as transplanting, harvesting, weeding, or pruning. For these crops, the timing of applications make hand labor activities likely following pendimethalin applications.

- Persons, including children, may be exposed to treated turfgrass (lawns) at residential sites frequently and for relatively long periods of time.

Based upon the above determinations, HED estimates that postapplication risks are not likely to be of concern for the following use-scenarios, **provided workers and others do not enter treated areas immediately following applications:**

- food, feed, and fiber crops, except for sugarcane and tobacco;
- golf-course and turf other than that on sod farms and residential sites;
- ornamental landscape plantings in commercial and residential sites; and
- rights-of-way and other noncrop areas.

However, HED is concerned about the postapplication risks at the following use-sites:

- tobacco and sugarcane (hand-transplanting tobacco and hand-planting or hand-aligning mechanically-planted sugarcane only);
- ornamentals grown for commercial (or research) purposes; and
- turf on sod farms and at residential sites.

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THE EFFECTS OBSERVED IN THE DOG STUDY SELECTED FOR RISK CHARACTERIZATION OF INTERMEDIATE EXPOSURE SCENARIOS DEMONSTRATE ACTUAL LIVER PATHOLOGY AT THE LOEL DOSE LEVEL. HOMEOWNER TURF EXPOSURE PATTERNS INDICATE THE LIKELIHOOD OF EXPOSURE TO INFANTS AND CHILDREN. THEREFORE, HED RECOMMENDS DISCUSSION WITH SRRD AND/OR THE REGISTRANT TO DETERMINE IF THIS USE SHOULD BE REREGISTERED.

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4. HED Recommendations for Risk Mitigation/Reduction

a. Tolerance Reassessment Summary

Tolerances for pendimethalin residues are currently expressed in terms of the combined residues of pendimethalin and its metabolite 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol [§180.361(a and c)] and, for peanut hulls only, in terms of the parent and aforementioned metabolite plus the metabolite 3-[(1-ethylpropyl)amino]-6-methyl-2,4-dinitrobenzyl alcohol [40 CFR §180.361(b)].

A summary of the pendimethalin tolerance reassessment and recommended modifications in commodity definitions are presented in Table 6.

Tolerances Listed Under 40 CFR §180.361(a)

Adequate data are available to reassess the established tolerances for pendimethalin residues in/on beans; bean forage; bean fodder; corn fodder; corn forage; corn grain; sweet corn; cottonseed; onions (dry bulb); peanuts; peanut hay; potatoes; sorghum fodder; sorghum forage; grain sorghum; soybeans; soybean forage; soybean hay; sugarcane; and sunflower seeds. [Note: Some commodity definitions must be corrected. See Table 6 for details.]

The tolerance for pendimethalin residues in/on peanut forage should be revoked since peanut forage is no longer considered to be a significant feed item according to the Livestock Feeds Table (Table II (September 1995)).

Available rice field trial data are deemed adequate to support the reregistration of pendimethalin for use on rice. The currently established tolerance on rice grain should be increased from 0.05 ppm to 0.1 ppm. A processing study on rice grain is outstanding.

Tolerances Needed Under 40 CFR §180.361(a)

Available rice field trial data are deemed adequate to support the reregistration of pendimethalin for use on rice. A tolerance for pendimethalin residues of concern in/on rice straw must be established. Available data indicate that a tolerance of 0.1 ppm would be appropriate.

As a result of changes in the Livestock Feeds Table (Table II (September 1995)), the Agency currently considers cotton gin byproducts a raw agricultural commodity (RAC). Data depicting pendimethalin residues of concern in/on cotton gin byproducts resulting from the maximum registered use of pendimethalin to cotton are hereby required. On receipt of the required cotton gin byproducts data, the need for tolerances for pendimethalin residues of concern will be determined.

Tolerances Listed Under 40 CFR §180.361(b)

The tolerance for residues in/on peanut hulls should be revoked since peanut hulls is no longer considered a significant feed item according to the Livestock Feeds Table (Table II (September 1995)).

Tolerances Listed Under 40 CFR §180.361(c)

HED concludes that available garlic magnitude of the residue data from field trials conducted in CA and OR are adequate to support a national registration for the use of pendimethalin on garlic and recommends that the currently established tolerance with regional registrations for pendimethalin residue of concern in/on garlic should be changed to a tolerance without regional registrations at the same level (0.1 ppm) and listed under 40 CFR §180.361(a).

Table 6. Tolerance Reassessment Summary for Pendimethalin.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Tolerances listed under 40 CFR §180.361(a):			
Beans, lima (dry,snap)	0.1	0.1	*Beans, succulent and dry*
Beans, forage	0.1	0.1	
Beans, hay	0.1	0.1	
Corn, fodder	0.1	0.1	*Corn, stover*
Corn, forage	0.1	0.1	
Corn, grain	0.1	0.1	*Corn, field* and *Corn, pop*
Corn, fresh (including sweet, K+CWHR)	0.1	0.1	*Corn, sweet (K+CWHR)*
Cottonseed	0.1	0.1	*Cotton, undelinted seed*
Onions, dry bulb	0.1	0.1	
Peanuts	0.1	0.1	
Peanut, hay	0.1	0.1	
Peanut, forage	0.1	Revoke	No longer listed in Livestock Feeds Table (Table II (September 1995)) as a significant feed item
Potatoes	0.1	0.1	
Rice, grain	0.05	0.1	The tolerance level must be increased to the analytical method's limit of quantitation (LOQ) for the combined residues of pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite.
Sorghum, fodder	0.1	0.1	*Sorghum, stover*
Sorghum, forage	0.1	0.1	
Sorghum, grain	0.1	0.1	
Soybeans	0.1	0.1	
Soybeans, forage	0.1	0.1	
Soybeans, hay	0.1	0.1	
Sugarcane	0.1	0.1	
Sunflower, seeds	0.1	0.1	

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Tolerances needed under 40 CFR §180.361(a):			
Cotton, gin byproducts	None	TBD[a]	Residue data are required.
Rice, straw	None	0.1	
Tolerances listed under 40 CFR §180.361(b):			
Peanut, hulls	0.25	Revoke	No longer listed in Livestock Feeds Table (Table II (September 1995)) as a significant feed item
Tolerances listed under 40 CFR §180.361(c):			
Garlic	0.1	0.1	HED hereby recommends that this tolerance should be listed under 40 CFR §180.361(a)

[a] TBD = To be determined. Reassessment of tolerance(s) cannot be made at this time because residue data are required.

b. CODEX Harmonization

There are no established or proposed Codex MRLs for pendimethalin residues. Therefore, there are no questions of compatibility with respect to Codex MRLs and U.S. tolerances.

c. Occupational/Residential Labeling Rationale

The Worker Protection Standard (WPS)

Scope of the WPS

The 1992 Worker Protection Standard for Agricultural Pesticides (WPS) established certain worker-protection requirements (personal protective equipment, restricted-entry intervals, etc.) to be specified on the label of all products that contain uses within the scope of the WPS. Uses within the scope of the WPS include all commercial (non-homeowner) and research uses on farms, forests, nurseries, and greenhouses to produce agricultural plants (including food, feed, and fiber plants, trees, turf grass, flowers, shrubs, ornamentals, and seedlings). Uses within scope include not only uses on plants, but also uses on the soil or planting medium in which the plants are (or will be) grown.

At this time some of the registered uses of pendimethalin are within the scope of the Worker Protection Standard for Agricultural Pesticides (WPS). Uses that are outside the scope of the WPS include use:

- on plants that are in ornamental gardens, parks, golf courses, and public or private lawns and grounds and that are intended only for decorative or environmental benefit. (However, pesticides used on sod farms ARE covered by the WPS).
- in a manner not directly related to the production of agricultural plants, including, for example, control of vegetation along rights-of-way and in other noncrop areas.

Compliance With the WPS

Any product whose labeling can be reasonably interpreted to permit use in the production of an agricultural plant on any farm, forest, nursery, or greenhouse must comply with the labeling requirements of PR Notice 93-7, "Labeling Revisions Required by the Worker Protection Standard (WPS)," and PR Notice 93-11, "Supplemental Guidance for PR Notice 93-7," which reflect the requirements of EPA's labeling regulations for worker protection statements (40 CFR part 156, subpart K). These labeling revisions are necessary to implement the Worker Protection Standard for Agricultural Pesticides (40 CFR part 170) and must be completed in accordance with, and within the deadlines specified in, PR Notices 93-7 and 93-11. Unless otherwise specifically directed in this RED, all statements required by PR Notices 93-7 and 93-11 are to be on the product label exactly as instructed in those notices.

- *After April 21, 1994, except as otherwise provided in PR Notices 93-7 and 93-11, the labeling of all products within the scope of those notices must meet the requirements of the notices when the products are distributed or sold by the primary registrant or any supplementally registered distributor.*

- *After October 23, 1995, except as otherwise provided in PR Notices 93-7 and 93-11, the labeling of all products within the scope of those notices must meet the requirements of the notices when the products are distributed or sold by any person.*

Personal Protective Equipment/Engineering Controls for Handlers

For each end-use product, PPE requirements for pesticide handlers are set during reregistration in one of two ways:

1. If EPA determines that no regulatory action must be taken as the result of the acute effects or other adverse effects of an active ingredient, the PPE for pesticide handlers will be based on the acute toxicity of the end-use product. For occupational-use products, PPE must be established using the process described in PR Notice 93-7 or more recent EPA guidelines.

2. If EPA determines that REGULATORY ACTION ON AN ACTIVE INGREDIENT MUST BE TAKEN as the result of very high acute toxicity or to certain other adverse effects, such as allergic effects or delayed effects (cancer, developmental toxicity, reproductive effects, etc.):

- *In the RED for that active ingredient, EPA may establish minimum or "baseline" handler PPE requirements that pertain to all or most end-use products containing that active ingredient.*
- *These minimum PPE requirements must be compared with the PPE that would be designated on the basis of the acute toxicity of the end-use product.*
- *The more stringent choice for each type of PPE (i.e., bodywear, hand protection, footwear, eyewear, etc.) must be placed on the label of the end-use product.*

Personal protective equipment requirements usually are set by specifying one or more pre-established PPE units – sets of items that are almost always required together. For example, if chemical-resistant gloves are required, then long-sleeve shirts, long pants, socks, and shoes are assumed and are also included in the required minimum attire. If the requirement is for two layers of body protection (coveralls over a long- or short-sleeve shirt and long or short pants), the minimum must also include (for all handlers) chemical-resistant footwear and chemical-resistant headgear for overhead exposures and (for mixers, loaders, and persons cleaning equipment) chemical-resistant aprons.

Occupational-Use Products

HED has determined that regulatory action regarding the establishment of active-ingredient-based minimum PPE requirements for occupational handlers must be taken for pendimethalin for certain handler use-situations. The MOE's were less than 100 for certain occupational handler (mixers, loaders, and applicators) use-scenarios, unless chemical-resistant gloves were used in addition to the baseline protection of long-sleeve shirt, long pants, shoes, and socks. HED is requiring active-ingredient-based protections for handlers of pendimethalin in these exposure situations: (1) mixing and loading emulsifiable concentrate formulations and (2) mixing, loading, and applying using low-pressure handwand equipment. In addition, since wettable powder formulations are currently contained in water-soluble packaging and HED's exposure and risk assessments were based on that assumption, HED will require wettable powder formulations of pendimethalin to be contained in water-soluble packaging. If the Registrant intends to register any wettable powder product not contained in water-soluble packaging, HED must first conduct an exposure risk assessment to determine if mitigation measures such as PPE would be necessary.

WPS and NonWPS Uses: Since potential handler exposure is similar for WPS and nonWPS uses, there is only one set of active-ingredient-based minimum (baseline) PPE requirements for occupational uses of pendimethalin (specified in Section V). These requirements must be followed in the labeling of all pendimethalin end-use products intended primarily for occupational use.

Homeowner-Use Products

HED is not establishing minimum (baseline) handler PPE for pendimethalin end-use products that are intended primarily for homeowner use, because the HED has determined that the frequency, duration, and degree of exposure by such handlers do not warrant such risk mitigation measures.

Postapplication/Entry Restrictions

Occupational-Use Products (WPS Uses)

Restricted-Entry Interval:

Under the Worker Protection Standard (WPS), interim restricted-entry intervals (REI's) for all uses within the scope of the WPS are based on the acute toxicity of the active ingredient. The toxicity categories of the active ingredient for acute dermal toxicity, eye irritation potential, and skin irritation potential are used to determine the interim WPS REI. If one or more of the three acute toxicity effects are in toxicity category I, the interim WPS REI is established at 48 hours. If none of the acute toxicity effects are in category I, but one or more of the three is classified as category II, the interim WPS REI is established at 24 hours. If none of the three acute toxicity effects are in category I or II, the interim WPS REI is established at 12 hours. A 48-hour REI is increased to 72 hours when an organophosphate pesticide is applied outdoors in arid areas. In addition, the WPS specifically retains two types of REI's established by the Agency prior to the promulgation of the WPS: (1) product-specific REI's established on the basis of adequate data, and (2) interim REI's that are longer than those that would be established under the WPS.

During the reregistration process, EPA considers all relevant product-specific information to decide whether there is reason to shorten or lengthen the previously established REI.

By default, PR Notice 93-7 specifies a 12 hour interim REI currently in effect. EPA notes that the 12-hour interim WPS REI was established because data indicated that pendimethalin was in toxicity category III/IV for acute dermal toxicity, skin irritation potential, and eye irritation potential.

During the reregistration process, HED has determined that the REI established under the WPS should be changed for some uses due to:

-the identification of intermediate toxicity endpoints of concern,
-the potential for significant postapplication worker exposure in certain crops,
-a significant number of reported incidences for pendimthalin,
-an absence of pendimethalin-specific exposure data for all use sites and scenarios, and
-the findings of HED's qualitative analysis of potential post-application exposure risk.

Therefore, HED is now increasing the REI on sugarcane and tobacco from 12 to 24 hours, until postapplication data to set specific REIs for these crops are available. **Thus, HED is establishing an interim 24-hour restricted-entry interval for uses on sugarcane and tobacco of all occupational-use products that contain pendimethalin and have use-directions for food, feed, and fiber crops.**

NOTE: AN INTERIM REI WILL BE ESTABLISHED FOR ORNAMENTAL AND TURFGRASS CROPS WITHIN THE SCOPE OF THE WPS PENDING THE OUTCOME OF THE PROPOSED MEETING WITH THE REGISTRANT.

Early-Entry PPE:

The WPS establishes very specific restrictions on entry by workers to areas that remain under a restricted-entry interval, if the entry involves contact with treated surfaces. Among those restrictions are a prohibition of routine entry to perform hand labor tasks and a requirement that personal protective equipment be worn. Under the WPS, these personal protective equipment requirements for persons who must enter areas that remain under a restricted-entry interval are based on the acute toxicity category of the active ingredient.

During the reregistration process, EPA considers all relevant product-specific information to decide whether there is reason to set personal protective equipment requirements that differ from those set through the WPS.

The RED requirements for early-entry PPE are set in one of two ways:

1. *If EPA determines that no regulatory action must be taken as the result of the acute effects or other adverse effects of an active ingredient, it establishes the early-entry PPE requirements on the basis of the acute dermal toxicity category, skin irritation potential category, and eye irritation potential category of the active ingredient.*

2. *If EPA determines that regulatory action on an active ingredient must be taken as the result of very high acute toxicity or to certain other adverse effects, such as allergic effects or delayed effects (cancer, developmental toxicity, reproductive effects), it may establish early-entry PPE requirements that are more stringent than would be established otherwise.*

Since pendimethalin is classified as category IV for skin irritation potential and IV for acute dermal toxicity, and HED has determined that no regulatory action must be taken due to the acute effects or other adverse effects of pendimethalin, the PPE for dermal protection required for early entry is the minimum early-entry PPE permitted under the WPS. Since pendimethalin is classified as toxicity category III for eye irritation potential, no protective eyewear is required.

WPS Notification Statement:

Under the WPS, the labels of some pesticide products must require employers to notify workers about pesticide-treated areas orally as well as by posting of the treated areas. The reregistration process also may decide that a product requires this type of "double notification."

HED has determined that double notification is not required for pendimethalin end-use products.

Occupational-Use Products (NonWPS Uses)

Since HED has concerns about post-application exposures to persons after nonWPS occupational uses of pendimethalin, it is establishing entry restrictions for all nonWPS occupational uses of pendimethalin end-use products. For specific requirements, refer to Section V of this document.

Homeowner-Use Products

Since HED has concerns about post-application exposures to persons after homeowner applications of pendimethalin, HED is establishing entry restrictions for all homeowner uses of pendimethalin end-use products. For specific requirements, refer to Section V of this document.

NOTE: THIS SECTION MAY BE AMENDED PENDING THE OUTCOME OF THE MEETING WITH THE REGISTRANT IN WHICH POST-APPLICATION RISKS AND HOMEOWNER CONCERNS WILL BE DISCUSSED.

Other Labeling Requirements

The Agency is also requiring other use and safety information to be placed on the labeling of all end-use products containing pendimethalin. For the specific labeling statements, refer to Section V of this document.

d. Occupational and Residential Labeling Requirements

Labeling Requirements for End-Use Products

PPE/Engineering Control Requirements for Pesticide Handlers

For sole-active-ingredient end-use products that contain pendimethalin, the product labeling must be revised to adopt the handler personal protective equipment/engineering control requirements set forth in this section. Any conflicting PPE requirements on the current labeling must be removed.

For **multiple-active-ingredient** end-use products that contain pendimethalin, the handler personal protective equipment/engineering control requirements set forth in this section must be compared to the requirements on the current labeling and the more protective must be retained. For guidance on which requirements are considered more protective, see PR Notice 93-7.

Products Intended Primarily for Occupational Use (WPS and nonWPS)

Minimum (Baseline) PPE/Engineering Control Requirements

HED is establishing minimum (baseline) engineering controls for occupational uses of pendimethalin end-use products formulated as wettable powders. All wettable powder formulations must be contained in water-soluble packaging.

HED is establishing minimum (baseline) personal protective equipment (PPE) requirements for some occupational uses of pendimethalin end-use products. The minimum (baseline) PPE for occupational uses of pendimethalin end-use products are:

For emulsifiable concentrate formulations:
"Mixers and loaders must wear:
- -- long-sleeved shirt and long pants,
- -- chemical-resistant gloves*, and
- -- shoes plus socks."

* For the glove statement, use the statement established for pendimethalin through the instructions in Supplement Three of PR Notice 93-7.

For water-dispersible granule, wettable powder, and emulsifiable concentrate formulations whose use directions reasonably permit application using hand-held sprayers:
"Handlers (mixers, loaders, and applicators) who apply this product using hand-held equipment or hoses must wear:
- -- long-sleeved shirt and long pants,
- -- chemical-resistant gloves*, and
- -- shoes plus socks."

* For the glove statement, use the statement established for pendimethalin through the instructions in Supplement Three of PR Notice 93-7.

Determining PPE Requirements for End-use Product Labels

The PPE that would be established on the basis of the acute toxicity category of the end-use product must be compared to the active-ingredient-based minimum (baseline) personal protective equipment specified above. The more protective PPE must be placed on the

product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

Placement in Labeling

The personal protective equipment requirements must be placed on the end-use product labeling in the location specified in PR Notice 93-7, and the format and language of the PPE requirements must be the same as is specified in PR Notice 93-7.

Products Intended Primarily for Homeowner Use

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THE EFFECTS OBSERVED IN THE DOG STUDY SELECTED FOR RISK CHARACTERIZATION OF INTERMEDIATE EXPOSURE SCENARIOS DEMONSTRATE ACTUAL LIVER PATHOLOGY AT THE LOEL DOSE LEVEL. HOMEOWNER TURF EXPOSURE PATTERNS INDICATE THE LIKELIHOOD OF EXPOSURE TO INFANTS AND CHILDREN. THEREFORE, HED RECOMMENDS DISCUSSION WITH SRRD AND/OR THE REGISTRANT TO DETERMINE IF THIS USE SHOULD BE REREGISTERED.

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Minimum (baseline) PPE Requirements

HED is not establishing active-ingredient-based minimum (baseline) handler PPE for pendimethalin end-use products that are intended primarily for homeowner use.

Determining PPE Requirements for End-Use Product Labels

Any necessary PPE for each pendimethalin end-use product intended primarily for homeowner use will be established on the basis of the end-use product's acute toxicity category.

Placement in Labeling

The personal protective equipment requirements, if any, must be placed on the end-use product labeling immediately following the precautionary statements in the labeling section "Hazards to Humans (and domestic animals)."

Entry Restrictions

For sole-active-ingredient end-use products that contain pendimethalin the product labeling must be revised to adopt the entry restrictions set forth in this section. Any conflicting entry restrictions on the current labeling must be removed.

For **multiple-active-ingredient** end-use products that contain pendimethalin the entry restrictions set forth in this section must be compared to the entry restrictions on the current labeling and the more protective must be retained. A specific time period in hours or days is considered more protective than "sprays have dried" or "dusts have settled."

Products Intended Primarily for Occupational Use

WPS Uses

Restricted-entry interval:

A 12-hour restricted-entry interval (REI) is required for uses on food, feed, and fiber crops within the scope of the WPS on all pendimethalin end-use products, with the exception of uses on sugarcane and tobacco.

A 24-hour restricted-entry interval (REI) is required for uses on sugarcane and tobacco crops within the scope of the WPS on all pendimethalin end-use products.

"Exception: if the product is soil-injected or soil-incorporated, the Worker Protection Standard, under certain circumstances, allows workers to enter the treated area if there will be no contact with anything that has been treated."

NOTE: AN REI WILL BE ESTABLISHED FOR TURF AND ORNAMENTAL USES WITHIN THE SCOPE OF THE WPS PENDING THE OUTCOME OF THE PROPOSED MEETING WITH THE REGISTRANT.

Early-entry personal protective equipment (PPE):

The PPE required for early entry is:
- coveralls,
- chemical-resistant gloves, and
- shoes plus socks,

Placement in labeling:

The REI and PPE required for early entry must be inserted into the standardized REI statement required by Supplement Three of PR Notice 93-7.

NonWPS uses

Entry restrictions:

The Agency is establishing the following entry restrictions for nonWPS occupational uses of pendimethalin end-use products:

For liquid applications:
"Do not enter or allow others to enter the treated area until sprays have dried."

For dry applications:
"Do not enter or allow others to enter the treated area until dusts have settled."

Placement in labeling:

If WPS uses are also on label -- Follow the instructions in PR Notice 93-7 for establishing a Non-Agricultural Use Requirements box, and place the appropriate nonWPS entry restrictions in that box.

If no WPS uses are on the label -- Place the appropriate nonWPS entry restrictions in the Directions for Use, under the heading "Entry Restrictions."

Products Intended Primarily for Homeowner Use

****

THE EFFECTS OBSERVED IN THE DOG STUDY SELECTED FOR RISK CAHARCTERIZATION OF INTERMEDIATE EXPOSURE SCENARIOS DEMONSTRATE ACTUAL LIVER PATHOLOGY AT THE LOEL DOSE LEVEL. HOMEOWNER TURF EXPOSURE PATTERNS INDICATE THE LIKELIHOOD OF EXPOSURE TO INFANTS AND CHILDREN. THEREFORE, HED RECOMMENDS DISCUSSION WITH SRRD AND/OR THE REGISTRANT TO DETERMINE IF THIS USE SHOULD BE REREGISTERED.

