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

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Mr. Brent Solomon
Valent USA Corp.
1401 Eye Street, N.W.
Suite 220
Washington, DC 20005

SUBJECT: NALED: The HED Chapter of the Reregistration Eligibility Decision Document (RED) for Naled (Case 0092)

Dear Mr. Solomon:

The Agency is in the process of revising the Human Health Assessment chapter for use in the Reregistration Eligibility Decision (RED) for Naled. A copy of the analyses completed July 13, 1995, are enclosed for your use.

The Agency provided Valent with the major components of the risk assessment in 1995. Valent submitted comments and incorporated several risk mitigation measures in response to this assessment. Because the Agency previously provided you with essentially the same assessment contained in the attached chapter and you have responded and provided mitigation measures in response to the Agency's assessment, EPA believes that Valent can reasonably identify gross errors in the enclosed chapter by August 10, 1998. Please keep in mind that the revised human health assessment will be sent to you for comment once it is complete.

If you have any questions or comments or questions, please contact Diane Isbell at (703) 308-8154.

Sincerely,

Richard P. Dumas

for Kathy S. Monk, Chief
Reregistration Branch II
Special Review and
Reregistration Division (7508W)

Enclosure

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

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MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: The HED Chapter of the Reregistration Eligibility Decision Document (RED) for Naled (Case 0092)

FROM: Mary R.A. Clock, Biologist
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

THRU: Karen Whitby, Acting Chief
Risk Characterization and Analysis Branch
Health Effects Division (7509C)
and
Stephanie Irene, Acting Director
Health Effects Division (7509C)

TO: Walt Waldrop, Acting Chief
Reregistration Branch
Special Review and Reregistration Division (7508W)

Please find attached the Human Health Assessment for the Naled Reregistration Eligibility Decision Document (RED). This chapter includes the Hazard Assessment from Pamela M. Hurley (Attachment 1), the Product and Residue Chemistry Assessments from Susan V. Hummel in CBRS (Attachment 2), Dietary Exposure Analysis from Steve Schaible (Attachment 3), and the Occupational and Residential Exposure Assessment from Peg Perrault (Attachment 4).

The naled metabolite DDVP (dichlorvos), which is a Group C carcinogen, is currently in Special Review. Although naled is structurally similar to DDVP, naled itself is not considered a carcinogen. The dietary exposure and risk assessment for naled includes DDVP residues resulting from the use of naled.

CC:	M.Clock/RCAB	P.Hurley/TOX	P.Perrault/OREB	S.Schaiable/SAB
	S.Hummel/CHEM	L.Dorsey/OREB	R.Forrest/RD	P.Deschamp/RCAB

Guidelines 61-3, 62-1, 62-2, 62-3, 63-7, 63-10, 63-11, 63-12, and 63-15. Data submitted by Chevron were reviewed in the Naled Reregistration Standard Update dated 6/8/90 for the Chevron 90% technical (EPA Reg. No. 62499-38), which was subsequently canceled, and the Amvac 90% technical. The Update required additional data concerning GLNs 61-1, 61-3, 62-1, 62-2, 63-10, and 63-15 for the Amvac 90% technical. All product chemistry data were required in the Update for the second Valent 90% technical (EPA Reg. No. 59639-43).

The Chevron data reviewed in the Naled Update for the Amvac 90% technical may apply to the Valent 90% technical (EPA Reg. No. 59639-73), provided Valent confirms that the manufacturing process and location have not changed since the transfer of the 90% technical from Amvac. In addition, if Valent confirms that the two Valent technicals now registered are the same, the submitted data may be applicable to both products.

Dichlorvos (DDVP), a naled metabolite and an impurity of technical naled, is currently in Special Review. Although naled is structurally similar to dichlorvos, based on a one-year dog study, naled itself is not assessed by HED as a carcinogen. The Agency's RfD/Peer Review Committee concluded that naled is classified as a "Group E" chemical (e.g. evidence of non-carcinogenicity for humans).

The current status of the product chemistry data requirements for the Valent naled products is presented in the attached data summary tables (Appendix 1). Refer to these tables for a listing of the outstanding product chemistry data requirements.

5. DATA REQUIREMENTS

Additional information must be provided by Valent concerning the composition of the two technical products and the manufacturing process and location before the Agency can determine whether the data submitted previously by Chevron are applicable to the Valent 90% technicals. If the Chevron data are not applicable, all product chemistry data except for Guideline 63-3 will be required for the Valent technicals. Provided that the registrant submits the data required in the attached data summary tables, and either certifies that the suppliers of beginning materials and the manufacturing process for the naled technical products have not changed since the last comprehensive product chemistry review or submits a complete updated product chemistry data package, HED has no objections to the reregistration of naled with respect to product chemistry data requirements.

Additional Product Chemistry data are required. Two naled 90% technicals are registered to Valent U.S.A. Corporation. A complete set of product chemistry data are required for one technical (EPA Reg. No. 59639-43). For the second technical (EPA Reg. No. 59639-73), a complete set of product chemistry data are required or some of the data requirements may be satisfied by a statement from the registrant that the manufacturing process and location has not changed since the transfer of the product from Amvac Chemical Corporation.

B. HUMAN HEALTH ASSESSMENT

I. HAZARD ASSESSMENT

The toxicology data base for naled for food and non-food uses is adequate to support reregistration eligibility.

a. Acute Toxicity

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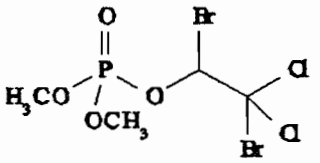
PRODUCT CHEMISTRY ASSESSMENT

1. DESCRIPTION OF CHEMICAL

Naled (1,2-dibromo-2,2-dichloroethyl dimethyl phosphate) is a non-systemic insecticide-acaricide used for fly/mosquito control on field, vegetable, and orchard crops, livestock, poultry, pets, buildings, and outdoor areas.