****

Entry restrictions:

The Agency is establishing the following entry restrictions for all homeowner uses of pendimethalin end-use products:

For liquid applications:
"Do not allow people or pets to touch treated plants until the sprays have dried."

For dry applications:
"Do not allow people or pets to enter the treated area until dusts have settled."

Placement in labeling:

Place the appropriate entry restrictions in the Directions for Use, under the heading "Entry Restrictions."

Other Labeling Requirements

Products Intended Primarily for Occupational Use

The Agency is requiring the following labeling statements to be located on all end-use products containing pendimethalin that are intended primarily for occupational use.

Application Restrictions

"Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application."

Engineering Controls

"When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides (40 CFR 170.240(d)(4-6), the handler PPE requirements may be reduced or modified as specified in the WPS."

User Safety Requirements

1. {Registrant: add the following statements if coveralls are required for pesticide handlers on the end-use product label:}

   Discard clothing or other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them.

2. {Registrant: add the following statement always:}

   Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."

- "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."

Products Intended Primarily for Home Use

Application Restrictions

"Do not apply this product in a way that will contact any person or pet, either directly or through drift. Keep people and pets out of the area during application."

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."

e. Required Occupational/Residential Exposure Studies and Recommendations

Required Handler Studies

No chemical-specific handler exposure data for pendimethalin exists and HED has low confidence in the data available for several pendimethalin use scenarios. Additional handler exposure studies are required. Requirements for such studies are addressed in Subdivision U of the Pesticide Assessment Guidelines. The required studies are necessary to provide data on mixers, loaders, and applicators for:

- high-volume turf sprayer applications with WP/WDG/liquid formulations;
- low-pressure handwand applications with WDG/liquid formulations;
- backpack sprayer applications with WDG/liquid formulations;
- rights-of-way applications with WDG/liquid formulations;
- tractor drawn solid broadcast spreader applications of granulars.

The study:

- a dermal exposure study (Guideline 231), and

Required Postapplication Studies

There are no pendimethalin-specific post-application exposure data available at this time. These chemical-specific data are necessary for HED to establish permanent restricted-entry intervals since an intermediate-term endpoint of concern has been identified. The Registrant must submit postapplication exposure studies. Requirements for such postapplication exposure studies are addressed by Subdivision K of the Pesticide Assessment Guidelines. Data are required to support the use of pendimethalin on the following crop groups/use sites:

- Food, feed, and fiber crops: (hand-transplanting tobacco and hand-planting or hand-aligning mechanically-planted sugarcane);
- Ornamental crops (transplanting ornamentals);
- Residential turfgrass; and
- Sod-farm turfgrass (harvesting).

Requirements for postapplication/reentry exposure studies are addressed by Subdivision K of the Pesticide Assessment Guidelines. The required data include:

Guidelines:

132-1(a) Foliar Residue Dissipation, if applicable
132-1(b) Soil Residue Dissipation
*133-3 Postapplication Dermal Passive Dosimetry Exposure

*Guideline 133-3 may be reserved at this time pending completion of the databases on agricultural and residential postapplication/reentry exposure currently being developed by the Agricultural Reentry Task Force and Outdoor Residential Exposure Task Force, *provided* the Registrant is a member of both Task Forces.

f. Required Product and Residue Chemistry Data and Recommendations

Product Chemistry

All pertinent data requirements are satisfied for the 90% T and the pendimethalin TGAI; however additional product-specific data (physical/chemical properties) are outstanding for the 86.8% and 60% FIs (Appendix 1, Product Chemistry Data Summary). Provided that the Registrant submits the data required in the attached data summary tables for the 86.8% and the 60% FIs, and either certifies that the suppliers of beginning materials and the manufacturing processes for the pendimethalin technical product and MPs have not changed since the last comprehensive product chemistry review or submits complete updated product chemistry data packages, HED has no objections to the reregistration of pendimethalin with respect to product chemistry data requirements.

Residue Chemistry

Radiovalidation data using samples from the potato metabolism study remain outstanding and are considered confirmatory. Tobacco magnitude of the residue remain outstanding and are considered confirmatory.

Pendimethalin residue data requirements for cotton gin byproducts which result from changes in the Livestock Feeds Table (Table II (September, 1995)) should be imposed at this time. However, this requirement should not impinge on the reregistration eligibility decision for pendimethalin. The need for additional tolerances and revisions to the exposure/risk assessments will be made upon receipt and evaluation of the required data.

Rice processing data remain outstanding and are considered confirmatory.

The available confined rotational crop study is not adequate. A new confined rotational crop study is required. This, however, will not preclude the reregistration of pendimethalin.

Appendices
1. Product Chemistry Data Summary
2. Residue Chemistry Science Assessments for the Reregistration of Pendimethalin

Attachments
1. Hazard Assessment
2. Product and Residue Chemistry Assessments
3. Dietary Exposure Analysis
4. Occupational and Residential Exposure Assessments.

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Appendix 2
Residue Chemistry Science Assessments Summary

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
171-3: Directions for Use	N/A	Yes[2]	See Table A.
171-4 (a): Plant Metabolism	N/A	No	00029803 00031219 00039535 00039537 00046278 00046280 00051963 00051965 00058478 00067293 00071121 00074621 00093698 00106779 00106795 00108317 00109915 41469901[3] 42467801[4] 42686401[5] 43154705[6]
171-4 (b): Animal Metabolism	N/A	No	00046275 00046293 00067288 00067289 00071124 41713901[7] 42467802[8]

Appendix 2
Residue Chemistry Science Assessments Summary

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
171-4 (c/d): Residue Analytical Methods	N/A	Yes[9]	00019004 00023780 00023781 00023782 00023796 00024823 00025820 00025821 00025822 00025827 00025828 00025831 00025832 00025833 00025837 00029018 00029020 00031212 00031214 00039519 00039520 00039521 00039522 00039526 00039527 00039528 00039529 00041898 00041901 00041904 00051958 00051959 00051960 00051961 00051962 00052558 00058835 00070962 00071120 00072810 00072822 00072823 00072824 00072825 00106752 00106791 00106808 00106830 41431001[10] 41827401[11] 41845801[12] 41982701[12] 42471901[8] 42471902[8] 42859202[13] 43068501[14] 43154704[15] 43185901[16]
171-4 (e): Storage Stability	N/A	No	40535101 42266301[17] 42471903[8]
171-4 (k): Magnitude of the Residue in Plants			
Root and Tuber Vegetables Group			
- Potatoes	0.1 [§180.361(a)]	No	00106797
Bulb Vegetables Group			
- Garlic	0.1 [§180.361(c)]	No[18]	40232501[19]

Appendix 2
Residue Chemistry Science Assessments Summary

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
- Onions (dry bulb)	0.1 [§180.361(a)]	No	41827401[20]
Legume Vegetables Group			
- Beans (succulent and dry)	0.1 Beans, lima (dry, snap) [§180.361(a)]	No	00039518[21] 00039519[21] 00039520[21] 00039521[21] 00039522[21] 00039523[21] 00039524[21] 00039534[21] 00081581[21]
- Soybeans	0.1 [§180.361(a)]	No	00025818 00029801 00041897
- Soybeans, aspirated grain fractions	None	No[22]	
Foliage of Legume Vegetables Group			
- Bean forage and hay	0.1 [§180.361(a)]	No	00039518[21] 00039519[21] 00039520[21] 00039521[21] 00039522[21] 00039523[21] 00039524[21] 00039534[21] 00081581[21]
- Soybean forage and hay	0.1 [§180.361(a)]	No	00025818 00029801 00161759 00161760 00161761 40185101[23]
Cereal Grains Group			
- Corn, grain	0.1 [§180.361(a)]	No[24]	00023786 00023787 00023788 00023789 00023790 00023791 00023792 00023793 00023794 00023795 00029029 00030697 00093697 00106820
- Corn, fresh	0.1 [§180.361(a)]	No	00074619[25] 00093719[25]
- Corn, field, aspirated grain fractions	None	No[22]	

Appendix 2
Residue Chemistry Science Assessments Summary

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
- Rice, grain	0.05 [§180.361(a)]	No[26]	00067283 00071120
- Rice, straw	None	No[27]	00067283 00071120
- Sorghum, grain	0.1 [§180.361(a)]	No	00106791 00106807 00114313
- Sorghum, grain, aspirated grain fractions	None	No[22]	
Forage, Fodder and Straw of Cereal Grains Group			
- Corn, forage and fodder	0.1 [§180.361(a)]	No[28]	00023786 00023787 00023788 00023789 00023790 00023791 00023792 00023793 00023794 00023795 00029028 00029029 00030697 00093697 00106820
- Sorghum, forage and fodder	0.1 [§180.361(a)]	No[28]	00106791 00106807 00114313
Miscellaneous Commodities			
- Cottonseed	0.1 [§180.361(a)]	No	00018997 00106752 00106829 41881201[29] 42858901[30]
- Cotton gin byproducts	None	Yes[31]	
- Peanuts	0.1 [§180.361(a)]	No	00106785
- Peanut, hulls	0.1 [§180.361(b)]	No[22]	00031215 00031216 00031217 00106785
- Peanut, forage	0.1 [§180.361(a)]	No[32]	00106785
- Peanut, hay	0.1 [§180.361(a)]	No	00106785
- Sugarcane	0.1 [§180.361(a)]	No	42859201[13]
- Sunflower, seeds	0.1 [§180.361(a)]	No	00134355
- Tobacco	None	Yes[33]	00129937
171-4(l): Magnitude of the Residues in Processed Food/Feed			
- Corn grain	None	No[34]	
- Cottonseed	None	No[34]	00106752

Appendix 2
Residue Chemistry Science Assessments Summary

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
- Peanuts	None	No[34]	00106785
- Potatoes	None	No[35]	00106797
- Rice Grain	None	Yes	
- Soybeans	None	No	00025818
- Sugarcane	None	No[36]	[PP#3F2765]
- Sunflower seed	None	No[34]	00134355
171-4 (f): Magnitude of the Residue - Potable Water	N/A	No	00046293 00071124
171-4 (g): Magnitude of the Residue - Fish	None	No[37]	00046293 00071124
171-4 (h): Magnitude of the Residue - Irrigated Crops	None	No[37]	
171-4 (i): Magnitude of the Residue - Food Handling	N/A	N/A	
171-4 (j): Magnitude of the Residue in Meat, Milk, Poultry, and Eggs	None	No[38]	
165-1: Rotational Crops (Confined)	N/A	Yes[39]	41806801[40]
165-2: Rotational Crops (Field)	None		

1. References were reviewed in the Pendimethalin Registration Standard (Guidance Document dated 3/85). References in bold were reviewed in the 4/90 Reregistration Standard Update. Otherwise, submissions were reviewed as noted.

2. The active pendimethalin labels are not consistent with respect to PHIs for certain crops and must be revised to specify a PHI for each crop with registered layby applications.

3. DEB Nos. 6570/6603/6604/7153, 1/29/91, R. Loranger and R. Perfetti.

4. CBRS No. 10678, DP Barcode D183220, 2/1/93, P. Deschamp and CBRS No. 11797, DP Barcode D190778, 6/16/93, P. Deschamp.

5. CBRS No. 11582, DP Barcode D189207, 6/16/93, P. Deschamp and CBRS No. 12673, DP Barcode D195890, 2/9/94, B. Cropp-Kohlligian.

6. CBRS No. 12673, DP Barcode D195890, 2/9/94, B. Cropp-Kohlligian and CBRS No. 13411, DP Barcode D200669, 11/15/94, B. Cropp-Kohlligian.

7. CBTS Nos. 7595/7596, 3/5/91, F. Griffith; CBTS Nos. 8859/8860, DP Barcode D170619, 4/29/92, F. Griffith; and CBTS No. 15375, DP Barcode D212340, 4/7/95, J. Stokes and B. Cropp-Kohlligian.

(continued)

Table B *(continued)*.

8. CBRS No. 10678 Addendum, DP Barcode D183220, 9/24/93, P. Deschamp.

9. Radiovalidation data from the potato metabolism study remain outstanding. Representative samples from the potato metabolism study must be analyzed using the currently accepted enforcement analytical method (CBRS No. 10678, DP Barcode No. D183220, 2/1/93, P. Deschamp).

10. CBRS Nos. 7507/7517, DP Barcodes D159827/D159905, 4/24/91, E. Zager.

11. PP#1E3965. CBTS No. 7887, DP Barcode D163268, 7/10/91, G.J. Herndon.

12. CBRS Nos. 8118/8515, DP Barcodes D165134/D167858, 5/15/92, E. Zager.

13. CBTS No. 11230, DP Barcode D193627, 7/25/94, R. Cook.

14. CBRS No. 13400, DP Barcode D200608, 7/24/95, B. Cropp-Kohlligian.

15. CBRS No. 13411, DP Barcode D200669, 11/15/94, B. Cropp-Kohlligian.

16. CBRS No. 13506, DP Barcode D201694, 11/15/94, B. Cropp-Kohlligian.

17. CBRS No. 9914, DP Barcode D178454, 10/22/93, P. Deschamp.

18. CBRS concludes that available garlic magnitude of the residue data from field trials conducted in CA and OR are adequate to support a national registration for the use of pendimethalin on garlic and recommends that the currently established tolerance with regional registrations for pendimethalin residues of concern in/on garlic should be changes to a tolerance without regional registrations at the same level (0.1 ppm) and listed under 40 CFR §180.361(a).

19. PP#7E3537. Memoranda by G. Otakie dated 8/20/87 and H. Fonouni dated 8/27/90.

20. PP#1E3965. CBTS No. 7887, DP Barcode D163268, 7/10/91, G.J. Herndon; CBTS No. 9616, DP Barcode D175936, 10/22/92, G.J. Herndon; CBTS No. 11391, DP Barcode D188216, 2/24/93, G.J. Herndon; and CBRS No. 9464, DP Barcode D174858, 9/24/93, P. Deschamp.

21. PP#1F2567. Memorandum, no CB No., no DP Barcode, 4/29/82, A. Smith.

22. As a result of changes in the Livestock Feeds Table (TABLE II (September 1995)), the Agency now considers aspirated grain fractions of soybeans, field corn, and grain sorghum as raw agricultural commodities (RACs). Residue chemistry data for these RACs are waived since pendimethalin is applied to soybeans, field corn, and grain sorghum very early in the growing season (i.e., preplant, preemergence and/or postemergence) and pendimethalin residues of concern in/on aspirated grain fractions of soybeans, field corn, and grain sorghum are unlikely to exceed the currently established tolerances on soybeans, field corn grain, and grain sorghum. No tolerances for pendimethalin residues of concern are needed for aspirated grain fractions of soybeans, field corn, and grain sorghum.

23. CB Nos. 5494/5495, 8/8/89, D. Edwards.

24. Data from field corn magnitude of the residue studies will be used to support the use of pendimethalin on pop corn.

Table B *(continued)*.

25. PP#2F2628. Memorandum, no CB No., no DP Barcode, 7/15/82, A. Smith.

26. As recommended in the 1984 Pendimethalin Registration Chemistry Chapter, the currently established rice grain tolerance should be increased from 0.05 ppm to 0.1 ppm.

27. Available rice field trial data are hereby deemed adequate to support a tolerance for pendimethalin residues of concern in/on rice straw. A tolerance of 0.1 ppm would be appropriate.

28. As a result of changes in the Livestock Feeds Table (TABLE II (September 1995)), the Agency now considers corn stover and sorghum stover as raw agricultural commodities (RACs). Available pendimethalin field trial data on corn/sorghum grain and corn/sorghum fodder (presumably the mature dried stalks with grain) reflecting the maximum use rates of pendimethalin to corn and sorghum demonstrated that pendimethalin residues of concern in/on corn grain, grain sorghum, corn fodder, and sorghum fodder were nondetectable (< 0.1 ppm). Hence, CBRS, concludes that adequate data are available to support tolerances for pendimethalin residues of concern in/on corn stover (mature dried stalks from which the grain or whole ear (cob and grain) have been removed) and sorghum stover (mature dried stalks from which the grain have been removed) at the limit of quantitation (LOQ) of the analytical method (0.1 ppm).

29. CB No. 8138, DP Barcode D165329, 9/18/91, K. Dockter

30. CBTS No. 12295, DP Barcode D193629, 8/1/94, G.J. Herndon.

31. As a result of changes in the Livestock Feeds Table (TABLE II (September 1995)), the Agency now considers cotton gin byproducts as a raw agricultural commodity (RAC). Data depicting pendimethalin residues of concern in/on cotton gin byproducts resulting from the maximum registered use rate of pendimethalin to cotton are hereby required. Cotton must be harvested by commercial equipment (stripper and mechanical picker) to provide an adequate representation of plant residue for the ginning process. At least 3 field trials for each type of harvesting (stripper and picker) are needed, for a total of six (6) field trials.

32. The established tolerances in/on peanut hulls and peanut forage should be revoked, since these are no longer considered to be significant feed items according to the Livestock Feeds Table (TABLE II (September 1995)).

33. CBRS has, considered available tobacco data (including available tobacco metabolism data (MRID 00031978) not previously reviewed) in light of recently issued guidance on this topic (memo by M. Metzger and E. Zager dated 7/17/95) and concludes that tobacco data are not adequate to assess human exposure to pendimethalin residues of concern on tobacco. Tobacco data remain outstanding. The registrant is directed to consult recently issued guidance on this topic (memo by M. Metzger and E. Zager dated 7/17/95) before proceeding with additional studies.

34. The Agency (Memorandum of Conference by J. Stokes and B. Cropp-Kohlligian dated 4/7/95) has accepted the registrant's argument that pendimethalin is not translocated to oil seeds and that residues would not concentrate in corn oil to levels above the established tolerance for corn grain (theoretical concentration factor 25x). As the other oilseeds with tolerances have theoretical concentration factors less than that of corn grain, additional processing studies on oil seeds are not required.

Table B *(continued)*.

35. Based on available potato field trial data (MRID 00106785) reflecting exaggerated application rates (2.67x) to potatoes, the Agency previously concluded (1984 Pendimethalin Registration Chemistry Chapter) that pendimethalin residues of concern were not expected to concentrate in potato processed commodities and a potato processing study was not required. No tolerances are required for pendimethalin residues of concern on potato processed commodities.

36. CBTS No. 11265, DP Barcode D187216, 2/11/93, R. Cook.

37. End-use product labels prohibit applications of pendimethalin to rice fields used for fish or crayfish production and prohibit the use of water from pendimethalin-treated rice fields for the irrigation of food or feed crops.

38. EPA has determined that based on (i) existing tolerances in 40 CFR §180.361(a), (ii) pending wheat/barley tolerances, and (iii) current livestock dietary burden calculations, there is no reasonable expectation of finite residues in animal tissues, milk, or eggs. This situation is provided for under 40 CFR §180.6(a)(3). No additional animal metabolism, analytical method, storage stability, or magnitude of the residue data are required for livestock (Memorandum of Conference by J. Stokes and B. Cropp-Kohlligian dated 4/7/95).

39. The registrant must submit a new confined rotational crop study conducted on three representative crops (small grain, leafy vegetable, and root crop) using [^{14}C]pendimethalin uniformly labeled in the ring position (CBRS No. 12685, DP Barcode D195941, 4/11/94, B. Cropp-Kohlligian). Once these data have been submitted the need for plant-back intervals will be determined.

40. This study was found unacceptable by EFGWB/EFED (H. Manning) and CBRS (CBRS No. 12685, DP Barcode D195941, 4/11/94, B. Cropp-Kohlligian).

Attachment 1

011842

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

JAN 30 1996

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: **PENDIMETHALIN, Reregistration Case No. 0187.** Toxicology Chapter for the Reregistration Eligibility Decision Document on Pendimethalin.

Tox. Chem. No.: 454BB
PC Code No.: 180501
CAS No.: 40487-42-1
DP Barcode No.: D221530
Submission No.: ~~S221530~~ S494478

From: William B. Greear, M.P.H. William B. Greear 1/30/96
Review Section 4, Toxicology Branch I
Health Effects Division (7509C)

To: Sherry Sterling/Jane Mitchell, PM Team 71
Reregistration Branch
Special Review and Reregistration Division (7508W)

Through: Marion P. Copley, D.V.M., Section Head Marion Copley 1/30/96
Review Section 4, Toxicology Branch I
Health Effects Division (7509C)

and

Karl P. Baetcke, Ph.D., Branch Chief
Toxicology Branch I
Health Effects Division (7509C)
1/30/96

Attached please find the Toxicology Chapter for the Reregistration Eligibility Decision document on pendimethalin. This chapter is to incorporated into the HED/RED for reregistration of pendimethalin.

TABLE OF CONTENTS

Human Health Assessment: Pendimethalin

1. Toxicology Assessment

The toxicology data base for pendimethalin is adequate and will support reregistration for current uses. There are not data gaps at this time.

a. Acute and Subchronic Toxicity

Acute Toxicity

The table below summarized the results of acute toxicity studies on pendimethalin and the toxicity categories for the different routes of administration.

ACUTE TOXICITY DATA FOR PENDIMETHALIN

TEST	RESULT	CATEGORY
Oral LD50 in rat (MRID 00026657)	LD_{50}(M) = 1250 mg/kg LD_{50}(F) = 1050 mg/kg	III
Dermal LD_{50} in rabbit (MRID 00026657)	LD_{50} > 5000 mg/kg	IV
Inhalation LC_{50} in rat (MRID 00073342)	LC_{50} > 320 mg/L (nominal concentration)	IV
Eye irritation in rabbit (MRID 00026657)	Slight conjunctival irritation	III
Dermal irritation in rabbit (MRID 00026657)	No irritation	IV
Dermal sensitization (MRID 00153767)	Nonsensitizing	N/A

Subchronic Toxicity

Oral

Rat:

In a 30-day feeding study in rats (MRID 000106754), pendimethalin technical (98.7%) was administered to groups of 10 males and 10 females RH Wistar rats in the diet at levels of 0, 800, 1,600 or 3,200 ppm (corresponding to 0, 80, 160, or 320 mg/kg/day). Urine was darker than controls in the 1,600 and

3,200 ppm groups. At 3,200 ppm there appeared to be increased liver weight. **The LOEL is 3,200 ppm (320 mg/kg/day) based on increased liver weight. The NOEL is 1,600 ppm (160 mg/kg/day).** Although this study is classified as Supplementary it provides useful information.

In a 13-week feeding study in rats (MRID 00156081), AC 92,553 (pendimethalin, 92.1%, Lot #AC3528-129-1) was administered to groups of 30 male and 30 female Charles River CD(SD)BR rats in the diet at levels of 0, 100, 500, or 5,000 ppm (corresponding to 0, 10, 50, or 500 mg/kg/day). At 5,000 ppm, rats displayed a dark yellow discoloration of the urine and yellow discoloration of abdominal fat. Body weight gain and food consumption were decreased. The hematocrit and hemoglobin levels were decreased and the number of platelets slightly increased in males. There was an increase in pale or mottled livers in males and dark red thyroids in both sexes at 5,000 ppm. The absolute weight of the liver was increased in males and females. Diffuse hypertrophy of the liver was also observed. **The LOEL is 5,000 ppm (500 mg/kg/day) based on decreased body weight gain the food consumption, decreased hematocrit and hemoglobin with an increase in platelets in males, increased liver weight, red thyroids, increased liver weights and hypertrophy of the liver. The NOEL is 500 ppm (mg/kg/day).**

In a second 13-week feeding study in rats (MRID 00059468), AC 92,553 technical (pendimethalin) was administered to groups of 25 male Long-Evans rats in the diet at levels of 0, 25, 50, 100, 500, or 2,500 ppm (corresponding to 0, 2.5, 5.0, 10.0, 50.0, or 250 mg/kg/day). The 2,500 ppm group was raised to 5,000 ppm (500 mg/kg/day) from week 8-13. There were no adverse effects noted with respect to mortality, body weight and gross and microscopic examination of mammary glands. **The LOEL was not determined. The NOEL was greater than 2,500 ppm (250 mg/kg/day).** Although this study is classified as Supplementary it provides useful information.

In a third 13-week study in rats (MRID 00059469), AC 92,553 technical pendimethalin was administered to Sprague-Dawley rats in the diet at 0 or 2,500 ppm (corresponding to 0 or 250 mg/kg/day). There were no adverse effects noted with respect to mortality, body weight and gross and microscopic examination of the mammary gland. **The LOEL was not determined. The NOEL was greater than 2,500 ppm (250 mg/kg/day).** Although this study is classified as Supplementary it provides useful information.

In a special 92-day thyroid function feeding study (MRID 42054601), AC 92,553 (pendimethalin, 92.6%, Lot #AC5213-72A) was administered to groups of 80 male CD[Crl:CD(SD)] rats at dose levels of 0, 100, or 5,000 ppm (corresponding to 0, 4.98, or 245.4 mg/kg/day) for 28 days. Groups of 20 male rats were sacrificed at 15, 29, 57 and 92 days. At 100 ppm there was

decreased total T_4, rT_3, total free T_4 and increased percent T_3, increased follicular cell height and decreased area occupied by colloid. At 5,000 ppm there were decreased body weight and food consumption compared to controls, increased thyroid weight, decreased total T_4, total T_3, rT_3, total free T_4 and [^{125}I]-T_4 to transthyretin bonding, increased percent free T_4, percent free T_3 and [^{125}I]-T_4 to albumin binding, increased follicular cell height and decreased area occupied by colloid and ultrastructural thyroid changes. Most parameters were reversible after treatment subsided except for decreased body weight. **The LOEL was 100 ppm (4.98 mg/kg/day) based on thyroid effects. The NOEL was less than 100 ppm (4.98 mg/kg/day).**

In a special 56-day feeding study to determine thyroid function (MRID 43135001), groups of 65-70 (5-15 per sacrifice time) male Crl:CD(SD) rats were treated at dose levels of 0, 500 or 5000 ppm (0, 31 or 292 mg/kg/day) of AC 92,553 (pendimethalin, 92.6%, Lot #AC5213-72A) in the diet for 28 days. A recovery period of up to 28 days was employed. There were no deaths or clinical signs of toxicity during or after the treatment period at either dose. At 500 ppm there was decreased total T_4 (38%), rT_3 (25%) and total free T_4 (28%) and increased percent free T_3 (13%), increased follicular cell height (40%) and decreased area occupied by colloid (51%) during treatment. At 5000 ppm, body weight (8%), body weight gain (29%) and food consumption (15%) were decreased compared to controls during the treatment period. Thyroid changes during treatment with 5000 ppm included: increased absolute (15%) and relative (23%) thyroid weight; decreased total T_4 (74%), total T_3 (25%), rT_3 (36%), total free T_4 (40%), and [^{125}I]-T_4 to transthyretin binding; increased percent free T_4 (117%), percent free T_3 (26%) and [^{125}I]-T_4 to albumin binding; increased follicular cell height (75%) and decreased area occupied by colloid (45%); ultrastructural thyroid changes were consistent with mild to moderate TSH stimulation except for the accumulation of dense-bodies in the cytoplasm which may be reaction products of AC 92,553. Most parameters were reversible after treatment subsided except for a slight decreased body weight compared to controls (7%) at 5000 ppm. There were no changes in TSH, total free T_3 or diameter of follicular cells. **The LOEL was 500 ppm (31 mg/kg/day) based on thyroid effects. The NOEL could not be determined.**

In a special 14-day feeding study to determine thyroid function (MRID 43135003), AC 92,553 (pendimethalin, 92.6%, Lot #AC5213-72A) was administered in the diet to groups of 10 male Crl:CD(SD) rats at dose levels of 0, 100 or 5,000 ppm (corresponding to 0, 10 or 500 mg/kg/day). At 5000 ppm AC 92,533 for 14 days, TSH was increased and T_4 and T_3 were decreased. No treatment related effects were observed for rT_3 levels, thyroid weight, ^{131}I uptake in MIT, DIT or T_4. There was a significant increase of ^{131}I uptake by the thyroid of rats in the 5000 ppm group and an increase in incorporation of ^{131}I in T_3. Total T_3 and

T_4 levels in the thyroid were not affected by treatment at 5,000 ppm. **The LOEL is 5,000 ppm (500 mg/kg/day) based on thyroid effects. The NOEL is 100 ppm (10 mg/kg/day).**

In a second special 14-day feeding study to determine biliary excretion and hepatic metabolism, AC 92,553 (pendimethalin, 92.98%, Lot #AC6539-77A) was administered to groups of 10 male Crl:CD(SD) rats at dose levels of 1, 100, or 5,000 ppm (corresponding to 0, 10, or 500 mg/kg/day). Ingestion of 5,000 ppm produced decreases in serum T_3 and T_4 with a compensatory increase in TSH. Also increased were liver weight, bile flow and cumulative biliary excretion of ^{125} I-T_4 with a slight increase in T_4-glucuronytransferase activity detected by generation of ^{125} I-T_4 glucuronide from ^{125} I-T_4 *in vitro* by hepatic microsomes. The increase in enzyme activity was also demonstrated *in vivo* by a significant increase in biliary excretion of ^{125} I-T_4-glucuronide. **The LOEL is 5,000 ppm (500 mg/kg/day) based on thyroid effects. The NOEL is 100 ppm (10 mg/kg/day).**

Dog:

In a 90-day feeding study (MRID 00026672), pendimethalin was administered to groups of 8 dogs at dose levels of 0, 62.5 250 or 1,000 mg/kg/day. Body weight loss was apparent at 250 and 1,000 mg/kg/day. **The LOEL is 250 mg/kg/day based on body weight loss. The NOEL is 62.5 mg/kg/day.** Although this study is classified as Supplementary it provides useful information.

In a 30-day feeding study in dogs (MRID 000106754) AC 92,553 technical (pendimethalin, 98.7%) was administered to groups of 2 male and 2 female beagles in the diet at dose levels of 0, 0.625% or 1.25% (corresponding to 0, 125 or 250 mg/kg/day). A third test group received 5% in the diet (corresponding to 1,000 mg/kg/day) for 30 days. The protocol was changed so that dogs received the compound by gelatin capsule from days 17 to 30. Food consumption and body weight were decreased in all treated groups compared to controls. **The LOEL was 125 mg/kg/day based on decreases in body weight and food consumption. The NOEL could not be determined.** Although this study is classified as Supplementary it provides useful information.

Mouse:

In a 30-day feeding study in mice (MRID 000106754), pendimethalin technical (98.7%) was administered to groups of 10 male and 10 female CF-1 mice in the diet at levels of 0, 500, 1,000 or 2,000 ppm (corresponding to 0, 75, 150 or 300 mg/kg/day). There were no adverse effects with respect to mortality, body weight, food consumption and organ weight. The LOEL was not determined. The NOEL is greater than 2,000 ppm (300 mg/kg/day). Although this study is classified as Supplementary it provides useful information.

Dermal

Rabbit:

In a 21-day dermal toxicity study (MRID 00026663), AC 92,553 (pendimethalin) was dermally applied to the back of 3 or 4 New Zealand white rabbits/group at dose levels of 0, 250, 500 or 1000 mg/kg/day. There were no adverse effects with respect to mortality, food and water intake, hematology, urinalysis and gross and microscopic pathology. **The systemic LOEL was not determined. The systemic NOEL is greater than 1000 mg/kg/day.**

b. Chronic Toxicity/Carcinogenicity

Rat:

In a 2-year study in rats (MRID 40174401), AC 92,533 (pendimethalin, 91.9%, Lot #AC3528-129-1), was administered to groups of 55 male and 55 female Crl:CD(SD)BR rats in the diet at levels of 0, 100, 500 or 5,000 ppm (corresponding to 0, 5, 25, or 250 mg/kg/day). Ten rats/sex/group were interim sacrificed as 12 months. At 5,000 ppm, survival in males was slightly decreased and body weight gain was decreased. There was decreased food consumption, increased gamma glutamyl transferase and cholesterol, increase in liver weight and/or liver body and/or brain weight ratios, generalized icterus, dark adipose tissue in females, diffusely dark thyroids, follicular cell hyperplasia of the thyroid and thyroid follicular cell adenoma. **The LOEL is 500 ppm (25 mg/kg/day) based on pigmentation of thyroid follicular cells in males and females. The NOEL is 100 ppm (5 mg/kg/day).**

In a second 2-year feeding study in rats (MRID 42027802), AC 92,533 (pendimethalin, 92.6%, Lot #AC5213-72A) was administered to groups of 125 male Sprague-Dawley (Crl:CD(SD)BR) at dose levels of 0, 1250, 2500, 3750, or 5000 ppm (corresponding to 0, 51, 103, 154, and 213 mg/kg/day). Fifteen rats/group were interim sacrificed at 1, 13, 26, 39 and 52 days. There was decreased colloid and increased cysts of the thyroid follicular cells and an increase in liver weight at 1250 ppm and above. At 2500 ppm and above there was increased pigment and hypertrophy of follicular cells, increased thyroid weight and an increase in eosinophilic and basophilic foci of cellular alteration, hepatocellular enlargement and hepatocellular intracytoplasmic inclusions. There was a decrease in body weight gain at 3750 ppm and above and hyperplasia of follicular cells. At 5000 ppm GGT and total cholesterol were increased and there was an increase in thyroid follicular adenomas. **The LOEL is less than or equal to 1250 ppm ($\leq$51 mg/kg/day) based on non-neoplastic thyroid follicular cell changes in increased liver weight. The NOEL was not determined.**

Mouse:

In an 18-month feeding study in mice (MRID 40909901), AC 92,533 (pendimethalin, 92.6%, Lot #AC5218-72A) was administered to groups of 65 male and 65 female Charles River CD-1 mice at dose levels of 100, 500, or 5,000 ppm (corresponding to 12.3, 62.3 and 622.1 mg/kg/day in males and 15.6, 78.3 and 806.9 mg/kg/day in females). There were 2 control groups consisting of 65 mice/sex each. Ten mice/sex were sacrificed at 12 months in 1 control and all treated groups. (One control group only consisted of 55 mice/sex.) At 5,000 ppm there was increased mortality in females, decreased body weight in females, increased absolute thyroid, liver and gall bladder weights and/or relative body and brain weight ratios in males and females and amyloidosis in males. **The LOEL is 5,000 ppm (622.1 mg/kg/day [M]; 806.99 mg/kg/day [F]) based on mortality, body weight decrease, organ weight changes and amyloidosis. The NOEL is 500 ppm (62.3 mg/kg/day [M]; 78.3 mg/kg/day [F]).**

Dog:

In a 2-year oral study in dogs (MRID 00058657), AC 92,533 (pendimethalin, 91.4%, Lot #77-02) was administered via capsule to groups of 4/sex beagle dogs at dose levels of 0, 12.5, 50 or 200 mg/kg/day. Serum alkaline phosphatase (SAP), liver weight and inflammation and hemosiderosis of the liver were increased at 50 mg/kg/day and above. Yellow color of the hair was observed in all treated dogs. **The LOEL is 50 mg/kg/day based on increased SAP, liver weights and liver pathology. The NOEL is 12.5 mg/kg/day.**

c. Developmental Toxicity

Rat:

Pendimethalin (94.2% a.i.) was administered in corn oil to groups of 30 mated Sprague-Dawley CD strain rats by gavage at daily dose levels of 0, 125, 250, or 500 mg/kg/day from gestation day 6 through 15 (MRID 00025752). Females were observed for signs of toxicity, and body weights were measured during gestation. Animals were sacrificed on gestation day 21 and reproductive observations were made and uteri were examined for live fetuses and intra-uterine deaths. Fetuses were weighed, sexed, and examined for external, visceral and skeletal alterations. There were no maternal or developmental effects noted at any dose level tested, and based on these results, the **NOELs for developmental and maternal toxicity are ≥500 mg/kg/day (highest dose tested).** Although this study is classified as Supplementary, when in conjunction with the rabbit developmental toxicity study (MRID 00117444) it will satisfy guideline requirement §83-3. It is not upgradable because an adequate dose range may not have been tested.

Rabbit:

Pendimethalin was administered in corn oil to groups of 20 artificially inseminated New Zealand White strain rabbits by gavage at dose levels of 0, 15, 30, or 60 mg/kg/day from gestation day 6 through 18 (MRID 00117444). Females were observed for signs of toxicity, and body weights were measured during gestation. Animals were sacrificed on gestation day 29 and reproductive observations were made and uteri were examined for live fetuses and intra-uterine deaths. Fetuses were weighed, sexed, and examined for external, visceral and skeletal alterations. **No maternal toxicity was reported at doses ≤60 mg/kg/day (highest dose tested). However, the range-finding study indicated that doses ≥ 125 mg/kg/day were associated with increased mortality** (3/5, 5/5 and 4/5 in the 125, 250, and 500 mg/kg/day, respectively compared with 0/5 in the control group). A slight increase in the mean incidence of skeletal anomalies in the mid- and high-dose groups which consisted of findings of less than twelve pairs of ribs (0/111, 1/118 and 4/107 fetuses in the control, mid-, and high-dose groups, respectively, not statistically significant) and/or missing or incompletely ossified vertebrae (0/111, 1/118 and 7/107 fetuses in the control, mid and high dose groups, respectively). No individual litter data or historical control data were available in the report to support a conclusion regarding the significance of these alterations. **A developmental toxicity NOEL could not be determined from this study. Although this study is Supplementary and does not satisfy §83-3 guideline requirements for a rabbit developmental toxicity study, it is upgradable pending receipt of individual litter data (fetal alterations) and historical control data. If, however, the additional data indicates the lack of any developmental or maternal effects at any dose, an additional developmental study (species to be determined) may be required.**

d. Reproductive Toxicity

In a 2-generation reproduction study (MRID 417252203), AC 92,533 (pendimethalin, 92.6%, Lot #AC5213-72A) was administered to groups of 25 male and 25 female Sprague-Dawley derived CFA-SD (IOPS-CAW) rats at dose levels of 0, 500, 2500 or 5000 ppm (corresponding to 0, 34, 172 and 346 mg/kg/day) in males and 0, 43, 216, 436 mg/kg/day in females). There were no clinical signs or changes in organ weight data. There was a minimal (5%) decrease in body weight gain and food consumption (possibly due to palatability) at 2500 ppm. At 5000 mg/kg/day the decrease in body weight gain was as high as 20 %. The LOEL for parental effects is 5000 ppm based on weight gain and food consumption depression. The NOEL for parental effects is 2500 ppm (172 and 216 mg/kg/day, in males and females, respectively). There were decreased pup weights during much of lactation at 5000 ppm. The LOEL for reproductive effects is 5000 ppm (346 and 436 mg/kg/day in males and female, respectively). The NOEL for

reproductive effects is 2500 ppm (172 and 216 mg/kg/day, in males and females, respectively).

In a 3-generation reproduction study (MRIDs 00026671, 0040304, 00059470) AC 92,533 technical (pendimethalin) was administered to groups of 10 male and 20 female Long-Evans rats at dose levels of 0, 500 or 5000 ppm (corresponding to 0, 25 and 250 mg/kg/day). At 5000 ppm there was a decrease in body weights in male and female parental animals. **The LOEL for parental toxicity is 5000 ppm (250 mg/kg/day) based on decreased body weights. The NOEL for parental toxicity is 500 ppm (25 mg/kg/day).** Pup body weight gain was decreased during lactation. There were possible decreases in pups born alive and pup survival. **The LOEL for reproductive toxicity is 5000 ppm (250 mg/kg/day) based on pup body weight gain and possible decreased pups born alive and pup survival . The NOEL for reproduotive toxicity is 500 ppm (25 mg/kg/day).**

e. Mutagenicity

There are acceptable studies to satisfy the initial mutagenicity testing requirements for all three categories (gene mutations, structural chromosomal aberrations, and other genotoxic effects). The positive Salmonella results in one study indicated that pendimethalin may have potential genotoxic activity. Subsequent assays for germ cell effects (Chinese hamster ovary cells and rat testicular cells) and additional Salmonella assays, submitted to address this concern, were all negative. No other mutagenicity studies are required at this time.

In a reverse gene mutation assay in bacteria (MRID 00153768), strains (TA1535, TA1537, TA1538, TA98, TA100) of S. typhimurium were exposed to AC 92,533 (pendimethalin, 92.2%, Lot #AC3528-129-1) at concentrations of 50, 158, 500, 1581 or 5000 µg/plate in the presence and absence of mammalian hamster S9. Subsequent tests with TA98, TA1538 and TA100 used dose levels of 250, 500, 1000, 3000 or 5000 µg/plate. AC 92,533 was tested up to the limit dose of 5000 µg/plate. A precipitate was formed at 5000 µg/plate. The positive controls did induce the appropriate responses in the corresponding strains. **This study was considered positive since there was evidence of a 2-fold dose-related increase in the number of induced mutant colonies over background at all doses from 50 to 5000 µg/plate.**

In a *Salmonella*/microsome plate incorporation assay and in an *Escherichia coli* WP2(uvrA) reverse mutation assay (MRID 43177801), strains TA98, TA100, TA1535, TA1537, TA1538 and WP2(uvrA) were exposed to pendimethalin at concentrations of 25, 50, 100 250, 500 and 750 µg/plate, with and without exogenous metabolic activation. Preparations for metabolic activation were made from Aroclor 1254 induced male Sprague-Dawley rat livers.

The test material was delivered in DMSO. No cytotoxicity was seen at any concentration of pendimethalin tested. The upper concentration was limited by test material solubility (a precipitate was observed at concentrations of 750 µg/plate and above). Positive and vehicle control values were appropriate. **There was no evidence of an increase number of mutant colonies over solvent control values at any concentration of pendimethalin tested, either with or without S9 mix.**

In a *Salmonella*/microsome plate incorporation and disk assay and in an *Escherichia coli* WP2(uvrA) reserve mutation assay (MRID 43135005), strains TA98, TA100, TA1535, TA1537, and WP2(uvrA) were exposed to pendimethalin (90.7% , Lot #AC8088-149) at 50, 158, 500, 1581 and 5000 µg/plate or 1000 µg/paper disk/plate, with and without exogenous metabolic activation. Preparations for metabolic activation were made from Aroclor 1254 induced male rat livers. The test material was delivered in DMSO. Cytogenetic determinations were not made or discussed in this study. The highest concentration was limited by solubility (a precipitate was seen at 1581 and 5000 µg/plate). Positive and vehicle controls were appropriate. **There was no evidence of induced mutant colonies over background vehicle control values at any concentration of pendimethalin tested in any strain with or without S9 mix.**

In a *Salmonella*/microsome plate incorporation and disk assay and in an *Escherichia coli* WP2(uvrA) reverse mutation assay (MRID 43135006), strains TA98, TA100, TA1535, TA1537, TA1538, and WP2(uvrA) were exposed to pendimethalin (99.5%, Lot #AC5042-52F) at concentrations of 50, 100, 250, 500, and 750 µg/plate without exogenous metabolic activation and to the same concentrations plus an additional concentration of 25 µg/plate with exogenous metabolic activation. A confirmatory assay tested concentrations of 25, 50, 100, 250, 500 and 750 µg/plate both with and without S9 mix. Preparations for metabolic activation were made from Aroclor 1254 induced male rat livers. The test material was delivered in DMSO. No cytogenicity was seen at any concentration tested up to 5000 µg/plate. The upper concentration tested was limited by solubility of the test material. Positive and vehicle control values were appropriate. **No evidence of a mutagenic response was seen at any dose in any strain with or without S9 mix in either assay.**

In a forward mutation study (MRID 43177802) at the HGPRT locus in Chinese hamster ovary CHO-K1-BH4 cells in culture, cells were exposed to pendimethalin (90.9%, Lot #AC5042-37D) at concentrations of 1, 5, 7.5, 10, 20, 30, 40, and 50 µg/ml in the absence of an exogenous metabolic activation system and to 10, 25, 50, 75, 100, 125, 150, and 175 µg/ml in the presence of an exogenous metabolic activation system (S9-mix). Preparations for metabolic activation were made from Aroclor 1254 induced male Sprague-Dawley rat liver. The test material was delivered in

DMSO. Cytotoxicity was unacceptably high at 30, 40 and 50 μg/ml in the absence of S9 mix and at 150, 150, and 175 μg/ml with S9 mix; therefore, mutagenicity was not evaluated at these concentrations. A yellow precipitate was seen at concentrations ≥50 μg/ml. Positive, negative, and vehicle control values were appropriate. **There was no evidence of induced mutant colonies over background either with or without S9 mix at any concentration evaluated in this study.**

In a chromosomal aberration study (MRID 00153770), Chinese hamster ovary (CHO) cells were exposed to AC 92,533 (pendimethalin, 92.2%, Lot #AC3528-129-1) at dose levels ranging from 5 to 25 μg/plate with or without rat liver S9 and at 12.5 to 100 μg/ml with rat liver S9. **There was no induction of chromosomal aberrations in CHO cells at dose levels of up to 25 μg/plate without S9 and up to 100 μg/ml with S9.**

In a mouse micronucleus study (MRID 42027801), AC 92,533 (pendimethalin, 92.98%, Lot #AC6539-77A) was administered to 5 male and 5 female ICR mice by gavage at dose levels of 313,625 or 1250 mg/kg. Administration of AC 92,533 did not cause a significant increase in the frequency of micronucleated polychromatic erythrocytes (MPEs) in bone marrow cells harvested 24, 48, or 72 hours posttreatment. Deaths and other signs of compound toxicity were seen in high-dose males and females. although there was no evidence of a cytotoxic effect on the target organ (bone marrow cells), the findings of overt toxicity at 1250 mg/kg (80% of the LD_{50}) clearly indicated that the maximum tolerated dose was achieved. Therefore, **AC 92,533 was adequately tested and found to be nonclastogenic in the mouse micronucleus assay.**

In an alkaline elution assay (MRID 43135007), three rats per dose per sacrifice time were given single i.p. doses of pendimethalin (90.7%, Lot #AC8088-149) at 1250, 2500 or 5000 mg/kg/body weight. (The alkaline elution assay detects DNA single strand breaks and DNA/DNA and DNA/protein crosslinks). The test compound was delivered in corn oil. Testicular cells were harvested 2, 6 and 24 hours after treatment. At the 6 hr sacrifice time, all rats receiving 2500 or 5000 mg/kg were lethargic while those receiving 1250 mg/kg appeared normal. At 24 hr, rats receiving 5000 mg/kg appeared lethargic and ungroomed with dehydrated intestinal tissue while all other rats at lower doses appeared normal. No testicular cell cytotoxicity as measured by trypan blue exclusion was evident at any test material dost or sacrifice time. All positive and vehicle control rats appeared normal at all sacrifice times and no testicular cytotoxicity was seen. **There was no evidence of DNA single strand break induction or DNA/DNA or DNA/protein crosslink formation at any dose or sacrifice time.**

f. Metabolism

In a metabolism study (MRID 00046275), when [^{14}C]pendimethalin was administered to rats, about 70% of the radioactivity was excreted in the feces and 20% in the urine within 24 hours. The excretion of radioactivity in the urine peaked at 6 to 12 hours wherein 11.2% of the dose was excreted. The maximum residual radioactivity in the tissues was found in the 6-hour samples (except for fat at 12 hours). The levels of radioactivity detected in liver, kidney, muscle, fat, and blood at 6 hours were 29.8, 16.9, 1.3, 12.2, and 5.4 ppm, respectively. Within 96 hours, the radioactivity found in the tissues was 0.3 ppm or less, except for fat which was 0.9 ppm. The major portion of the radioactivity that was excreted in the feces was identified as the parent compound. Pendimethalin is metabolized in rats mainly through oxidation of the 4-methyl group attached to the benzene ring as well as oxidation of the alkyl side chain of the N-substituted dinitroaniline compound. Pendimethalin is rapidly eliminated from the body with 70% being excreted in the feces primarily unchanged as parent compound and 20% in the urine within 24 hours. It is mainly metabolized through oxidation of the 4-methyl group on the benzene ring and the alkyl side chain.

g. Carcinogenicity Classification

Cancer Classification and Basis: The HED Cancer Peer Review Committee classified pendimethalin as a "Group C", possible human carcinogen, "based on statistically significant increased trend and pairwise comparison between the high dose group and controls for thyroid follicular cell adenomas in male and female rats". They recommended that for the purpose of risk characterization, the RfD approach should be used for quantification of human risk. (HED report dated July 24, 1992). The RfD committee (meeting dated 1/5/96) determined that the hypothesis that thyroid tumors associated with pendimethalin are due to a thyroid-pituitary imbalance can be supported.

h. Endpoints Used for Risk Assessment

The Health Effects Division Less-Than-Lifetime/Peer Review Committee considered the toxicity data available for this chemical at a meeting held on January 5, 1996. Based upon a review of the toxicology database for the chemical listed above, toxicology endpoints and dose levels of concern have been identified for use in risk assessments corresponding to the categories below.

Dermal absorption: There were no dermal absorption studies and no appropriate toxicity studies available to allow an estimation of the dermal absorption by a route to route comparison of toxicity. However, structurally related chemicals: oryzalin, trifluralin and ethalfluralin have dermal absorption studies (in

monkeys) indicating that absorption is 2.3%, ≈1%, and 2.8% percent, respectively. The solubilities (water) for pendimethalin and related chemicals, oryzalin, ethalflualin and trifluralin are similar: 0.5 ppm, 2.5 ppm, 0.3 ppm and < 1 ppm, respectively. Therefore, for risk characterization purposes, it is estimated that absorption for pendimethalin will be no greater than 10 %.

Acute Dietary Endpoint (One Day): An acute dietary endpoint and dose for use in risk assessment was not identified; there are no toxicologic endpoints of concern for acute dietary risk.

Short Term Occupational or Residential Exposure (1 to 7 Days): In a 21-day dermal toxicity study (MRID 00026663), AC 92,553 (pendimethalin) was dermally applied to the back of 3 or 4 New Zealand white rabbits/group at dose levels of 0, 250, 500 or 1000 mg/kg/day. There were no adverse effects with respect to mortality, food and water intake, hematology, urinalysis and gross and microscopic pathology. **The systemic LOEL was not determined. The systemic NOEL is greater than 1000 mg/kg/day. therefore a risk assessment is not needed.**

Intermediate Term Occupational or Residential (1 Week to Several Months): The endpoint for use in risk assessment is the NOEL of 12.5 mg/kg/day (assume 10% dermal absorption) from the chronic dog study. A MOE of 100 is considered adequate. The effects observed at 50 mg/kg/day and higher include increased alkaline phosphatase activity in the blood, increased liver weight and hepatic pathology including inflammation and hemosiderosis. Effects observed at similar doses at earlier time points, in special hormonal rat studies, included thyroid endocrine changes and increased liver weight as described above. **Comments about studies and/or endpoint:** Although this is a chronic dog study it is felt that the study is appropriate since some effects relating to thyroid endocrine disruption occur in other studies at 31 mg/kg/day and progress in severity at 51 mg/kg/day and are observed as early as 15 to 28 days.

Chronic Occupational or Residential Exposure (greater than 90 Days): The endpoint for use in this risk assessment is the NOEL of 12.5 mg/kg/day (assume 10 % dermal absorption) from the chronic dog study. The effects observed at the LOEL of 50 mg/kg/day and higher are described above. **Comments about studies and/or endpoint:** This is the same NOEL used for the RfD.

Inhalation Occupational or Residential Exposure: There are no endpoints of concern therefore this risk assessment is not required.

RfD and Basis: The HED RfD/Peer Review Committee established the RfD for pendimethalin at 0.13 mg/kg/day. An uncertainty factor

(UF) of 100 was used. The NOEL of 12.5 mg/kg/day from the chronic toxicity study was used. The LOEL of 50 mg/kg/day, was based on increased alkaline phosphatase activity in the blood, increased liver weight and hepatic pathology including inflammation and hemosiderosis.

2. References

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00026672 Feinman, H.; Bistner, S.; Daniels, M.; et al. (1973) Report: Subacute Oral Toxicity Studies--AC 92553--Beagle Dogs: Laboratory No. 1421. (Unpublished study received on unknown date under 4G1451; prepared by Food and Drug Research Laboratories, Inc., submitted by American Cyanamid Co., Princeton, N.J.; CDL: 093868-U)

00040304 Rapp, W.R.; Kasner, J.A.; Wilson, N.H.; et al. (1974) A Three Generation Reproduction Study of AC 92,553 in Rats: Project No. 72R-748. (Unpublished study received Sep 27, 1974 under 5F1556; prepared by Bio/dynamics, Inc., submitted by American Cyanamid Co., Princeton, NJ; CDL:094232-C)

00046275 Zulalian, J. (1973) CL 92,553: Metabolism III. Isolation and Identification of Metabolites Present in Urine, Feces, and Selected Tissues of Rats Treated with Carbon-14 CL 92,553 [-N--(1-Ethyl-propyl)-2,6-dinitro-3,4-xylidine], Prowl Herbicide: Project No. 2-463. (Unpublished study received Sep 27, 1974 under 5F1556; submitted by American Cyanamid Co., Princeton, N.J.;CDL:094475-B)

00058657 Cueto, C., Jr.; Manus, A.G. (1979) Two-Year Toxicity Study in Dogs: AC 92,553: LBI Project No. 20755. Final rept. (Unpublished study received Feb 26, 1981 under 241-243; prepared by Litton Bionetics, Inc., submitted by American Cyanamid Co.,

Princeton, N.J.; CDL:244444-A; 244445)

00059468 Rapp, W.R.; Smith, J.M.; Kasner, J. (1973) A 3 and 24 Month Oral Toxicity and Carcinogenicity Study of Compound AC 92,553 in Rats: Project No. 72R-746. Three month interim rept. (Unpublished study received Dec 21, 1973 under unknown admin. no.;prepared by Bio/dynamics, Inc., submitted by American CyanamidCo., Princeton, N.J.; CDL:130681-L)

00059469 Tegeris, A.S. (1973) Final Report to ... on the Effect of Mammary Glands of a Ninety-Day Male Rat Feeding Study with AC 92,553. (Unpublished study received Dec 21, 1973 under unknown admin. no.; prepared by Pharmacopathics Research Laboratories, Inc.,submitted by American Cyanamid Co., Princeton, N.J.; CDL:130681-M)

00059470 Bio/dynamics, Incorporated (1973) A Three Generation Reproduction Study of AC 92,553 in Rats: Project No. 72R-748. Unpublished study received Dec 21, 1973 under unknown admin. no.; submitted American Cyanamid Co., Princeton, NJ; CDL:130681-N)

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00117444 Wolfe, G.; Mistretta, L.; Durloo, R. (1982) Teratology Study in Rabbits: AC 92,553 Technical: Project No. 362-164. Final rept. (Unpublished study received Oct 28, 1982 under 241-243; prepared by Hazleton Laboratories America, Inc., submitted by American Cyanamid Co., Princeton, NJ; CDL:248659-A)

00153767 Costello, B. (1985) Dermal Sensitization Study with AC 92,553 Lot #AC 3528-129-1 in Guinea Pigs: Project No. 85-4639A. Unpublished study prepared by Biosearch, Inc. 18 p.

00153768 Allen, J. (1985) Bacterial/Microsome Reverse Mutation (Ames) Test on AC 92,553 (Lot AC 3528-129-1): Project No. 0166. Unpublished study prepared by American Cyanamid Co. 31 p.

00153770 SanSebastian, J. (1985) In vitro Chromosomal Aberration Analysis in Chinese Hamster Ovary (CHO) Cells: AC 92,553: PH 320-AC-001-85. Unpublished study prepared by Pharmakon Research International, Inc. 34 p.

00153771 Barfknecht, T. (1985) Rat Hepatocyte Primary Culture/DNA Repair Test: AC 92,553: PH 311-AC-002-85. Unpublished study prepared by Pharmakon Research International, Inc. 100 p.

00156081 Fischer, J. (1986) AC 92,553: A 13-Week Rat Feeding Study: Project No. 0166: Toxicology Report AX86-1. Unpublished study prepared by American Cyanamid Co. 805 p.

40174401 Weltman, R. (1987) Chronic Dietary Toxicity and Oncogenicity Study in Rats Fed with AC 92,553 Prowl Herbicide :HLA Study No. 6123- 112. Unpublished study prepared by Hazleton Laboratories America, Inc. 1874 p.

40909901 Johnson, D. (1988) Chronic Dietary Toxicity and Oncogenicity Study with AC 92,553 in Mice: Report No. 141-028. Unpublished study prepared by International Research and Development Corp. 2052 p.

41725203 Irvine, L.; Boughton, P. (1990) Pendimethalin: Dietary Rat Two-Generation Reproduction Toxicity Study with AC 92,553: Lab Project Number: CBG/2/90. Unpublished study prepared by Toxicol Labs Ltd. and American Cyanamid Co. 717 p.

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42054601 Fischer, J. (1991) 92-Day Thyroid Function Study in Rats with AC 92,553: Lab Project Nimber: T-0270. Unpublished study prepared by American Cyanamid Co. 171 p.

43135001 Fischer, J. (1993) 56-Day Thyroid Function Study in Albino Rats with AC 92,533. Study No. AX-93-1, E2366. Report to EPA dated May, 28,1993.

Appendix 1
Product Chemistry Data Summary

011842

Case No. 0187
Chemical No. 108501

Case Name: Pendimethalin
Registrant: American Cyanamid Company
Product(s): 90% T (EPA Reg. No. 241-245)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	Y	CSF dated 9/11/91 [c]
61-2	Starting Materials and Manufacturing Process	Y	00153762 [d], 00158623
61-3	Discussion of Formation of Impurities	Y	00153762 [d], 00152847
62-1	Preliminary Analysis	Y	00153762 [d], 41111301
62-2	Certification of Ingredient Limits	Y	00153762 [d], 41111301, 41725201 [f], CSF dated 9/11/91 [c]
62-3	Analytical Methods to Verify the Certified Limits	Y	00153762 [d], 41111301, 41725201 [f]
63-2	Color	Y	00153762 [d]
63-3	Physical State	Y	00153762 [d]
63-4	Odor	Y	00153762 [d]
63-5	Melting Point	Y	00153762 [d]
63-6	Boiling Point	N/A [a]	
63-7	Density, Bulk Density or Specific Gravity	Y	00153762 [d]
63-8	Solubility	Y	00153762 [d]
63-9	Vapor Pressure	Y	00153762 [d]
63-10	Dissociation Constant	Y	00153762 [d]
63-11	Octanol/Water Partition Coefficient	Y	00153762 [d]
63-12	pH	Y	00153762 [d]
63-13	Stability	Y	00153762 [d]
63-14	Oxidizing or Reducing Action	Y	00153762 [d]
63-15	Flammability	Y	00153762 [d]
63-16	Explodability	Y	00153762 [d]
63-17	Storage Stability	Y	00161758
63-18	Viscosity	N/A [a]	
63-19	Miscibility	N/A [a]	
63-20	Corrosion Characteristics	Y	00153762 [d]

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] **Bolded** citations were reviewed in the Pendimethalin Reregistration Standard Update dated 3/19/90; and all other citations were reviewed as noted.

[c] CBRS No. 8683, D169168, 10/1/92, F. Toghrol.

[d] CBRS No. 789, 6/13/86, G. Makhijani.

[e] CBRS No. 790, 6/25/86, G. Makhijani.

[f] CBRS No. 7507 and 7517, D159827 and D159905, 4/24/91, E. Zager.

[g] Data are not required because the TGAI/MP is a solid at room temperature.

Appendix 1
Product Chemistry Data Summary

Case No. 0187
Chemical No. 108501

Case Name: Pendimethalin
Registrant: American Cyanamid Company
Product(s): 86.8% FI (EPA Reg. No. 241-291)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	Y	40392101
61-2	Starting Materials and Manufacturing Process	Y	40392101
61-3	Discussion of Formation of Impurities	Y [c]	
62-1	Preliminary Analysis	N/A [d]	
62-2	Certification of Ingredient Limits	Y	40392101
62-3	Analytical Methods to Verify the Certified Limits	Y [c]	
63-2	Color	N	
63-3	Physical State	N	
63-4	Odor	N	
63-5	Melting Point	N/A [d]	
63-6	Boiling Point	N/A [d]	
63-7	Density, Bulk Density or Specific Gravity	N	
63-8	Solubility	N/A [d]	
63-9	Vapor Pressure	N/A [d]	
63-10	Dissociation Constant	N/A [d]	
63-11	Octanol/Water Partition Coefficient	N/A [d]	
63-12	pH	N	
63-13	Stability	N/A [d]	
63-14	Oxidizing or Reducing Action	N	
63-15	Flammability	N	
63-16	Explodability	N	
63-17	Storage Stability	N	
63-18	Viscosity	N	
63-19	Miscibility	N	
63-20	Corrosion Characteristics	N	

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] The referenced citation was reviewed by the Registration Division (RD) in a letter dated 11/18/87 from R. Taylor of RD to M. Galley of American Cyanamid.

[c] Based on the manufacturing process, only impurities present in the technical source product will be present in the FI. The manufacturing process for the FI does not include any conditions (i.e., heat or changes in pH) or ingredients which will change the composition of the TGAI.

[d] Not applicable; TGAI/PAI data requirements will be satisfied by the technical source product.

[e] An analytical method has been submitted and evaluated for technical pendimethalin and formulations under submissions for the 90% T and 60% FI (CBRS No. 789, 6/13/86, G. Makhijani; and CBRS No. 685, 5/1/85, W. Anthony); this method is adequate for enforcement purposes for the 86.8% FI.

Appendix 1
Product Chemistry Data Summary

Case No. 0187
Chemical No. 108501

Case Name: Pendimethalin
Registrant: American Cyanamid Company
Product(s): 60% FI (EPA Reg. No. 241-281)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	Y	00154789
61-2	Starting Materials and Manufacturing Process	Y	00154789
61-3	Discussion of Formation of Impurities	Y [c]	
62-1	Preliminary Analysis	N/A [d]	
62-2	Certification of Ingredient Limits	Y	00154789
62-3	Analytical Methods to Verify the Certified Limits	Y	00154789
63-2	Color	Y	00154789
63-3	Physical State	Y	00154789
63-4	Odor	Y	00154789
63-5	Melting Point	N/A [d]	
63-6	Boiling Point	N/A [d]	
63-7	Density, Bulk Density or Specific Gravity	Y	00154789
63-8	Solubility	N/A [d]	
63-9	Vapor Pressure	N/A [d]	
63-10	Dissociation Constant	N/A [d]	
63-11	Octanol/Water Partition Coefficient	N/A [d]	
63-12	pH	N	
63-13	Stability	N/A [d]	
63-14	Oxidizing or Reducing Action	Y	00154789
63-15	Flammability	Y	00154789
63-16	Explodability	N	
63-17	Storage Stability	N	
63-18	Viscosity	Y	00154789
63-19	Miscibility	N	
63-20	Corrosion Characteristics	N	

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] The referenced citation was reviewed under CBRS No. 685, 5/1/85, W. Anthony.

[c] Based on the manufacturing process, only impurities present in the technical source product will be present in the FI. The manufacturing process for the FI does not include any conditions (i.e., heat or changes in pH) or ingredients which will change the composition of the TGAI.

[d] Not applicable; TGAI/PAI data requirements will be satisfied by the technical source product.

Attachment 2

011842

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DEC 12 1995

MEMORANDUM

SUBJECT: **Product and Residue Chemistry Chapters for the Pendimethalin Reregistration Eligibility Decision (RED) Document.**
CBRS No.: 16592
DP Barcode No.: D221531
Chemical No.: 108501
Reregistration Case No.: 0187

FROM: Bonnie Cropp-Kohlligian, Environmental Scientist
Reregistration Section II
Chemistry Branch II: Reregistration Support
Health Effects Division [7509C]

THRU: Edward Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division [7509C]

TO: Lois Rossi, Chief
Reregistration Branch
Special Review and Reregistration Division [7508W]

AND

Debra Edwards, [redacted]
Risk Characterization and Analysis Branch
Health Effects Division [7509C]

Attached are the Product and Residue Chemistry Chapters for the Pendimethalin RED Document. These documents were prepared by Dynamac Corporation and have been revised by CBRS, HED to reflect branch policies.

PRODUCT CHEMISTRY

All pertinent data requirements are satisfied for the 90% T and the pendimethalin TGAI; however additional product-specific data (physical/chemical properties) are outstanding for the 86.8% and 60% FIs. Provided that the registrant submits the data required in the attached data summary tables for the 86.8% and the 60% FIs, and either certifies that the suppliers of beginning materials and the manufacturing processes for the pendimethalin technical product and MPs have not changed since the last comprehensive product chemistry review or submits complete updated product chemistry data packages, CBRS has no objections to the reregistration of pendimethalin with respect to product chemistry data requirements.

RESIDUE CHEMISTRY

Adequate goat and poultry metabolism studies are available. The Agency has determined that there is no reasonable expectation of finite pendimethalin residues of concern in animal commodities (40 CFR §180.6(a)(3)). No additional animal metabolism, analytical methods, storage stability, and magnitude of the residue data are required. Tolerances for pendimethalin residues of concern in livestock commodities are not needed.

The qualitative nature of the residue in plants is understood. Pendimethalin *per se* and its 3,5-dinitrobenzyl alcohol metabolite are the residues of concern in/on plant commodities.

Adequate methods are available for data collection and tolerance enforcement. Radiovalidation data using samples from the potato metabolism study remain outstanding and are considered confirmatory.

Available storage stability data adequately support the plant magnitude of the residue data.

The reregistration requirements for magnitude of the residue in/on beans (succulent and dry); bean forage; bean fodder; corn stover (fodder); corn forage; field corn; pop corn; sweet corn (K+CWHR); cottonseed; garlic; onions (dry bulb); peanuts; peanut hay; potatoes; rice grain; rice straw; sorghum stover (fodder); sorghum forage; grain sorghum; soybeans; soybean forage; soybean hay; sugarcane; and sunflower seeds have been satisfied. Tobacco magnitude of the residue remain outstanding and are considered confirmatory.

Pendimethalin [redacted] data requirements for cotton gin byproducts which result from changes in the Liv[redacted] Table (TABLE II (September, 1995)) should be imposed at this time. However, [redacted] should not impinge on the reregistration eligibility decision for pendimethalin. The need for additional tolerances and revisions to the exposure/risk assessments will be made upon receipt and evaluation of the required data.

Adequate data are available to demonstrate that residues do not concentrate in commodities derived from corn, cottonseed, peanuts, potatoes, soybeans, sugarcane, and sunflower seeds.

Rice processing data remain outstanding and are considered confirmatory.

The available confined rotational crop study is not adequate. A new confined rotational crop study is required. This, however, will not preclude the reregistration of pendimethalin.

DIETARY EXPOSURE ASSESSMENT

The dietary exposure assessment for pendimethalin will be based on tolerance level residues and proposed tolerance levels as indicated herein. Since tolerance level residues will be used, the risk assessment will likely be upper bound.

The major uncertainty in the assessment is the lack of rice processing data. CBRS recommends that in the absence of rice processing data, dietary exposure assessments for rice bran should be based on the maximum theoretical concentration factor for residues in rice bran (8x) and the currently established tolerance on rice grain (0.1 ppm). [Note: All other processing data indicate that pendimethalin residues of concern do not concentrate in commodities derived from corn, cottonseed, peanuts, potatoes, soybeans, sugarcane, and sunflower seeds.]

Notes to the PM:

1. **Uses of pendimethalin to nonbearing orchard crops have been considered nonfood uses under the assumption that all end-use product labels permitting such uses include a 12-month harvest restriction on treated foods/feeds.**

2. **The Special Local Needs (SLN) registrations of pendimethalin to carrots and alfalfa grown for seed have been considered nonfood uses under the assumptions that all SLN labels permitting such uses include appropriate label restrictions to ensure that the treated crop is not diverted for consumption by humans and is not fed to livestock and that the states involved have an adequate mechanism to ensure that the treated crop is not diverted for consumption by humans and is not fed to livestock.**

3. **Having consulted the Pendimethalin LUIS report prepared by BEAD (9/25/95) for the Pendimethalin RED document describing registered uses of pendimethalin to onions and shallots, CBRS concludes that the established tolerance for pendimethalin residues of concern in/on onion (dry bulb) also applies to the currently registered use of pendimethalin on shallots (dry bulb only). End-use product labels must specify shallots (dry bulb only).**

4. **Having consulted the Pendimethalin LUIS report prepared by BEAD (9/25/95) for the Pendimethalin RED document describing registered uses of pendimethalin to beans and lupines, CBRS concludes that the established tolerance for pendimethalin residues of concern in/on beans applies to the currently registered use of pendimethalin on lupines.**

Attachments: Product and Residue Chemistry Chapters for the Pendimethalin Reregistration Eligibility Decision (RED) Document.

cc: BLCKohlligian (CBRS), Pendimethalin SF, Pendimethalin Reg. Std. File, RF, Circulate, DRES (E. Doyle), Dynamac.

RDI: RPerfetti: 12/8/95 EZager:12/8/95

7509C:CBRS:BLCKohlligian:CM#2:Rm 805B:703-305-7462:12/7/95.

PENDIMETHALIN

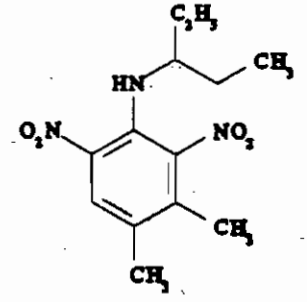
REREGISTRATION ELIGIBILITY DECISION:

PRODUCT CHEMISTRY CONSIDERATIONS

Shaughnessy No. 108501; Case No. 0187

DESCRIPTION OF CHEMICAL

Pendimethalin [N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine] is a selective herbicide registered for control of broadleaf weeds and grassy weed species.



Empirical Formula:	$C_{13}H_{19}N_3O_4$
Molecular Weight:	281.3
CAS Registry No.:	40487-42-1
Shaughnessy No.:	108501

IDENTIFICATION OF ACTIVE INGREDIENT

Pendimethalin is an orange-yellow crystalline solid with a melting point of 54-58 C. It is soluble in chlorinated hydrocarbons and aromatic solvents such as methylene chloride, acetone, and xylene, but only soluble in water at <0.5 ppm at 20 C. Pendimethalin is stable under acidic and alkaline conditions.

MANUFACTURING-USE PRODUCTS

A search of the Reference Files System (REFS) conducted 9/14/95 identified three pendimethalin manufacturing-use products (MPs) registered to American Cyanamid Company under Shaughnessy No. 108501: the 90% technical (T; EPA Reg. No. 241-245), and the 86.8% and 60% formulation intermediates (FIs; EPA Reg. Nos. 241-291 and 241-281, respectively). Only the American Cyanamid 90% T, and 86.8% and 60% FIs are subject to a reregistration eligibility decision.

REGULATORY BACKGROUND

The Pendimethalin Reregistration Standard dated 7/20/84 and Guidance Document dated 3/85 required additional data for the American Cyanamid 90% T. The Pendimethalin Reregistration Standard Update dated 3/19/90 required additional data concerning GLNs 62-2 and 62-3 for the 90% T. As was Agency policy at that time, data pertaining to the 86.8% and 60% FIs were not reviewed in the Update because the products were registered after the Guidance Document was issued. Data concerning the FIs have since been evaluated by either the Chemistry Branch or Registration Division (RD).

In addition because pendimethalin contains dinitroanilines, a discussion of the potential for formation of nitrosamines and analysis of the 90% T for the presence of nitrosamines formed during manufacture and storage of the product was required. Submitted data indicate that no volatile nitrosamines are present (<0.5 ppm) and that total nonvolatile nitrosamines are present at less than 100 ppm. The Agency had previously determined that concentrations of N-nitroso-pendimethalin below 135 ppm were required to maintain the associated upper risk below $1x10^{-6}$ (45 FR 49600).

The current status of the product chemistry data requirements for American Cyanamid pendimethalin products is presented in the attached data summary tables. Refer to these tables for a listing of the outstanding product chemistry data requirements.

CONCLUSIONS

All pertinent data requirements are satisfied for the 90% T and the pendimethalin TGAI; however additional product-specific data (physical/chemical properties) are outstanding for the 86.8% and 60% FIs. Provided that the registrant submits the data required in the attached data summary tables for the 86.8% and the 60% FIs, and either certifies that the suppliers of beginning materials and the manufacturing processes for the pendimethalin technical product and MPs have not changed since the last comprehensive product chemistry review or submits complete updated product chemistry data packages, CBRS has no objections to the reregistration of pendimethalin with respect to product chemistry data requirements.

AGENCY MEMORANDA CITED IN THIS DOCUMENT

CBRS No(s).:	685
Subject:	Pendimethalin; New Manufacturing Use Product.
From:	W. Anthony
To:	R. Taylor
Dated:	5/1/85
MRID(s):	00154789

CBRS No(s).:	789
Subject:	American Cyanamid Company - Response to the Product Chemistry Chapter of the Pendimethalin Registration Standard.
From:	G. Makhijani
To:	R. Taylor/V.K. Walters and A. Rispin
Dated:	6/13/86
MRID(s):	00153762

CBRS No(s).:	790
Subject:	Response to Pendimethalin Registration Standard by American Cyanamid Company.
From:	G. Makhijani
To:	R. Taylor/V.K. Walters and A. Rispin
Dated:	6/25/86
MRID(s):	00152847

CBRS No(s).:	None; RD Letter
Subject:	Prowl Herbicide Flaked (Revised Confidential Statement of Formula), EPA Registration No. 241-291, Your Letter Dated October 28, 1987.
From:	R. Taylor
To:	M. Galley, American Cyanamid Agricultural Research Division
Dated:	11/18/87
MRID(s):	40392101

CBRS No(s).:	7507 and 7517
DP Barcode(s):	D159827 and D159905
Subject:	American Cyanamid Company: Response to the Pendimethalin Reregistration Standard: Methodology and Product Chemistry.
From:	E. Zager
To:	L. Rossi and R. Engler
Dated:	4/24/91
MRID(s):	41725201

CBRS No(s).:	8683
DP Barcode(s):	D169168
Subject:	Pendimethalin Reregistration. (ID# 108501). American Cyanamid Response to Product Chemistry Data Requirements.
From:	F. Toghrol
To:	L. Rossi
Dated:	10/1/92
MRID(s):	CSF dated 9/11/91

Case No. 0187
Chemical No. 108501

Case Name: Pendimethalin
Registrant: American Cyanamid Company
Product(s): 90% T (EPA Reg. No. 241-245)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	Y	CSF dated 9/11/91 [c]
61-2	Starting Materials and Manufacturing Process	Y	**00153762 [d], 00158623**
61-3	Discussion of Formation of Impurities	Y	00153762 [d], 00152847
62-1	Preliminary Analysis	Y	**00153762 [d], 41111301**
62-2	Certification of Ingredient Limits	Y	**00153762 [d], 41111301,** 41725201 [f], CSF dated 9/11/91 [c]
62-3	Analytical Methods to Verify the Certified Limits	Y	**00153762 [d], 41111301,** 41725201 [f]
63-2	Color	Y	00153762 [d]
63-3	Physical State	Y	**00153762 [d]**
63-4	Odor	Y	00153762 [d]
63-5	Melting Point	Y	**00153762 [d]**
63-6	Boiling Point	N/A [a]	
63-7	Density, Bulk Density or Specific Gravity	Y	**00153762 [d]**
63-8	Solubility	Y	00153762 [d]
63-9	Vapor Pressure	Y	**00153762 [d]**
63-10	Dissociation Constant	Y	00153762 [d]
63-11	Octanol/Water Partition Coefficient	Y	**00153762 [d]**
63-12	pH	Y	00153762 [d]
63-13	Stability	Y	**00153762 [d]**
63-14	Oxidizing or Reducing Action	Y	00153762 [d]
63-15	Flammability	Y	**00153762 [d]**
63-16	Explodability	Y	00153762 [d]
63-17	Storage Stability	Y	**00161758**
63-18	Viscosity	N/A [a]	
63-19	Miscibility	N/A [a]	
63-20	Corrosion Characteristics	Y	00153762 [d]

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] **Bolded** citations were reviewed in the Pendimethalin Reregistration Standard Update dated 3/19/90; and all other citations were reviewed as noted.

[c] CBRS No. 8683, D169168, 10/1/92, F. Toghrol.

[d] CBRS No. 789, 6/13/86, G. Makhijani.

[e] CBRS No. 790, 6/25/86, G. Makhijani.

[f] CBRS No. 7507 and 7517, D159827 and D159905, 4/24/91, E. Zager.

[g] Data are not required because the TGAI/MP is a solid at room temperature.

Case No. 0187
Chemical No. 108501

Case Name: Pendimethalin
Registrant: American Cyanamid Company
Product(s): 86.8% FI (EPA Reg. No. 241-291)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	Y	40392101
61-2	Starting Materials and Manufacturing Process	Y	40392101
61-3	Discussion of Formation of Impurities	Y [c]	
62-1	Preliminary Analysis	N/A [a]	
62-2	Certification of Ingredient Limits	Y	40392101
62-3	Analytical Methods to Verify the Certified Limits	Y [c]	
63-2	Color	N	
63-3	Physical State	N	
63-4	Odor	N	
63-5	Melting Point	N/A [a]	
63-6	Boiling Point	N/A [a]	
63-7	Density, Bulk Density or Specific Gravity	N	
63-8	Solubility	N/A [a]	
63-9	Vapor Pressure	N/A [a]	
63-10	Dissociation Constant	N/A [a]	
63-11	Octanol/Water Partition Coefficient	N/A [a]	
63-12	pH	N	
63-13	Stability	N/A [a]	
63-14	Oxidizing or Reducing Action	N	
63-15	Flammability	N	
63-16	Explodability	N	
63-17	Storage Stability	N	
63-18	Viscosity	N	
63-19	Miscibility	N	
63-20	Corrosion Characteristics	N	

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] The referenced citation was reviewed by the Registration Division (RD) in a letter dated 11/18/87 from R. Taylor of RD to M. Galley of American Cyanamid.

[c] Based on the manufacturing process, only impurities present in the technical source product will be present in the FI. The manufacturing process for the FI does not include any conditions (i.e., heat or changes in pH) or ingredients which will change the composition of the TGAI.

[d] Not applicable; TGAI/PAI data requirements will be satisfied by the technical source product.

[e] An analytical method has been submitted and evaluated for technical pendimethalin and formulations under submissions for the 90% T and 60% FI (CBRS No. 789, 6/13/86, G. Makhijani; and CBRS No. 685, 5/1/85, W. Anthony); this method is adequate for enforcement purposes for the 86.8% FI.

Case No. 0187
Chemical No. 108501

Case Name: Pendimethalin
Registrant: American Cyanamid Company
Product(s): 60% FI (EPA Reg. No. 241-281)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	Y	00154789
61-2	Starting Materials and Manufacturing Process	Y	00154789
61-3	Discussion of Formation of Impurities	Y [c]	
62-1	Preliminary Analysis	N/A [d]	
62-2	Certification of Ingredient Limits	Y	00154789
62-3	Analytical Methods to Verify the Certified Limits	Y	00154789
63-2	Color	Y	00154789
63-3	Physical State	Y	00154789
63-4	Odor	Y	00154789
63-5	Melting Point	N/A [d]	
63-6	Boiling Point	N/A [d]	
63-7	Density, Bulk Density or Specific Gravity	Y	00154789
63-8	Solubility	N/A [d]	
63-9	Vapor Pressure	N/A [d]	
63-10	Dissociation Constant	N/A [d]	
63-11	Octanol/Water Partition Coefficient	N/A [d]	
63-12	pH	N	
63-13	Stability	N/A [d]	
63-14	Oxidizing or Reducing Action	Y	00154789
63-15	Flammability	Y	00154789
63-16	Explodability	N	
63-17	Storage Stability	N	
63-18	Viscosity	Y	00154789
63-19	Miscibility	N	
63-20	Corrosion Characteristics	N	

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] The referenced citation was reviewed under CBRS No. 685, 5/1/85, W. Anthony.

[c] Based on the manufacturing process, only impurities present in the technical source product will be present in the FI. The manufacturing process for the FI does not include any conditions (i.e., heat or changes in pH) or ingredients which will change the composition of the TGAI.

[d] Not applicable; TGAI/PAI data requirements will be satisfied by the technical source product.

Pendimethalin

REREGISTRATION ELIGIBILITY DECISION

RESIDUE CHEMISTRY CONSIDERATIONS

Shaughnessy No. 108501; Case No. 0187

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Pendimethalin

REREGISTRATION ELIGIBILITY DECISION

RESIDUE CHEMISTRY CONSIDERATIONS

Shaughnessy No. 108501; Case No. 0187

INTRODUCTION

Pendimethalin [N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzamine] is a herbicide registered for use on numerous food/feed crops. Pendimethalin is manufactured by American Cyanamid Co. under the trade names Pentagon®, Prowl®, Pursuit®, and Squadron®. Formulations registered for food/feed uses include emulsifiable concentrates (ECs), soluble concentrates/liquid (SC/L), and water dispersable granules (WDG). Pendimethalin is applied to soil as preplant, preemergence, and postemergence applications, including at layby, with ground or aerial equipment.

REGULATORY BACKGROUND

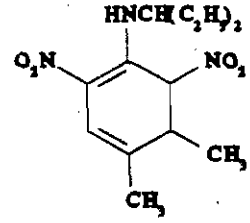
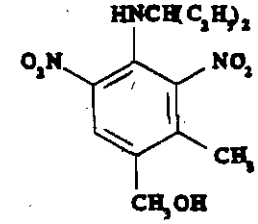
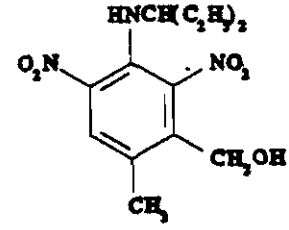
The Pendimethalin Guidance Document was issued 3/85. Pendimethalin was the subject of a Reregistration Standard Update issued 4/13/90. These documents summarized regulatory conclusions regarding the available residue chemistry data. The 1990 Update specified that additional data were required for reregistration purposes. Several submissions of data have been received since the Update. The information contained in this document outlines the current Residue Chemistry Science Assessments with respect to the reregistration of pendimethalin.

Tolerances of 0.1 ppm (except 0.05 ppm for rice grain) are established for the combined residues of pendimethalin [N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine] and its metabolite 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol in/on beans, corn (field and fresh), cottonseed, onions (dry bulb), peanuts, potatoes, grain sorghum, soybeans, sugarcane, and sunflower seeds [40 CFR §180.361(a)]. A tolerance of 0.25 ppm has been established for the combined residues of pendimethalin and its metabolites 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol and 3-[(1-ethylpropyl)amino]-6-methyl-2,4-dinitrobenzyl alcohol in/on peanut hulls [40 CFR §180.361(b)]. A tolerance with regional registration of 0.1 ppm has been established for the combined residues of pendimethalin and its metabolite 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol in/on garlic [40 CFR §180.361(c)]. The molecular structures of pendimethalin and currently regulated metabolites are depicted in Figure 1.

The Agency has recently updated the Livestock Feeds Table [Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Table II (September, 1995)]. Additional residue data are now required for some commodities as a result of changes in Table II; these

data requirements have been incorporated into this document. These new data requirements will be imposed at the issuance of the Pendimethalin RED but should not impinge on the reregistration eligibility decision for pendimethalin. The need for additional tolerances and for revisions to exposure/risk assessments will be determined upon receipt of the required residue chemistry data.

Figure 1. Chemical names and structures of pendimethalin and its metabolites.

Common/Chemical Names	Structures
Pendimethalin N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine	
3,5-Dinitrobenzyl alcohol metabolite 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol	
2,4-Dinitrobenzyl alcohol metabolite 3-[(1-ethylpropyl)amino]-6-methyl-2,4-dinitrobenzyl alcohol	

SUMMARY OF SCIENCE FINDINGS

GLN 171-3: Directions for Use

A REFs search conducted 9/14/95 indicated that there are eight pendimethalin end-use products (EPs) with food/feed uses registered to American Cyanamid Co. These EPs are presented below.

EPA Reg. No.	Acceptance Date	Formulation Class	Product Name
241-243	7/95	4 lb/gal EC	Prowl® Herbicide
241-244	2/87	3 lb/gal EC	Prowl® 3E Herbicide
241-268	7/95	60% WDG	Pentagon® DG Herbicide
241-297	2/91	2 lb/gal SC/L	Squadron® Herbicide
241-315	1/93	2.7 lb/gal EC	Pursuit® Plus Herbicide
241-327	2/95	2 lb/gal SC/L	Squadron® Herbicide
241-331	10/95	3 lb/gal EC	Pursuit® Plus EC Herbicide
241-337*	5/95	3.3 lb/gal EC	Prowl® 3.3 EC Herbicide

* Including SLN Nos. ID930012, MT930003, NV920004, NY940003, OR930001, OR930002, UT920004, WA920015, WA920034, WY920005.

The labels under EPA Reg Nos. 241-268, -327, -331, -337 require a 12-hour re-entry interval. A re-entry interval is not specified on any other label.

The active pendimethalin labels are not consistent with respect to PHIs for certain crops (Table A). The labels must be revised to specify a PHI for each crop with registered layby applications.

A comprehensive summary of the registered food/feed use patterns of pendimethalin, based on the product labels registered to American Cyanamid, is presented in Table A. Uses of pendimethalin to nonbearing orchard crops are considered nonfood uses assuming that all end-use product labels permitting such uses include a 12-month harvest restriction on treated foods/feeds. The Special Local Needs (SLN) registration of pendimethalin to carrots grown for seed in Washington (WA920015) is considered a nonfood use assuming that the SLN label includes appropriate label restrictions to ensure that the treated crop is not diverted for consumption by humans and is not fed to livestock. The Special Local Needs (SLN) registration of pendimethalin to carrots grown for seed in Oregon (OR930002) is considered a nonfood use assuming that the SLN label includes appropriate label restrictions and the State of Oregon has an adequate mechanism to ensure that the treated crop is not diverted for consumption by humans and is not fed to livestock. The Special Local Needs (SLN) registrations of pendimethalin to alfalfa grown for seed may be considered nonfood uses

assuming that the SLN labels include appropriate label restrictions and the individual states have adequate mechanisms to ensure that the treated crop is not diverted for consumption by humans and is not fed to livestock.

A tabular summary of the residue chemistry science assessments for reregistration of pendimethalin is presented in Table B. The conclusions listed in Table B regarding the reregistration eligibility of pendimethalin food/feed uses are based on the use patterns registered by the basic producer, American Cyanamid Co. When end-use product DCIs are developed (e.g., at issuance of the RED), RD should require that all end-use product labels (e.g., MAI labels, SLNs, and products subject to the generic data exemption) be amended such that they are consistent with the basic producer labels.

GLN 171-4 (a): Plant Metabolism: The qualitative nature of the residue in plants is understood based on adequate studies conducted with [^{14}C]pendimethalin on potatoes and sweet corn. The results of these studies are supported by additional corn, cotton, dry bean, lima bean, peanut, potato, red table beet, rice, snapbean, soybean, sugarcane, and wheat metabolism data. Pendimethalin *per se* and its 3,5-dinitrobenzyl alcohol metabolite are the residues of concern.

The current tolerance expressions specify the combined residues of pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite and, for peanut hulls, the 2,4-dinitrobenzyl alcohol metabolite as well.

GLN 171-4 (b): Animal Metabolism: Adequate goat and poultry metabolism studies are available. The Agency has determined that there is no reasonable expectation of finite pendimethalin residues of concern in animal commodities (40 CFR §180.6(a)(3)). No additional animal metabolism, analytical methods, storage stability, and magnitude of the residue data are required. Tolerances for pendimethalin residues of concern in livestock commodities are not needed.

GLN 171-4 (c/d): Residue Analytical Methods: Adequate methods are available for data collection and tolerance enforcement. Methods I through IV in PAM Vol. II are gas chromatography/electron capture (GC/ECD) methods. Methods used for data collection are essentially the same as the PAM Vol. II methods.

Radiovalid[redacted] using samples from the potato metabolism study remain outstanding and are consid[redacted]rmatory.

The FDA PESTDATA database dated 1/94 (PAM Volume I, Appendix I) indicates that pendimethalin is completely recovered (>80%) by Multiresidue Methods Section 302 (Luke method; Protocol D) and 303 (Mills, Onley, Gaither method; Protocol E, nonfatty), and partially recovered (50-80%) by Multiresidue Method Section 304 (Mills fatty food method; Protocol E, fatty).

GLN 171-4 (e): Storage Stability Data: CBRS concludes that available storage stability data on almonds (representative of oilseeds), alfalfa seed (representative of non-oily seeds), onions, potatoes, soybean forage and hay, wheat straw, and alfalfa forage and hay adequately support the plant magnitude of the residue data. No additional storage stability data are required.

GLN 171-4 (k): Magnitude of the Residue in Plants: The reregistration requirements for magnitude of the residue in/on beans (succulent and dry); bean forage; bean fodder; corn stover (fodder); corn forage; field corn; pop corn; sweet corn (K+CWHR); cottonseed; garlic; onions (dry bulb); peanuts; peanut hay; potatoes; rice grain; rice straw; sorghum stover (fodder); sorghum forage; grain sorghum; soybeans; soybean forage; soybean hay; sugarcane; and sunflower seeds have been satisfied. Tobacco magnitude of the residue remain outstanding and are considered confirmatory.

Pendimethalin residue data requirements for cotton gin byproducts which result from changes in the Livestock Feeds Table (TABLE II (September, 1995)) should be imposed at this time. However, this requirement should not impinge on the reregistration eligibility decision for pendimethalin. The need for additional tolerances and revisions to the exposure/risk assessments will be made upon receipt and evaluation of required data.

GLN 171-4 (l): Magnitude of the Residue in Processed Food/Feed: Adequate data are available to demonstrate that pendimethalin residues of concern do not concentrate in commodities derived from corn, cottonseed, peanuts, potatoes, soybeans, sugarcane, and sunflower seeds. Rice processing data remain outstanding and are considered confirmatory.

GLN 171-4 (j): Magnitude of the Residue in Meat, Milk, Poultry, and Eggs: The Agency has determined that there is no reasonable expectation of finite pendimethalin residues of concern in animal commodities (40 CFR §180.6(a)(3)). Therefore, livestock feeding studies and tolerances on livestock commodities are not required.

GLN 165-1 and 165-2: Rotational Crops: The available confined rotational crop study is not adequate. A new confined rotational crop study is required. This, however, will not preclude the reregistration of pendimethalin.

TABLE A. FOOD/FEED USE PATTERNS SUBJECT TO REREGISTRATION FOR PENDIMETHALIN (CASE 0187).

Site Application Type Application Timing Application Equipment[a]	Form [EPA Reg. No.]	Max. Single Application Rate (lb ai/A)			Max. # Apps.[b]	Use Limitations
Beans (dry, lima, snap, chickpeas, southern peas (cowpeas), sweet lupines						
Soil Preplant incorporated, preemergence (sweet lupines only) Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268]	Soil Coarse Medium Fine	So. States 0.75 1.0 1.5	No. States 1.0 1.5 1.5	1	Preplant incorporated only on chickpeas, dry beans, lima beans, snap beans, and southern peas (cowpeas) Do not feed lupine hay or forage or graze livestock in treated fields
Corn (field)						
Soil[c] Preemergence, postemergence (broadcast) Ground, aerial	4 lb/gal EC [241-243] 3 lb/gal EC [241-244] 3.3 lb/gal EC [241-337] 60% WDG [241-268] 2.7 lb/gal EC [241-331]	Soil Coarse Medium Fine	1-1.5[d] 1.5-2[d] 1.5-2[d]		1	Livestock may graze or be fed forage 21 days after layby application
Layby (incorporated)		Soil Coarse Medium Fine	0.75-1.0[e] 1.0-1.5[e] 1.0-1.5[e]			

(continued; footnotes follow.)

Table A. (continued)

Site Application Type Application Timing Application Equipment[a]	Form [EPA Reg. No.]	Max. Single Application Rate (lb ai/A)			Max. # Apps.[b]	Use Limitations
Corn (sweet)						
Soil Preemergence, postemergence (broadcast) Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268] 2.7 lb/gal EC [241-331]	<u>Soil</u> Coarse Medium Fine	1-1.5[d] 1.5-2[d] 1.5-2[d]		1	May be applied preemergence only to sweet corn (all varieties) in AZ, CA, ID, MT, OR, TX, WA; preemergence or postemergence application to processing varieties only in IL, MN, NY, WY Early postemergence application only allowed in AL, FL, GA
Cotton						
Soil Preplant incorporated, preemergence Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 3 lb/gal EC [241-244] 60% WDG [241-268]	<u>Soil</u> Coarse Medium Fine	0.75 1.0 1.5	<u>No-till</u> 1.0 1.5 2.0	2	Do not graze or feed forage Do not use on no-till cotton in CA
Postemergence layby Ground						Layby application permitted in AZ, CA, NM, and TX only 60 day PHI
Garlic						
Soil Preemergence, postemergence Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268]	<u>Soil</u> Coarse Medium Fine	0.75 1.0 1.5		1	5-month PHI Regional registration for AZ, CA, NV, OR only Not to be used on peat or muck soils

(continued; footnotes follow.)

Table A. (continued)

Site Application Type Application Timing Application Equipment[a]	Form [EPA Reg. No.]	Max. Single Application Rate (lb ai/A)		Max. # Apps.[b]	Use Limitations
Onions (dry bulb)					
Soil Pre-transplant Postemergence Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268]	Soil Coarse Medium Fine	0.75 1.0 1.5	1	45-day PHI (except CA) 60-day PHI in CA
		Muck	(2 in ID, OR, WA) 2	3	Do not use on muck soils in CA
Soil Preemergence, postemergence	NY940003	Muck	2	2	45-day PHI
Peanuts					
Soil[c] Pre-plant incorporated Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268]	TX, OK, NM AL, GA, FL Other	0.75 1.5 1.0	1	Do not use in CA Do not use on peat or muck soils
Potatoes					
Soil[c] Preemergence, postemergence Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268]	Soil Coarse Medium Fine	0.75 1-1.5[d] 1.5	1	

(continued; footnotes follow.)

Table A. (continued)

Site Application Type Application Timing Application Equipment[a]	Form [EPA Reg. No.]	Max. Single Application Rate (lb ai/A)		Max. # Apps.[b]	Use Limitations
Rice					
Soil Early postemergence preemergence Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268]	Soil Coarse Medium Fine	0.75 1.0 1.0	1	Do not apply to rice fields used for fish or crayfish production Do not use straw for feed [241-243, -268, -337] Do not use on water-seeded rice Do not use water from treated fields for irrigating food or feed crops Do not use in CA Do not use on peat or muck soils
Sorghum (grain)					
Soil[c] Postemergence incorporated Ground	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268]	Soil Coarse Medium Fine	0.75-1[c] 1.0-1.5[c] 1.5	1	Livestock may graze or be fed forage 21 days after application

(continued; footnotes follow.)

Table A. (continued)

Site Application Type Application Timing Application Equipment[a]	Form [EPA Reg. No.]	Max. Single Application Rate (lb ai/A)			Max. # Apps.[b]	Use Limitations
Soybeans						
Soil[c] Preplant, preplant incorporated preemergence Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268] 2.7 lb/gal EC [241-315] [241-331] 2 lb/gal SC/L [241-297] 2 lb/gal SC/L [241-327]	Soil Coarse Medium Fine		0.75-1[d] 1-1.5[d] 2.0	1	85-day PHI (241-315, -331) 90-day PHI (241-327, -297) Do not graze or feed treated soybean forage, hay, or straw to livestock (241-297, -315, -327, -331) Livestock can graze or be fed soybean forage from treated fields (241-243, -268, -337) Do not use in CA (241-243, -268, -337)
Sugarcane						
Soil Broadcast or banded Preemergence, postemergence through layby Ground, aerial	3.3 lb/gal EC [241-337] 60% WDG [241-268]	Hawaii 4 Other states 3			2	90 day PHI Do not graze treated fields or feed forage or fodder to livestock A maximum of 6 lb ai/A may be applied per season
Sunflowers						
Soil[c] Preplant incorporated Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268]	Soil Coarse Medium Fine	So. States 0.75 1.0 1.5	No. States 1.0 1.5 1.5	1	Do not feed forage or graze livestock in treated fields Do not use on peat or muck soils

(continued; footnotes follow.)

Table A. (continued)

Site Application Type Application Timing Application Equipment[a]	Form [EPA Reg. No.]	Max. Single Application Rate (lb ai/A)			Max. # Apps.[b]	Use Limitations
Tobacco						
Soil Preplant incorporated Ground, aerial	4 lb/gal EC [241-243] 3.3 lb/gal EC [241-337] 60% WDG [241-268]	Soil	MD, VA, NC, SC, GA, FL	Other states	2	
		Coarse	1.0	1.0		
		Medium	1.0	1.0		
		Fine	1.25	1.25		
Soil Layby ground		Soil			2	Layby application should be directed to soil between rows
		Coarse	0.75			
		Medium	1.0			
		Fine	1.0			
Crops grown for seed						
Carrots (grown for seed)						
Soil Layby Ground	OR930002 WA920015	2			1	Do not harvest carrots from treated areas for food or feed Seed must be labeled "not for human or animal consumption" Seed screenings may not be used for food or feed

(continued; footnotes follow.)

Table A. (continued)

Site Application Type Application Timing Application Equipment[a]	Form [EPA Reg. No.]	Max. Single Application Rate (lb ai/A)	Max. # Apps.[b]	Use Limitations
Alfalfa (grown for seed)				
Soil Postemergence Ground	ID930012 MT930003 NV920004 OR930001 UT920004 WA920034 WY920005	4	1-4 (max 4	Apply to dormant alfalfa Do not feed or graze Do not cut for forage Do not use harvested seed for sprouting Processed seed must be labeled "not for human or animal consumption"

[a] Unless otherwise specified, application using irrigation equipment is prohibited.
[b] In cases when more than one application is allowed, no repeat treatment interval is specified.
[c] Chemigation application allowed.
[d] The lower maximum rate is specified for soils with organic matter up to 1.5% and the higher maximum rate is listed for soils with organic matter to >3%.
[e] The lower maximum rate is specified for southern states and the higher maximum rate is listed for northern states.

Table B. Residue Chemistry Science Assessments for Reregistration of Pendimethalin.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
171-3: Directions for Use	N/A	Yes[2]	See Table A.
171-4 (a): Plant Metabolism	N/A	No	00029803 00031219 00039535 00039537 00046278 00046280 00051963 00051965 00058478 00067293 00071121 00074621 00093698 00106779 00106795 00108317 00109915 41469901[3] 42467801[4] 42686401[5] 43154705[6]
171-4 (b): Animal Metabolism	N/A	No	00046275 00046293 00067288 00067289 00071124 41713901[7] 42467802[8]

(continued; footnotes follow)

Table B. *(continued)*.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
171-4 (c/d): Residue Analytical Methods	N/A	Yes[9]	00019004 00023780 00023781 00023782 00023796 00024823 00025820 00025821 00025822 00025827 00025828 00025831 00025832 00025833 00025837 00029018 00029020 00031212 00031214 00039519 00039520 00039521 00039522 00039526 00039527 00039528 00039529 00041898 00041901 00041904 00051958 00051959 00051960 00051961 00051962 00052558 00058835 00070962 00071120 00072810 00072822 00072823 00072824 00072825 00106752 00106791 00106808 00106830 41431001[10] 41827401[11] 41845801[12] 41982701[12] 42471901[8] 42471902[8] 42859202[13] 43068501[14] 43154704[15] 43185901[16]
171-4 (e): Storage Stability	N/A	No	40535101 42266301[17] 42471903[8]
171-4 (k): Magnitude of the Residue in Plants			
Root and Tuber Vegetables Group			
- Potatoes	0.1 [§180.361(a)]	No	00106797
Bulb Vegetables Group			
- Garlic	0.1 [§180.361(c)]	No[18]	40232501[19]

(continued; footnotes follow)

Table B. *(continued)*.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
- Onions (dry bulb)	0.1 [§180.361(a)]	No	41827401[20]
Legume Vegetables Group			
- Beans (succulent and dry)	0.1 Beans, lima (dry, snap) [§180.361(a)]	No	00039518[21] 00039519[21] 00039520[21] 00039521[21] 00039522[21] 00039523[21] 00039524[21] 00039534[21] 00081581[21]
- Soybeans	0.1 [§180.361(a)]	No	00025818 00029801 00041897
- Soybeans, aspirated grain fractions	None	No[22]	
Foliage of Legume Vegetables Group			
- Bean forage and hay	0.1 [§180.361(a)]	No	00039518[21] 00039519[21] 00039520[21] 00039521[21] 00039522[21] 00039523[21] 00039524[21] 00039534[21] 00081581[21]
- Soybean forage and hay	0.1 [§180.361(a)]	No	00025818 00029801 00161759 00161760 00161761 40185101[23]
Cereal Grains Group			
- Corn, grain	0.1 [§180.361(a)]	No[24]	00023786 00023787 00023788 00023789 00023790 00023791 00023792 00023793 00023794 00023795 00029029 00030697 00093697 00106820
- Corn, fresh	0.1 [§180.361(a)]	No	00074619[25] 00093719[25]
- Corn, field, aspirated grain fractions	None	No[22]	

(continued; footnotes follow)

Table B. *(continued)*.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must no Additional Data Be Submitted?	References[1]
- Rice, grain	0.05 [§180.361(a)]	No[26]	00067283 00071120
- Rice, straw	None	No[27]	00067283 00071120
- Sorghum, grain	0.1 [§180.361(a)]	No	00106791 00106807 00114313
- Sorghum, grain, aspirated grain fractions	None	No[22]	
Forage, Fodder and Straw of Cereal Grains Group			
- Corn, forage and fodder	0.1 [§180.361(a)]	No[28]	00023786 00023787 00023788 00023789 00023790 00023791 00023792 00023793 00023794 00023795 00029028 00029029 00030697 00093697 00106820
- Sorghum, forage and fodder	0.1 [§180.361(a)]	No[28]	00106791 00106807 00114313
Miscellaneous Commodities			
- Cottonseed	0.1 [§180.361(a)]	No	00018997 00106752 00106829 41881201[29] 42858901[30]
- Cotton gin byproducts	None	Yes[31]	
- Peanuts	0.1 [§180.361(a)]	No	00106785
- Peanut, hulls	0.1 [§180.361(b)]	No[32]	00031215 00031216 00031217 00106785
- Peanut, forage	0.1 [§180.361(a)]	No[32]	00106785
- Peanut, hay	0.1 [§180.361(a)]	No	00106785
- Sugarcane	0.1 [§180.361(a)]	No	42859201[13]
- Sunflower, seeds	0.1 [§180.361(a)]	No	00134355
- Tobacco	None	Yes[33]	00129937
171-4(l): Magnitude of the Residues in Processed Food/Feed			
- Corn grain	None	No[34]	
- Cottonseed	None	No[34]	00106752

(continued; footnotes follow)

Table B. *(continued)*.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References[1]
- Peanuts	None	No[34]	00106785
- Potatoes	None	No[35]	00106797
- Rice Grain	None	Yes	
- Soybeans	None	No	00025818
- Sugarcane	None	No[36]	[PP#3F2765]
- Sunflower seed	None	No[34]	00134355
171-4 (f): Magnitude of the Residue - Potable Water	N/A	No	00046293 00071124
171-4 (g): Magnitude of the Residue - Fish	None	No[37]	00046293 00071124
171-4 (h): Magnitude of the Residue - Irrigated Crops	None	No[37]	
171-4 (i): Magnitude of the Residue - Food Handling	N/A	N/A	
171-4 (j): Magnitude of the Residue in Meat, Milk, Poultry, and Eggs	None	No[38]	
165-1: Rotational Crops (Confined)	N/A	Yes[39]	41806801[40]
165-2: Rotational Crops (Field)	None		

1. References were reviewed in the Pendimethalin Registration Standard (Guidance Document dated 3/85). References in bold were reviewed in the 4/90 Reregistration Standard Update. Otherwise, submissions were reviewed as noted.

2. The active pendimethalin labels are not consistent with respect to PHIs for certain crops and must be revised to specify a PHI for each crop with registered layby applications.

3. DEB Nos. 6570/6603/6604/7153, 1/29/91, R. Loranger and R. Perfetti.

4. CBRS No. 10678, DP Barcode D183220, 2/1/93, P. Deschamp and CBRS No. 11797, DP Barcode D190778, 6/16/93, P. Deschamp.

5. CBRS No. 11582, DP Barcode D189207, 6/16/93, P. Deschamp and CBRS No. 12673, DP Barcode D195890, 2/9/94, B. Cropp-Kohlligian.

6. CBRS No. 12673, DP Barcode D195890, 2/9/94, B. Cropp-Kohlligian and CBRS No. 13411, DP Barcode D200669, 11/15/94, B. Cropp-Kohlligian.

7. CBTS Nos. 7595/7596, 3/5/91, F. Griffith; CBTS Nos. 8859/8860, DP Barcode D170619, 4/29/92, F. Griffith; and CBTS No. 15373, DP Barcode D212340, 4/7/95, J. Stokes and B. Cropp-Kohlligian.

8. CBRS No. 10678 Addendum, DP Barcode D183220, 9/24/93, P. Deschamp.

(continued)

Table B *(continued)*.

9. Radiovalidation data from the potato metabolism study remain outstanding. Representative samples from the potato metabolism study must be analyzed using the currently accepted enforcement analytical method (CBRS No. 10678, DP Barcode No. D183220, 2/1/93, P. Deschamp).

10. CBRS Nos. 7507/7517, DP Barcodes D159827/D159905, 4/24/91, E. Zager.

11. PP#1E3965. CBTS No. 7887, DP Barcode D163268, 7/10/91, G.J. Herndon.

12. CBRS Nos. 8118/8515, DP Barcodes D165134/D167858, 5/15/92, E. Zager.

13. CBTS No. 11230, DP Barcode D193627, 7/25/94, R. Cook.

14. CBRS No. 13400, DP Barcode D200608, 7/24/95, B. Cropp-Kohlligian.

15. CBRS No. 13411, DP Barcode D200669, 11/15/94, B. Cropp-Kohlligian.

16. CBRS No. 13506, DP Barcode D201694, 11/15/94, B. Cropp-Kohlligian.

17. CBRS No. 9914, DP Barcode D178454, 10/22/93, P. Deschamp.

18. CBRS concludes that available garlic magnitude of the residue data from field trials conducted in CA and OR are adequate to support a national registration for the use of pendimethalin on garlic and recommends that the currently established tolerance with regional registrations for pendimethalin residues of concern in/on garlic should be changes to a tolerance without regional registrations at the same level (0.1 ppm) and listed under 40 CFR §180.361(a).

19. PP#7E3537. Memoranda by G. Otakie dated 8/20/87 and H. Fonoumi dated 8/27/90.

20. PP#1E3965. CBTS No. 7887, DP Barcode D163268, 7/10/91, G.J. Herndon; CBTS No. 9616, DP Barcode D175936, 10/22/92, G.J. Herndon; CBTS No. 11391, DP Barcode D188216, 2/24/93, G.J. Herndon; and CBRS No. 9464, DP Barcode D174858, 9/24/93, P. Deschamp.

21. PP#1F2567. Memorandum, no CB No., no DP Barcode, 4/29/82, A. Smith.

22. As a result of changes in the Livestock Feeds Table (TABLE II (September 1995)), the Agency now considers aspirated grain fractions of soybeans, field corn, and grain sorghum as raw agricultural commodities (RACs). Residue chemistry data for these RACs are waived since pendimethalin is applied to soybeans, field corn, and grain sorghum very early in the growing season (i.e., preplant, preemergence and/or postemergence) and pendimethalin residues of concern in/on aspirated grain fractions of soybeans, field corn, and grain sorghum are unlikely to exceed the currently established tolerances on soybeans, field corn grain, and grain sorghum. No tolerances for pendimethalin residues of concern are needed for aspirated grain fractions of soybeans, field corn, and grain sorghum.

23. CB Nos. 5494/5495, 8/8/89, D. Edwards.

24. Data from field corn magnitude of the residue studies will be used to support the use of pendimethalin on pop corn.

25. PP#2F2628. Memorandum, no CB No., no DP Barcode, 7/15/82, A. Smith.

Table B *(continued)*.

26. As recommended in the 1984 Pendimethalin Registration Chemistry Chapter, the currently established rice grain tolerance should be increased from 0.05 ppm to 0.1 ppm.

27. Available rice field trial data are hereby deemed adequate to support a tolerance for pendimethalin residues of concern in/on rice straw. A tolerance of 0.1 ppm would be appropriate.

28. As a result of changes in the Livestock Feeds Table (TABLE II (September 1995)), the Agency now considers corn stover and sorghum stover as raw agricultural commodities (RACs). Available pendimethalin field trial data on corn/sorghum grain and corn/sorghum fodder (presumably the mature dried stalks with grain) reflecting the maximum use rates of pendimethalin to corn and sorghum demonstrated that pendimethalin residues of concern in/on corn grain, grain sorghum, corn fodder, and sorghum fodder were nondetectable (< 0.1 ppm). Hence, CBRS, concludes that adequate data are available to support tolerances for pendimethalin residues of concern in/on corn stover (mature dried stalks from which the grain or whole ear (cob and grain) have been removed) and sorghum stover (mature dried stalks from which the grain have been removed) at the limit of quantitation (LOQ) of the analytical method (0.1 ppm).

29. CB No. 8138, DP Barcode D165329, 9/18/91, K. Dockter

30. CBTS No. 12295, DP Barcode D193629, 8/1/94, G.J. Herndon.

31. As a result of changes in the Livestock Feeds Table (TABLE II (September 1995)), the Agency now considers cotton gin byproducts as a raw agricultural commodity (RAC). Data depicting pendimethalin residues of concern in/on cotton gin byproducts resulting from the maximum registered use rate of pendimethalin to cotton are hereby required. Cotton must be harvested by commercial equipment (stripper and mechanical picker) to provide an adequate representation of plant residue for the ginning process. At least 3 field trials for each type of harvesting (stripper and picker) are needed, for a total of six (6) field trials.

32. The established tolerances in/on peanut hulls and peanut forage should be revoked, since these are no longer considered to be significant feed items according to the Livestock Feeds Table (TABLE II (September 1995)).

33. CBRS has, considered available tobacco data (including available tobacco metabolism data (MRID 00031978) not previously reviewed) in light of recently issued guidance on this topic (memo by M. Metzger and E. Zager dated 7/17/95) and concludes that tobacco data are not adequate to assess human exposure to pendimethalin residues of concern on tobacco. Tobacco data remain outstanding. The registrant is directed to consult recently issued guidance on this topic (memo by M. Metzger and E. Zager dated 7/17/95) before proceeding with additional studies.

34. The Agency (Memorandum of Conference by J. Stokes and B. Cropp-Kohlligian dated 4/7/95) has accepted the registrant's argument that pendimethalin is not translocated to oil seeds and that residues would not concentrate in corn oil to levels above the established tolerance for corn grain (theoretical concentration factor 25x). As the other oilseeds with tolerances have theoretical concentration factors less than that of corn grain, additional processing studies on oil seeds are not required.

35. Based on available potato field trial data (MRID 00106785) reflecting exaggerated application rates (2.67x) to potatoes, the Agency previously concluded (1984 Pendimethalin Registration Chemistry Chapter) that pendimethalin residues of concern were not expected to concentrate in potato processed commodities and a potato processing study was not required. No tolerances are required for pendimethalin residues of concern on potato processed commodities.

36. CBTS No. 11265, DP Barcode D187216, 2/11/93, R. Cook.

Table B *(continued)*.

37. End-use product labels prohibit applications of pendimethalin to rice fields used for fish or crayfish production and prohibit the use of water from pendimethalin-treated rice fields for the irrigation of food or feed crops.

38. EPA has determined that based on (i) existing tolerances in 40 CFR §180.361(a), (ii) pending wheat/barley tolerances, and (iii) current livestock dietary burden calculations, there is no reasonable expectation of finite residues in animal tissues, milk, or eggs. This situation is provided for under 40 CFR §180.6(a)(3). No additional animal metabolism, analytical method, storage stability, or magnitude of the residue data are required for livestock (Memorandum of Conference by J. Stokes and B. Cropp-Kohlligian dated 4/7/95).

39. The registrant must submit a new confined rotational crop study conducted on three representative crops (small grain, leafy vegetable, and root crop) using [^{14}C]pendimethalin uniformly labeled in the ring position (CBRS No. 12685, DP Barcode D195941, 4/11/94, B. Cropp-Kohlligian). Once these data have been submitted the need for plant-back intervals will be determined.

40. This study was found unacceptable by EFGWB/EFED (H. Manning) and CBRS (CBRS No. 12685, DP Barcode D195941, 4/11/94, B. Cropp-Kohlligian).

TOLERANCE REASSESSMENT SUMMARY

Tolerances for pendimethalin residues are currently expressed in terms of the combined residues of pendimethalin and its metabolite 4-[(1-ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol [§180.361(a and c)] and, for peanut hulls only, in terms of the parent and aforementioned metabolite plus the metabolite 3-[(1-ethylpropyl)amino]-6-methyl-2,4-dinitrobenzyl alcohol [40 CFR §180.361(b)].

A summary of the pendimethalin tolerance reassessment and recommended modifications in commodity definitions are presented in Table C.

Tolerances Listed Under 40 CFR §180.361(a)

Adequate data are available to reassess the established tolerances for pendimethalin residues in/on beans; bean forage; bean fodder; corn fodder; corn forage; corn grain; sweet corn; cottonseed; onions (dry bulb); peanuts; peanut hay; potatoes; sorghum fodder; sorghum forage; grain sorghum; soybeans; soybean forage; soybean hay; sugarcane; and sunflower seeds. [Note: Some commodity definitions must be corrected. See Table C for details.]

The tolerance for pendimethalin residues in/on peanut forage should be revoked since peanut forage is no longer considered to be a significant feed item according to the Livestock Feeds Table (TABLE II (September 1995)).

Available rice field trial data are deemed adequate to support the reregistration of pendimethalin for use on rice. The currently established tolerance on rice grain should be increased from 0.05 ppm to 0.1 ppm. A processing study on rice grain is outstanding.

Tolerances Needed Under 40 CFR §180.361(a)

Available rice field trial data are deemed adequate to support the reregistration of pendimethalin for use on rice. A tolerance for pendimethalin residues of concern in/on rice straw must be established. Available data indicate that a tolerance of 0.1 ppm would be appropriate.

As a result of changes in the Livestock Feeds Table (TABLE II (September 1995)), the Agency currently considers cotton gin byproducts a raw agricultural commodity (RAC). Data depicting pendimethalin residues of concern in/on cotton gin byproducts resulting from the maximum registered use of pendimethalin to cotton are hereby required. On receipt of the required cotton gin byproducts data, the need for tolerances for pendimethalin residues of concern will be determined.

Tolerances Listed Under 40 CFR §180.361(b)

The tolerance for residues in/on peanut hulls should be revoked since peanut hulls is no longer considered a significant feed item according to the Livestock Feeds Table (TABLE II (September 1995)).

Tolerances Listed Under 40 CFR §180.361(c)

CBRS concludes that available garlic magnitude of the residue data from field trials conducted in CA and OR are adequate to support a national registration for the use of pendimethalin on garlic and recommends that the currently established tolerance with regional registrations for pendimethalin residue of concern in/on garlic should be changed to a tolerance without regional registrations at the same level (0.1 ppm) and listed under 40 CFR §180.361(a).

Table C. Tolerance Reassessment Summary for Pendimethalin.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Tolerances listed under 40 CFR §180.361(a):			
Beans, lima (dry,snap)	0.1	0.1	*Beans, succulent and dry*
Beans, forage	0.1	0.1	
Beans, hay	0.1	0.1	
Corn, fodder	0.1	0.1	*Corn, stover*
Corn, forage	0.1	0.1	
Corn, grain	0.1	0.1	*Corn, field* and *Corn, pop*
Corn, fresh (including sweet, K+CWHR)	0.1	0.1	*Corn, sweet (K+CWHR)*
Cottonseed	0.1	0.1	*Cotton, undelinted seed*
Onions, dry bulb	0.1	0.1	
Peanuts	0.1	0.1	
Peanut, hay	0.1	0.1	
Peanut, forage	0.1	Revoke	No longer listed in Livestock Feeds Table (Table II (September 1995)) as a significant feed item
Potatoes	0.1	0.1	
Rice, grain	0.05	0.1	The tolerance level must be increased to the analytical method's limit of quantitation (LOQ) for the combined residues of pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite
Sorghum, fodder	0.1	0.1	*Sorghum, stover*
Sorghum, forage	0.1	0.1	
Sorghum, grain	0.1	0.1	
Soybeans	0.1	0.1	
Soybeans, forage	0.1	0.1	
Soybeans, hay	0.1	0.1	
Sugarcane	0.1	0.1	
Sunflower, seeds	0.1	0.1	

Is not here

Peanut Hulls

Peas, shell removed

Peas, vine

Peas, w/pods

Herb not in TIS

Add for DRES

Shallots

Table C *(continued)*.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/*Correct Commodity Definition*
Tolerances needed under 40 CFR §180.361(a):			
Cotton, gin byproducts	None	TBD[a]	Residue data are required.
Rice, straw	None	0.1	
Tolerances listed under 40 CFR §180.361(b):			
Peanut, hulls	0.25	Revoke	No longer listed in Livestock Feeds Table (Table II (September 1995)) as a significant feed item
Tolerances listed under 40 CFR §180.361(c):			
Garlic	0.1	0.1	CBRS hereby recommends that this tolerance should be listed under 40 CFR §180.361(a)

[a] TBD = To be determined. Reassessment of tolerance(s) cannot be made at this time because residue data are required.

CODEX HARMONIZATION

There are no established or proposed Codex MRLs for pendimethalin residues. Therefore, there are no questions of compatibility with respect to Codex MRLs and U.S. tolerances.

AGENCY MEMORANDA CITED IN THIS DOCUMENT

CBTS No.:	None
DP Barcode:	None
Subject:	PP#1F2567: Pendimethalin in Beans. Evaluation of residue data and analytical method.
From:	A. Smith, RCB
To:	R.J. Taylor, RD
Dated:	4/29/82
MRID(s):	00039518 00039519 00039520 00039521 00039522 00039523 00039524 00039534 00081581

CBTS No.:	None
DP Barcode:	None
Subject:	PP#2F2628: Pendimethalin in Sweet Corn. Evaluation of residue data and analytical method.
From:	A. Smith, RCB
To:	R.J. Taylor, RD
Dated:	7/15/82
MRID(s):	00074619 and 00093719

DEB No.:	5494/5495
DP Barcode:	None
Subject:	Pendimethalin Registration Standard Followup: Response to Residue Chemistry Data Requirements.
From:	D. Edwards, RCB
To:	J. Yowell, RD
Dated:	9/8/89
MRID(s):	40185101 and 40185102

DEB Nos.:	6570/6603/6604/7153
DP Barcode:	None
Subject:	Plant metabolism and processing study requirement for re-registration of pendimethalin.
From:	R. Loranger, CBTS and R. Perfetti, CBRS
To:	R. Engler, HED and L. Rossi, SRRD
Dated:	1/29/91
MRID(s):	41469901

CBTS No.: 7595 and 7596
DP Barcode: None
Subject: PP#3F2788 - Pendimethalin (Prowl®) on/in Barley and Wheat.
From: F. Griffith, CBTS
To: R. Taylor, HED
Dated: 3/5/91
MRID(s): 41713901

CBRS Nos.: 7507/7517
DP Barcode: D159827/D159905
Subject: American Cyanamide Company: Response to the Pendimethalin Registration Standard: Methodology and Product Chemistry.
From: E. Zager, CBRS
To: L. Rossi, SRRD and R. Engler, HED
Dated: 4/24/91
MRID(s): 41431001 and 41725201

CBTS No.: 7887
DP Barcode: D163268
Subject: PP#1E3965. Pendimethalin (Prowl®) for Use in/on Onions. Evaluation of Analytical Method and Residue Data.
From: G. Herndon, CBTS
To: H. Jamerson/A. Beard, HED
Dated: 7/10/91
MRID(s): 41827401

CBTS No.: 8138
DP Barcode: D165329
Subject: Request to Add Layby Use on Cotton to the Prowl® (pendimethalin) Label
From: K. Dockter, CBTS
To: R. Taylor, RD
Dated: 9/18/91
MRID(s): 41881201 and 41881202

CBTS No.: 8859 and 8860
DP Barcode: D170619
Subject: PP#3F2788 - Pendimethalin on/in Barley and Wheat
From: F. Griffith, CBTS
To: R. Taylor, RD
Dated: 4/29/92
MRID(s): None

CBRS No.: 8118 and 8515
DP Barcode: D165134 and D167858
Subject: Reregistration of Pendimethalin. Residue Analytical Methods.
From: E. Zager, CBRS
To: L. Rossi/T. Stowe, SRRD
Dated: 5/15/92
MRID(s): 41982701 and 41845801

CBRS No.: 9616
DP Barcode: D175936
Subject: PP#1E3965. Pendimethalin (Prowl®) for Use in/on Onions. Amendment of 3/3/92.
From: G. Herndon, CBTS
To: H. Jamerson/L. Fried, HED
Dated: 10/22/92
MRID(s): None

CBTS No.: 9863
DP Barcode: D178174
Subject: Addressing Request to Add Layby Use on Cotton to the Prowl® (pendimethalin) Label
From: G.J. Herndon, CBTS
To: V. Walters/R. Taylor, RD
Dated: 1/6/93
MRID(s): 42266301-42266307

CBRS No.: 10678
DP Barcode: D183220
Subject: Reregistration of Pendimethalin. Nature of the residue in Potatoes.
From: P. Deschamp, CBRS
To: L. Rossi/T. Stowe
Dated: 2/1/93
MRID(s): 42467801

CBTS No.: 11256
DP Barcode: D187216
Subject: PP2F2765. Pendimethalin on Sugarcane. Response to Office of General Counsel comments regarding sugarcane processing data.
From: R.Cook, CBTS
To: R. Taylor, RD
Dated: 2/11/93
MRID(s): None

CBTS No.: 11391
DP Barcode: D188216
Subject: PP#1E3965. Pendimethalin (Prowl®) for Use in/on Onions. Reevaluation of 10/22/92 Memo of G.J. Herndon Based on Additional Data Submitted from a Metabolism Study on Potatoes.
From: G. Herndon, CBTS
To: H. Jamerson, RD
Dated: 2/24/93
MRID(s): None

CBRS No.: 11797
DP Barcode: D190778
Subject: Reregistration of Pendimethalin. American Cyanamid Response to Potato Metabolism Study Deficiencies.
From: P. Deschamp, CBRS
To: J. Mitchell, SRRD
Dated: 6/16/93
MRID(s): None

CBRS No.: 11582
DP Barcode: D189207
Subject: Reregistration of Pendimethalin. Nature of the Residue in Sweet Corn.
From: P. Deschamp, CBRS
To: T. Stowe, SRRD
Dated: 6/16/93
MRID(s): 42686401

CBRS No.: None
DP Barcode: None
Subject: Pendimethalin and its Alcohol Metabolite (CL 202,347) through FDA Multi-Residue Protocols A through E.
From: L. Edwards, CBRS
To: H. Hundley, ACB
Dated: 9/24/93
MRID(s): None

CBRS No.: 10678 Addendum
DP Barcode: D183220
Subject: Reregistration of Pendimethalin. Poultry Metabolism, Residue Analytical Methods, Storage Stability Data.
From: P. Deschamp, CBRS
To: L. Rossi/T. Stowe, SRRD
Dated: 9/24/93
MRID(s): 42467802, 42471902, 42471903 and 42471901

CBRS No.: 9464
DP Barcode: D174858
Subject: Reregistration of Pendimethalin. Status of Data Reviews: Ruminant Metabolism and Onion (dry bulb) Field Trials.
From: P. Deschamp, CBRS
To: L. Rossi, SRRD
Dated: 9/24/93
MRID(s): 41713901 and 41827401

CBRS No.: 9914
DP Barcode: D178454
Subject: Reregistration of Pendimethalin. Storage Intervals and Conditions of Crop Field Trial Residue Samples
From: P. Deschamp, CBRS
To: L. Rossi, SRRD
Dated: 10/22/93
MRID(s): 42266301-07

CBRS No.: 12673
DP Barcode: D195890
Subject: Pendimethalin Reregistration. Storage Stability Data Submitted to Support Previously Submitted Sweet Corn Metabolism Data.
From: B. Cropp-Kohlligian, CBRS
To: L. Rossi/W. Waldrop, SRRD
Dated: 2/9/94
MRID(s): None

CBRS No.: 12685
DP Barcode: D195941
Subject: Pendimethalin Reregistration. Re-evaluation of Previously Reviewed Confined Rotational Crop Study (MRID 41806801).
From: B. Cropp-Kohlligian, CBRS
To: L. Rossi/W. Waldrop, SRRD
Dated: 4/11/94
MRID(s): None

CBTS No. 11230
DP Barcode: D193627
Subject: Amended use of pendimethalin on sugarcane in Hawaii
From: R. Cook, CBTS
to: R. Taylor, RD
Dated: 7/25/94
MRID(s): 42859201 and 42859202

CBTS No.: 12295
DP Barcode: 193629
Subject: Addressing Request to Add Layby Use on Cotton to the Prowl® (pendimethalin) Label
From: G.J. Herndon, CBTS
To: E. Allen/R. Taylor, RD
Dated: 8/1/94
MRID(s): 42858901

CBRS No.: 13411
DP Barcode: D200669
Subject: Pendimethalin Reregistration. Registrant's Responses to Agency Reviews of Previously Submitted Ruminant Metabolism; Analytical Method Validation, and Sweet Corn Metabolism Data.
From: B. Cropp-Kohlligian, CBRS
To: W. Waldrop/J. Mitchell, SRRD
Dated: 11/15/94
MRID(s): 43154703 - 43154705

CBRS No.: 13506
DP Barcode: D201694
Subject: Pendimethalin Reregistration. Analytical Method Radiovalidation for Residues of Pendimethalin in/on Corn Plants.
From: B. Cropp-Kohlligian, CBRS
To: W. Waldrop/J. Mitchell, SRRD
Dated: 11/15/94
MRID(s): 43185901

CBTS No.: 15373
DP Barcode: D212340
Subject: Pendimethalin. Discussion of Need for Processing Studies for Oilseeds. Discussion of Adequacy of Ruminant Metabolism Study. Discussion of Other Chemistry Data Requirements.
From: J. Stokes, CBTS and B. Cropp-Kohlligian, CBRS
To: W. Waldrop/J. Mitchell, SRRD
Dated: 4/7/95
MRID(s): None

CBRS No.:	13400
DP Barcode:	D200608
Subject:	Pendimethalin. Analytical method description required by CBRS to support previously submitted alfalfa storage stability data for the purposes of reregistration. Confirmatory analytical method required by CBTS to support the pending registration of pendimethalin on barley/wheat (PP#3F2788).
From:	B. Cropp-Kohlligian
To:	W. Waldrop/J. Mitchell, SRRD
Dated:	7/24/95
MRID(s):	43068501 and 43147801

Attachment 3

011842

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

FEB 21 1996

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

Memorandum

SUBJECT: **Pendimethalin** (PC Code 108501): Dietary Risk Assessment in Support of the Reregistration Eligibility Document (RED) Case No. 0187

FROM: Mary R.A. Clock, Biologist
Risk Characterization and Analysis Branch
Health Effects Division

TO: Paula Deschamp, Section Chief
Risk Characterization and Analysis Branch
Health Effects Division

THROUGH: Elizabeth A. Doyle, Ph.D., Section Chief
Dietary Risk Evaluation Section
Scientific Analysis Branch
Health Effects Division

and

William Burnam, Branch Chief
Scientific Analysis Branch
Health Effects Division

Action Requested

Provide an estimate of chronic risk from the uses of pendimethalin which are currently registered and being supported for reregistration.

Discussion

Toxicological Endpoints

The Dietary Risk Evaluation System (DRES) chronic exposure analysis used a Reference Dose (RfD) of 0.13 mg/kg bwt/day. The NOEL is taken from a two year feeding study in dogs. At the next higher dose level (50 mg/kg bwt/day), increases in serum alkaline phosphatase and liver weight and other hepatic lesions were observed. An uncertainty level of 100 was applied to account for both the interspecies extrapolation and intraspecies variability (G.Ghali memo, "RfD/Peer Review Report of Pendimethalin", report date 2/6/96).

The Toxicology Endpoint Selection Document for pendimethalin requires the assessment of chronic dietary risk (TES report date 1/17/96). The endpoint for chronic dietary risk assessment is the RfD of 0.13 mg/kg bwt/day.

Pendimethalin has been classified as a group C, possible human carcinogen, by the HED Carcinogenicity Peer Review Committee based upon "statistically significant increased trend and pairwise comparison between the high dose group and controls for thyroid follicular cell adinomas in male and female rats." The Committee recommended that for the purpose of risk characterization, the RfD approach should be used for quantification of human risk (HED CPR Report, 7/24/92).

Residue Information

Food uses evaluated in the DRES analysis were the published uses of pendimethalin listed in 40 CFR § 180.275 and the Tolerance Index System (TIS). The analysis used tolerance level residues for commodities with registered pendimethalin tolerances.

Reassessed Tolerances:

In the Product and Residue Chemistry Chapter of the Reregistration Eligibility Document (B. Cropp-Kohlligian, 12/12/95), CBRS has concluded that tolerances for pendimethalin on rice be increased from 0.05 ppm to 0.1 ppm due to the analytical method's limit of quantification for the combined residues of pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite. In the same memo, CBRS recommended that the tolerance for onions (dry bulb) be applied to shallots (dry bulb only).

In the DRES analysis, both rice and dry bulb shallots were included at these recommended tolerance levels. See Table 1 for all the commodities and tolerances included in this analysis.

Results

In order to estimate a worst case chronic dietary risk from uses being supported in reregistration, tolerance level residues were used in the analysis to calculate a Theoretical Maximum Residue Contribution (TMRC). These exposure estimates were then compared to the RfD for pendimethalin for chronic dietary risk. See Tables 2 and 3 for a summary of the TMRCs and percentages of the RfD.

Chronic Exposure from Pendimethalin for Reregistration

Using Tolerances

The Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population from all currently published tolerances are listed below. See also Table 3.

Subgroup	Exposure	% Reference Dose
U.S. population	0.000319	0.25
Children (1-6)	0.000693	0.53

The DRES analysis for the published uses and reassessed tolerances of pendimethalin indicate that the overall U.S. population would receive 0.25 percent of the RfD and the highest

subgroup, children ages 1-6 years, would receive 0.53 percent of the RfD. Therefore, the chronic dietary risk posed from pendimethalin is not of concern for the reregistration scenario.

cc: E.Doyle/SAB
M.Clock/RCAB

TABLE 1

CHEMICAL INFORMATION FOR CASWELL NUMBER 454BB DATE: 01/30/96 PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Pendimethalin Caswell #454BB CAS No. 40487-42-1 A.I. CODE: 108501 CFR No. 180.361	2yr feeding- dog NOEL= 12.5000 mg/kg 0.00 ppm LEL= 50.0000 mg/kg 0.00 ppm ONCO: C (HCPRC)	Increased liver weights & alkaline phosphatase; lesions of the liver. Doses by geletin capsule. No carcinogenicity data is available.	PADI UF -->100 OPP RfD= 0.130000 EPA RfD= 0.040000	Chronic feed/onco- rat	HED reviewed 07/25/86 EPA deferred 08/19/86 EPA verified 09/16/87 Revised HED RfD 1/5/96 final report pending On IRIS.

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
14007AA	GARLIC	4E3537			0.1000
14011AA	ONIONS-DRY-BULB (CIPOLLINI)	1E3965			0.1000
14011DA	ONIONS-DEHYDRATED OR DRIED	1E3965			0.1000
14013AA	POTATOES(WHITE)-WHOLE	9F2134			0.1000
14013AB	POTATOES(WHITE)-UNSPECIFIED	9F2134			0.1000
14013AC	POTATOES(WHITE)-PEELED	9F2134			0.1000
14013DA	POTATOES(WHITE)-DRY	9F2134			0.1000
14013HA	POTATOES(WHITE)-PEEL ONLY	9F2134			0.1000
14017AA	SHALLOTS	1E3965			0.1000
15001AC	BEANS-DRY-LIMA	1F2567			0.1000
15005AA	CORN,SWEET	2F2628			0.1000
15006AA	PEANUTS-WHOLE	6F1741			0.1000
15018AA	SUNFLOWER-SEEDS	0F2373			0.1000
15029AA	SOYBEANS-SPROUTED SEEDS	6F1704			0.1000
24002EA	CORN,GRAIN-ENDOSPERM	5F1556			0.1000
24002HA	CORN,GRAIN-BRAN	5F1556			0.1000
24002SA	CORN SUGAR	5F1556			0.1000
24004AA	RICE-ROUGH	0F2401			0.1000
24004AB	RICE-MILLED	0F2401			0.1000
24006AA	SORGHUM (INCLUDING MILO)	9F2246			0.1000
25003SA	CANE SUGAR	3F2765			0.1000
25003SB	SUGAR-MOLASSES	3F2765			0.1000
27002OA	CORN,GRAIN-OIL	5F1556			0.1000
27003OA	COTTONSEED-OIL	5F1556			0.1000
27003WA	COTTONSEED-MEAL	5F1556			0.1000
27007OA	PEANUTS-OIL	6F1741			0.1000
27010OA	SOYBEANS-OIL	6F1704			0.1000
27011OA	SUNFLOWER-OIL	0F2373			0.1000
28023AA	SOYBEANS-UNSPECIFIED	6F1704			0.1000
28023AB	SOYBEANS-MATURE,SEEDS DRY	6F1704			0.1000
28023WA	SOYBEANS-FLOUR, FULL FAT	6F1704			0.1000
28023WB	SOYBEANS-FLOUR, LOW FAT	6F1704			0.1000
28023WC	SOYBEANS-FLOUR,DEFATTED	6F1704			0.1000

Table 2

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS DATE: 01/30/96 PAGE: 1

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
Pendimethalin Caswell #45488 CAS No. 40487-42-1 A.I. CODE: 108501 CFR No. 180.361	2yr feeding- dog NOEL= 12.5000 mg/kg 0.00 ppm LEL= 50.0000 mg/kg 0.00 ppm ONCO: C (HCPRC)	Increased liver weights & alkaline phosphatase; lesions of the liver. Doses by gelatin capsule. No carcinogenicity data is available.	PADI UF -->100 OPP RfD= 0.130000 EPA RfD= 0.040000	Chronic feed/onco- rat	HED reviewed 07/25/86 EPA deferred 08/19/86 EPA verified 09/16/87 Revised HED RfD 1/5/96 final report pending On IRIS.

POPULATION SUBGROUP	TOTAL THRC (MG/KG BODY WEIGHT/DAY) CURRENT THRC*	NEW THRC**	NEW THRC AS PERCENT OF RFD	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES ARC	2RFD
U.S. POPULATION - 48 STATES	0.000319	0.000319	0.245196	0.000000		
U.S. POPULATION - SPRING SEASON	0.000310	0.000310	0.238480	0.000000		
U.S. POPULATION - SUMMER SEASON	0.000319	0.000319	0.245768	0.000000		
U.S. POPULATION - FALL SEASON	0.000321	0.000321	0.246935	0.000000		
U.S. POPULATION - WINTER SEASON	0.000315	0.000315	0.242215	0.000000		
NORTHEAST REGION	0.000296	0.000296	0.227777	0.000000		
NORTH CENTRAL REGION	0.000327	0.000327	0.251852	0.000000		
SOUTHERN REGION	0.000327	0.000327	0.251842	0.000000		
WESTERN REGION	0.000308	0.000308	0.237145	0.000000		
HISPANICS	0.000365	0.000365	0.280825	0.000000		
NON-HISPANIC WHITES	0.000311	0.000311	0.239168	0.000000		
NON-HISPANIC BLACKS	0.000327	0.000327	0.251509	0.000000		
NON-HISPANIC OTHERS	0.000329	0.000329	0.253008	0.000000		
NURSING INFANTS (< 1 YEAR OLD)	0.000209	0.000209	0.160737	0.000000		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.000667	0.000667	0.513272	0.000000		
FEMALES (13+ YEARS, PREGNANT)	0.000220	0.000220	0.168868	0.000000		
FEMALES 13+ YEARS, NURSING	0.000249	0.000249	0.191745	0.000000		
CHILDREN (1-6 YEARS OLD)	0.000693	0.000693	0.533161	0.000000		
CHILDREN (7-12 YEARS OLD)	0.000508	0.000508	0.390596	0.000000		
MALES (13-19 YEARS OLD)	0.000349	0.000349	0.268465	0.000000		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000294	0.000294	0.225870	0.000000		
MALES (20 YEARS AND OLDER)	0.000244	0.000244	0.187973	0.000000		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000208	0.000208	0.159882	0.000000		

*Current THRC does not include new or pending tolerances.
**New THRC includes new, pending, and published tolerances.

Table 3

TOLERANCE ASSESSMENT SUMMARY FOR Pendimethalin DATE: 01/30/96
CASWELL #45488

ANALYSIS FOR POPULATION SUB-GROUP: U.S. POPULATION - 48 STATES

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.000319	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	0.245	% OF THE ADI.

NO NEW TOLERANCES ARE IN THE FILE.

NO OTHER PENDING TOLERANCES ARE IN THE FILE

ANALYSIS FOR POPULATION SUB-GROUP: CHILDREN (1-6 YEARS OLD)

EXISTING TOLERANCES (PUBLISHED ONLY)		
RESULT IN A TMRC OF:	0.000694	MG/KG/DAY
THE EXISTING TMRC IS EQUIVALENT TO:	0.533	% OF THE ADI.

NO NEW TOLERANCES ARE IN THE FILE.

NO OTHER PENDING TOLERANCES ARE IN THE FILE

Attachment 4

011842

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

FEB 20 1996

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: OCCUPATIONAL AND RESIDENTIAL EXPOSURE ASSESSMENT AND RECOMMENDATIONS FOR THE REREGISTRATION ELIGIBILITY DECISION DOCUMENT FOR PENDIMETHALIN

TO: Mike Metzger, Branch Chief
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

FROM: John Leahy, Environmental Protection Specialist

THRU: Alan P. Nielsen, Section Head
Reregistration Section II
Occupational and Residential Exposure Branch
Health Effects Division (7509C)

Larry C. Dorsey, Chief
Occupational and Residential Exposure Branch
Health Effects Division (7509C)

Please find the OREB review of pendimethalin.

DP Barcode:	D221532
Pesticide Chemical Codes:	108501
EPA Reg. Nos.:	241-337, 241-305, 10404-52, 241-268, 538-195, 538-214-10404, 538-188, 10404-74, 241-297, 241-340, 538-251
EPA MRID Nos.:	None
LUIS Report Date:	9/5/95
PHED:	Yes, Version 1.1

Occupational-use products and homeowner-use products

At this time products containing pendimethalin are intended for both occupational and homeowner uses.

Acute Toxicity

The toxicological data base for pendimethalin is adequate and will support reregistration. Guideline studies for acute toxicity indicate that pendimethalin (test material not identified) is classified as category III for acute oral toxicity, category IV for acute dermal toxicity, category IV for acute inhalation toxicity, category III for eye irritation potential, and category IV for dermal irritation.[3] Pendimethalin is not classified as a skin sensitizer.[3]

Other Endpoints of Concern

The *Toxicological Selection Endpoint Document*, dated January 17, 1996, indicates that there are toxicological endpoints of concern for pendimethalin. Two endpoints have been identified: a short-term NOEL of 1,000 mg/kg/day (21-day dermal study using New Zealand white rabbits, no adverse effects at the highest dose tested); and, an intermediate-term NOEL of 12.5 mg/kg/day (chronic dog study, according to the EPA's endpoint selection document, "although this is a chronic dog study, it is felt that the study is appropriate since some effects relating to thyroid endocrine disruption occur in other studies at 21 mg/kg/day and progress in severity at 51 mg/kg/day and are observed as early as 15 to 28 days").[3] Because the short-term study was a dermal toxicity study, it is not necessary to apply a dermal absorption value. However, for the intermediate-term toxicity study, a dermal absorption of 10 percent is used.[3] Additionally, pendimethalin has been classified as a "Group C" possible human carcinogen and the Toxicological Selection Endpoint Document recommends using the RfD approach for quantification of human risk. However, no chronic exposures to pendimethalin have been identified. The RfD for pendimethalin is 0.13 mg/kg/day.[3]

Handler Exposures & Assumptions

EPA has determined that there is potential exposure to persons handling pendimethalin. Handler exposures may occur to:

- occupational handlers involved in food, feed, fiber, ornamental, turf, rights-of-way and other noncrop treatments, and
- homeowner handlers making applications to residential turf and gardens.

No handler exposure studies were conducted by the registrant for pendimethalin.

EPA has determined that there is potential exposure to mixers, loaders, applicators, or other handlers during usual use-patterns associated with pendimethalin. Based on the use patterns and potential exposures described above, thirteen major exposure scenarios were

Table 1. Short-Term and Intermediate-Term Exposure of Pendimethalin

Exposure Scenario (Scen. #)	Baseline Dermal Unit Exposure[a] (mg/lb ai)	Baseline Inhalation Unit Exposure[b] (µg/lb ai)	Application Rate[c] (lb ai/acre)	Daily Acres Treated[d]	Daily Dermal Exposure[e] (mg/day)	Daily Inhalation Exposure[f] (mg/day)	Daily Total Exposure[g] (mg/day)
Mixer/Loader Exposure							
Mixing/Loading Water Dispersible Granulars (Dry Flowables) for Rights-of-Way Spraying (1a)	0.07	0.8	3.96	10	2.8	0.032	2.8
Mixing/Loading Water Dispersible Granulars (Dry Flowables) for Groundboom Applications (1b)			3.96	80	22.2	0.25	22.5
Mixing/Loading Wettable Powders (water soluble packets) for Groundboom Applications(2)	0.02 (wtr. sol. pk.)	0.2 (wtr. sol. pk.)	3.0	80	4.8	0.048	4.8
Loading Granulars for Solid Broadcast Applications (3)	0.005	1.7	3.0	80	1.2	0.41	1.6
Mixing/Loading Liquid (E.C.) for Aerial Applications and Irrigation Systems (4a)	2.9	1.2	1.98	800	4,594	1.9	4,596
Mixing/Loading Liquid (E.C.) for Rights-of-Way Spraying (4b)			4.0	10	116	0.048	116
Mixing/Loading Liquid (E.C.) for Groundboom Applications (4c)			1.98	80	459	0.19	459
Applicator Exposure							
Aerial-Fixed Wing - enclosed cockpit (liquid) (5)	0.005	0.07	1.98	800	7.9	0.11	8.0
Rights-of-Way (6)	1.2	3.9	4.0	10	48	0.16	48.2
Groundboom Tractor (7)	0.015	0.7	3.96	80	4.8	0.22	5.0
Solid Broadcast Spreader (tractor drawn) (8)	0.01	1.2	3.0	80	2.4	0.29	2.7
Flagger							
Flagging (liquid) (9)	0.01	0.3	1.98	800	15.8	0.48	16.3
Mixer/Loader/Applicator							
Backpack (spot treatment) (10)	2.6	30	3.96	(H) 1,000[h] *(O) 1.0*	(H) 0.24 *(O) 10.3*	(H) 0.003 *(O) 0.12*	(H) 0.24 *(O) 10.4*
Low Pressure Handwand (spot treatment) (11)	103.8	31.2	3.96	(H) 1,000[h] (O) 1.0	(H) 9.4 (O) 411	(H) 0.003 (O) 0.12	(H) 9.4 (O) 411.1
Residential Broadcast Spreader (12)	2.9	6.3	3.0	1.0	8.7	0.019	8.7
High Volume Turf Sprayer (13)	0.77	1.4	3.96	8	24.4	0.044	24.4

Baseline dermal unit exposures represent long pants, long sleeve shirts, no gloves, open mixing/loading, enclosed cockpit, open cab tractor.
Baseline inhalation unit exposure represents no respirator.
Application rates were derived from the following labels (EPA Reg. Nos.): E.C. 241-337 and 241-305, Granular 538-188, WDG 10404-52, 241-340, and 241-268 (CA only), WP 538-195 (water soluble packets only).
Values represent the area [(H) = homeowner, (O) = occupational] which can be used in a single day to complete treatments for each exposure scenario of concern.
Daily dermal exposure (mg/day) = Exposure (mg/lb ai) * Max. Appl. Rate (lb ai/acre or lb ai/gal) * Max. Treated (acres or gallons of spray solution).
Daily inhalation exposure (mg/day) = Exposure (ug/lb ai) * (1mg/1000ug) conversion * Max Appl Rate (lb ai/A or lb ai/gal) * Max Treated (acres or gallons of spray solution).
Daily total exposure (mg/day) = Daily dermal exposure + Daily inhalation exposure.

NA = Not applicable since previous MOE was over 100.
Daily dermal dose = daily dermal exposure / 70 kg.
Baseline Total Dose = (daily dermal exposure + daily inhalation exposure)/70 kg.
Dermal MOE = NOEL (short-term NOEL = 1,000 mg/kg/day)/ daily dermal dose.
Total MOE = NOEL (short-term NOEL = 1,000 mg/kg/day) / daily total dose.
Additional PPE for Scenario 4a = single layer clothing and chemical resistant gloves.

Exposure Scenario (Scen. #)	Baseline Daily Dermal Dose (mg/kg/day)[c]	Baseline Daily Absorbed Dermal Dose (mg/kg/day)[b]	Baseline Total Daily Absorbed Dose (mg/kg/day)[c]	Baseline Dermal MOE[d]	Baseline Total MOE[e]	Risk Mitigation Measure					
						Additional PPE[f]					
						Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (ug/lb ai)	Daily Dermal Absorbed Dose (mg/kg/day)[b]	Daily Total Absorbed Dose (mg/kg/day)[c]	Dermal MOE[d]	Total MOE[e]
Mixer/Loader/Applicator											
Backpack Sprayer (10)	(O) 0.15	(O) 0.015	(O) 0.017	(O) 833	(O) 735	NA	NA	NA	NA	NA	NA
Low Pressure Handwand (11)	(O) 5.9	(O) 0.59	(O) 0.59	(O) 21	(O) 21	4.1	31.2	0.023	0.025	543	500
Residential Broadcast Spreader (12)	0.12	0.012	0.012	1,042	1,042	NA	NA	NA	NA	NA	NA
High Volume Turf Sprayer (13)	0.35	0.035	0.036	357	347	NA	NA	NA	NA	NA	NA

NA Not applicable since previous MOE was over 100.
Daily dermal dose = daily dermal exposure/70 kg.
Baseline absorbed dermal dose = daily dermal dose * dermal absorption rate 10.0%.
Baseline total absorbed dose = (daily absorbed dermal exposure + daily inhalation exposure)/70 kg.
Dermal MOE = NOEL (intermediate-term NOEL = 12.5 mg/kg/day) / daily absorbed dermal dose.
Total MOE = NOEL (intermediate-term NOEL = 12.5 mg/kg/day) / daily total absorbed dose.
Additional PPE = for Scenario 4a, b, c = Single layer of clothing and chemical resistant gloves.
for Scenario 11 = Single layer of clothing and chemical resistant gloves.

Exposure Scenario (Number)	Data Source	Standard Assumptions[a] (8-hr work day)	Comments[b]
Flagger			
Liquids (9)	PHED V1.1	800 acres	Baseline: "Best Available" grades: Hands, dermal, and inhalation acceptable grades. Hands = 16 replicates; Dermal = 16 to 18 replicates; Inhalation = 18 replicates. High confidence in dermal and inhalation data. PHED data used for baseline, no PFs were necessary.
Mixer/Loader Applicator			
Backpack Sprayer (spot treatment) (10)	PHED V1.1	Homeowner: 1,000ft²; Occupational: 1 acre	Baseline: "Best Available" grades: Hands and dermal grades A,B,C, inhalation acceptable grades. Hands = 11 replicates; Dermal = 9 to 11 replicates; Inhalation = 11 replicates. Low confidence in dermal and inhalation data. PHED data used for baseline was derived from single layer clothing and chemical resistant gloves; a 90% PF was used to remove the chemical resistant gloves to simulate a no glove scenario.
Low Pressure Handwand (11)	PHED V1.1	Homeowner: 1,000ft²; Occupational: 1 acre	Baseline: "Best Available" grades: Hands, dermal, and inhalation all grades. Hands = 70 replicates; Dermal = 25 to 96 replicates; Inhalation = 96 replicates. Low confidence in both dermal and inhalation data. PPE: "Best Available" grades: Hands acceptable grades, dermal all grades. Hands = 15 replicates; Dermal = 25 to 96 replicates. Low confidence in dermal data.. PHED data used for baseline and PPE values, no PFs were necessary.
Residential Broadcast Spreader (12)	PHED V1.1	1 acre	Baseline: "Best Available" grades: Hands and dermal grades A,B,C, inhalation acceptable grades. Hands = 15 replicates; Dermal = 15 (no head data) replicates; Inhalation = 15 replicates. Low (no head data) confidence in dermal and high confidence in inhalation data. PHED data used for baseline, no PF were necessary.
High Volume Turf Sprayer (13)	PHED V1.1	8 acres	Baseline: "Best Available" grades: Hands and dermal all grades, inhalation acceptable grades. Hands = 14 replicates; Dermal = 14 (no head data) replicates; Inhalation = 14 replicates. Low confidence in dermal and low to medium confidence in inhalation data. PHED data used for baseline was derived from single layer clothing and chemical resistant gloves; a 90% PF was used to remove the chemical resistant gloves to simulate a no glove scenario.

a Standard Assumptions based on an 8-hour work day as estimated by OREB. HEAD data were not available.

b "Best Available" grades are defined by OREB SOP for meeting Subdivision U Guidelines. Best available grades are assigned as follows: matrices with grades A and B data and a minimum of 15 replicates; if not available, then grades A, B, and C data and a minimum of 15 replicates; if not available, then all data regardless of the quality and number of replicates. Data confidence are assigned as follows:

High = grades A and B and 15 or more replicates per body part
Medium = grades A, B, and C and 15 or more replicates per body part
Low = grades A, B, C, D, and E or any combination of grades with less than 15 replicates

(RISK)

Occupational and Residential

Risk From Handler Exposures

Table 2 presents the risk assessment for the short-term toxicity endpoint of concern, while Table 3 presents the risk assessment for the intermediate-term toxicity endpoint of concern. Table 4 summarizes the caveats and parameters specific to each exposure scenario and corresponding risk assessment.

Daily Dose is calculated using the following formula:

Daily Dose (mg ai/kg bw/day) =
Unit Exposure (mg ai/lb ai) x Use (lb ai/A) x Daily Acres Treated (A/day) / Body Wt (kg)

The following assumptions are made:

- Some commercial mixers, loaders, flaggers, and applicators are exposed more than 7 days in a three-month (ninety-day) period (reasonable worse-case estimate). Therefore, the exposure/risk assessment for commercial handlers must use both short-term (less than 7 days per year) and intermediate-term (7 or more days per year) toxicological endpoints.
- Aerial applicators are in enclosed cockpits.
- Wettable powder formulations are contained in water-soluble packaging (all currently registered wettable powder products are in water soluble packaging).
- Homeowner handlers would be exposed fewer than 7 days in a three-month (ninety-day) period. Therefore, the exposure/risk assessment for homeowner handlers uses only the short-term toxicological endpoint.

These calculations of daily dose to pendimethalin by handlers are used to assess the risk to those handlers.

The following equation is for determining the risk (MOE) from short-term and intermediate-term exposures.

MOE = NOEL / Total Absorbed Dose

mechanical cultivation, given the timing of applications (early season) and the crops involved. Exceptions include hand-transplanting tobacco and hand-planting or hand-aligning mechanically-planted sugarcane seed pieces in recently treated areas;

- most applications to ornamentals and turf are to established plants and are often broadcast over the entire ornamental and turf foliage, thus increasing potential exposure risk from foliar contact with such treated foliage;

- workers entering turf and ornamental production areas following pendimethalin applications may perform hand-labor tasks such as transplanting, harvesting, weeding, or pruning. For these crops, the timing of applications make hand labor activities likely following pendimethalin applications.

- workers entering rights-of-way and other noncrop areas would likely perform non-hand-labor tasks;

- landscape and grounds maintenance workers performing tasks in commercial landscape plantings may perform hand-labor tasks, such as hoeing, thinning, or weeding, but exposures to treated surfaces are likely to be infrequent and short in duration;

- golf course workers may be exposed while mowing, tending greens, or performing other maintenance tasks, but their exposures are likely to be limited and relatively short in duration;

- persons, including children, may be exposed to treated turfgrass (lawns) at residential sites frequently and for relatively long periods of time.

- persons, including children, may be exposed to treated ornamentals at residential sites, but their exposures are likely to be limited and of short duration.

Given the above, HED estimates that postapplication risks are likely to be acceptable in the following use-scenarios, provided workers and others do not enter treated areas immediately following applications:

- food, feed, and fiber crops, except for sugarcane and tobacco;

- golf-course and turf other than that on sod farms and residential sites;

- ornamental landscape plantings in commercial and residential sites; and

- rights-of-way and other noncrop areas.

However, HED is concerned that postapplication risks are questionable at the following use-sites:

PostApplication Studies

The registrant must submit postapplication exposure studies as confirmatory data. Requirements for such postapplication exposure studies are addressed by Subdivision K of the Pesticide Assessment Guidelines. Data are required to support the use of pendimethalin on the following crop groups/use sites:

- Food, feed, and fiber crops: (hand-transplanting tobacco and hand-planting or hand-aligning mechanically-planted sugarcane);
- Ornamental crops (transplanting ornamentals);
- Residential turfgrass; and
- Sod-farm turfgrass (harvesting).

Requirements for postapplication/reentry exposure studies are addressed by Subdivision K of the Pesticide Assessment Guidelines. The required data include:

Guidelines:	132-1(a)	Foliar Residue Dissipation, if applicable
	132-1(b)	Soil Residue Dissipation
	*133-3	Postapplication Dermal Passive Dosimetry Exposure
	*133-4	Postapplication Inhalation Passive Dosimetry Exposure

*Guidelines 133-3 and 133-4 may be reserved at this time pending completion of the databases on agricultural and residential postapplication/reentry exposure currently being developed by the Agricultural Reentry Task Force and Outdoor Residential Exposure Task Force, *provided* the registrant is a member of both Task Forces.

- *After October 23, 1995, except as otherwise provided in PR Notices 93-7 and 93-11, the labeling of all products within the scope of those notices must meet the requirements of the notices when the products are distributed or sold by any person.*

Personal Protective Equipment/Engineering Controls for Handlers

For each end-use product, PPE requirements for pesticide handlers are set during reregistration in one of two ways:

1. If EPA determines that no regulatory action must be taken as the result of the acute effects or other adverse effects of an active ingredient, the PPE for pesticide handlers will be based on the acute toxicity of the end-use product. For occupational-use products, PPE must be established using the process described in PR Notice 93-7 or more recent EPA guidelines.

2. If EPA determines that REGULATORY ACTION ON AN ACTIVE INGREDIENT MUST BE TAKEN as the result of very high acute toxicity or to certain other adverse effects, such as allergic effects or delayed effects (cancer, developmental toxicity, reproductive effects, etc.):

- *In the RED for that active ingredient, EPA may establish minimum or "baseline" handler PPE requirements that pertain to all or most end-use products containing that active ingredient.*
- *These minimum PPE requirements must be compared with the PPE that would be designated on the basis of the acute toxicity of the end-use product.*
- *The more stringent choice for each type of PPE (i.e., bodywear, hand protection, footwear, eyewear, etc.) must be placed on the label of the end-use product.*

Personal protective equipment requirements usually are set by specifying one or more pre-established PPE units -- sets of items that are almost always required together. For example, if chemical-resistant gloves are required, then long-sleeve shirts, long pants, socks, and shoes are assumed and are also included in the required minimum attire. If the requirement is for two layers of body protection (coveralls over a long- or short-sleeve shirt and long or short pants), the minimum must also include (for all handlers) chemical-resistant footwear and chemical-resistant headgear for overhead exposures and (for mixers, loaders, and persons cleaning equipment) chemical-resistant aprons.

Occupational-Use Products

EPA has determined that regulatory action regarding the establishment of active-ingredient-based minimum PPE requirements for occupational handlers must be taken for pendimethalin for certain handler use-situations. The MOE's were less than 100 for certain occupational handler (mixers, loaders, and applicators) use-scenarios, unless chemical-resistant gloves were used in addition to the baseline protection of long-sleeve shirt, long pants, shoes, and socks. EPA is requiring active-ingredient-based protections for handlers of pendimethalin in these exposure situations: (1) mixing and loading emulsifiable concentrate formulations and (2) mixing, loading, and applying using low-pressure handwand equipment.

The WPS REI in effect until now was 12 hours. This was an interim REI placed on pendimethalin products by PR Notice 93-7. EPA notes that the 12-hour interim WPS REI was established because data indicated that pendimethalin was in toxicity category III/IV for acute dermal toxicity, skin irritation potential, and eye irritation potential.

During the reregistration process, EPA has determined that the REI established under the WPS should be changed for some uses due to non-acute toxicity endpoints of concern, potential for significant postapplication worker exposure in certain crops, and an absence of exposure data for all use sites and scenarios. Therefore, EPA is now increasing the REI on sugarcane and tobacco from 12 to 24 hours, until postapplication data to set specific REIs for these crops are available. Thus, EPA is establishing a 24-hour restricted-entry interval for uses on sugarcane and tobacco of all occupational-use products that contain pendimethalin and have use-directions for food, feed, and fiber crops. This interim REI is being established due to the intermediate-term toxicity endpoint of concern that has been identified, the lack of pendimethalin-specific postapplication exposure data, and EPA's qualitative analysis of potential post-application exposure risk.

Early-Entry PPE:

The WPS establishes very specific restrictions on entry by workers to areas that remain under a restricted-entry interval, if the entry involves contact with treated surfaces. Among those restrictions are a prohibition of routine entry to perform hand labor tasks and a requirement that personal protective equipment be worn. Under the WPS, these personal protective equipment requirements for persons who must enter areas that remain under a restricted-entry interval are based on the acute toxicity category of the active ingredient.

During the reregistration process, EPA considers all relevant product-specific information to decide whether there is reason to set personal protective equipment requirements that differ from those set through the WPS.

The RED requirements for early-entry PPE are set in one of two ways:

1. *If EPA determines that no regulatory action must be taken as the result of the acute effects or other adverse effects of an active ingredient, it establishes the early-entry PPE requirements on the basis of the acute dermal toxicity category, skin irritation potential category, and eye irritation potential category of the active ingredient.*

2. *If EPA determines that regulatory action on an active ingredient must be taken as the result of very high acute toxicity or to certain other adverse effects, such as allergic effects or delayed effects (cancer, developmental toxicity, reproductive effects), it may establish early-entry PPE requirements that are more stringent than would be established otherwise.*

(RED SECTION V - LABELING REQUIREMENTS)

LABELING REQUIREMENTS FOR END-USE PRODUCTS

PPE/Engineering Control Requirements for Pesticide Handlers

For sole-active-ingredient end-use products that contain pendimethalin, the product labeling must be revised to adopt the handler personal protective equipment/engineering control requirements set forth in this section. Any conflicting PPE requirements on the current labeling must be removed.

For multiple-active-ingredient end-use products that contain pendimethalin, the handler personal protective equipment/engineering control requirements set forth in this section must be compared to the requirements on the current labeling and the more protective must be retained. For guidance on which requirements are considered more protective, see PR Notice 93-7.

Products Intended Primarily for Occupational Use (WPS and nonWPS)

Minimum (Baseline) PPE/Engineering Control Requirements

EPA is establishing minimum (baseline) engineering controls for occupational uses of pendimethalin end-use products formulated as wettable powders. All wettable powder formulations must be contained in water-soluble packaging.

EPA is establishing minimum (baseline) personal protective equipment (PPE) requirements for some occupational uses of pendimethalin end-use products. The minimum (baseline) PPE for occupational uses of pendimethalin end-use products are:

For emulsifiable concentrate formulations:
"Mixers and loaders must wear:
- long-sleeved shirt and long pants,
- chemical-resistant gloves*, and
- shoes plus socks."

* For the glove statement, use the statement established for pendimethalin through the instructions in Supplement Three of PR Notice 93-7.

For water-dispersible granule, wettable powder, and emulsifiable concentrate formulations whose use directions reasonably permit application using hand-held sprayers:

"Handlers (mixers, loaders, and applicators) who apply this product using hand-held equipment or hoses must wear:
- long-sleeved shirt and long pants,
- chemical-resistant gloves*, and
- shoes plus socks."

For **multiple-active-ingredient** end-use products that contain pendimethalin the entry restrictions set forth in this section must be compared to the entry restrictions on the current labeling and the more protective must be retained. A specific time period in hours or days is considered more protective than "sprays have dried" or "dusts have settled."

Products Intended Primarily for Occupational Use

WPS Uses

Restricted-entry interval:

A 12-hour restricted-entry interval (REI) is required for uses on food, feed, and fiber crops within the scope of the WPS on all pendimethalin end-use products, with the exception of uses on sugarcane and tobacco.

A 24-hour restricted-entry interval (REI) is required for uses on sugarcane and tobacco crops within the scope of the WPS on all pendimethalin end-use products.

"Exception: if the product is soil-injected or soil-incorporated, the Worker Protection Standard, under certain circumstances, allows workers to enter the treated area if there will be no contact with anything that has been treated."

Early-entry personal protective equipment (PPE):

The PPE required for early entry is:

- -- coveralls,
- -- chemical-resistant gloves, and
- -- shoes plus socks,

Placement in labeling:

The REI and PPE required for early entry must be inserted into the standardized REI statement required by Supplement Three of PR Notice 93-7.

NonWPS uses

Entry restrictions:

2. The Agency is establishing the following entry restrictions for nonWPS occupational uses of pendimethalin end-use products:

"Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application."

Engineering Controls

"When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides (40 CFR 170.240(d)(4-6), the handler PPE requirements may be reduced or modified as specified in the WPS."

User Safety Requirements

1. {Registrant: add the following statements if coveralls are required for pesticide handlers on the end-use product label:}

Discard clothing or other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them.

2. {Registrant: add the following statement always:}

Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."
- "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."

Products Intended Primarily for Home Use

Application Restrictions

"Do not apply this product in a way that will contact any person or pet, either directly or through drift. Keep people and pets out of the area during application."

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."

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Chemical:	**Pendimethalin (ANSI)**
PC Code:	**108501**
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