Empirical Formula:	$C_4H_7O_4PBr_2Cl_2$
Molecular Weight:	381
CAS Registry No.:	300-76-5
Shaughnessy No.:	034401

2. IDENTIFICATION OF ACTIVE INGREDIENT

Pure naled is a white solid with a melting point of 27 C and a vapor pressure of 2 x 10^{-4} mm Hg at 20 C. Naled is practically insoluble in water, has limited solubility in aliphatic solvents, and is highly soluble in oxygenated solvents such as ketones and alcohols.

3. MANUFACTURING-USE PRODUCTS

A search of the Reference Files System (REFS) conducted 3/16/94 identified two naled manufacturing-use products (MPs) registered to Valent U.S.A. Corporation as 90% technicals (EPA Reg. Nos. 59639-43 and 59639-73). The Valent 90% T (EPA Reg. No. 59639-73) was originally registered to Amvac Chemical Corporation (EPA Reg. No. 5481-198) in 1985. This product was subsequently transferred to Chevron (EPA Reg. No. 62499-44) on 10/2/91, then to Valent on 1/13/92. The second Valent 90% technical (EPA Reg. No. 59639-43) was registered to Valent on 12/1/89.

The two 90% technicals for which data requirements were addressed in the Naled Guidance Document dated 6/83, were identified in the Naled Reregistration Standard Update dated 6/8/90 as the Chevron 90% technical (EPA Reg. Nos. 62499-14 and 62499-38). These products were canceled on 6/16/92. Only the Valent 90% technicals are subject to a reregistration eligibility decision.

4. REGULATORY BACKGROUND

Amvac produced the technical material for the 90% technicals addressed in the 6/83 Guidance Document; thus, when Amvac applied for me-too registration of its own 90% technical (EPA Reg. No. 5481-198) in 1985, the Agency determined that data submitted by Chevron and reviewed in the Naled Guidance Document dated 6/83 were applicable to the Amvac 90% technical (MRID 00138846). The Guidance Document required additional product chemistry data concerning

The acute oral studies indicated that naled was more toxic when administered as an aqueous suspension in 0.5% carboxymethylcellulose than when administered as a corn oil preparation.

Acute Toxicity

Test	Result	Category
Acute Oral LD_{50} (rat) [1]	Corn oil vehicle: 325 mg/kg (males); 230 mg/kg (females) Carboxymethylcellulose vehicle: [2] 191 mg/kg (males); 92 mg/kg (females)	II
Acute Dermal LD_{50} (rabbit) [3]	390 mg/kg (males) 360 mg/kg (females)	II
Acute Inhalation LC_{50} (rat) [4]	0.20 mg/L (males) 0.19 mg/L (females) for 4 hr. exposure	II
Eye Irritation (rabbit) [5]	Severe irritation	I
Dermal Irritation (rabbit) [6]	Corrosive (escharotic)	I
Skin Sensitization (guinea pig) [7]	Weakly positive	N/A

[1] MRID 00142660
[2] A preliminary study to a cytogenetics assay obtained somewhat lower oral LD_{50} values of 85.1 mg/kg/day for male rats and 81.2 mg/kg/day for females using carboxymethylcellulose as the vehicle. (MRID 00142665)
[3] MRID 00146493
[4] MRID 00146494
[5] MRID 00074826. Test material = Dibrom 14 Concentrate (85% naled).
[6] MRID 00074825. Test material = Dibrom 14 Concentrate (85% naled).
[7] MRID 00074657
N/A = not applicable

b. Subchronic Toxicity

In a 13-week inhalation study, male and female Fischer-344 rats were exposed (whole body) to filtered air (control group) or aerosols containing 0.2, 1, or 6 μg/L of naled for 6 hours/day, 5 days/week. Additional control and high concentration groups were allowed to recover for 6 weeks. Exposure to the highest concentration of 6 μg/L resulted in clinical signs of toxicity manifest as tremors, salivation, nasal discharge, abnormal respiration, and anogenital staining. The clinical signs were consistent with cholinergic effects and the observed inhibition of cholinesterase activity relative to the control group. Brain cholinesterase was inhibited at 6 μg/L. Plasma and RBC cholinesterases were inhibited at 1 and 6 μg/L. Only plasma cholinesterase continued to be inhibited six weeks after exposure to the high concentration. No other treatment-related effects were observed. The NOEL for cholinesterase inhibition was 0.2 μg/L, and the LOEL was 1 μg/L based on depression of plasma and RBC cholinesterase activities. The NOEL for systemic toxicity was 1 μg/L, and the LOEL was 6 μg/L based on clinical signs of toxicity. (MRID 00164224)

A 28-day dermal study was conducted with male and female CD/Sprague-Dawley rats.

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Naled was applied to intact skin at dose levels of 0, 1, 20, or 80 mg/kg/day for 6 hour/day, 5 days/week. Carboxymethylcellulose was used as the vehicle. The two highest doses were extremely irritating to the skin producing severe erythema and edema, necrosis, and exfoliation. After 28 days, histopathological findings in the skin included acute ulcerative inflammation, necrosis, and epidermal hyperplasia. Exposure to 20 and 80 mg/kg/day also produced systemic toxicity. Body weight gain by males was depressed despite increased food consumption. Plasma, RBC, and brain cholinesterases were inhibited by 20 and 80 mg/kg/day relative to the control group. Other treatment-related findings were confined to the 80 mg/kg/day groups. Liver and adrenal weights of females were increased. Clinical chemistry changes were suggestive of mild renal effects. Blood urea nitrogen was increased and creatinine, total protein, and albumin were decreased in both sexes. No treatment-related histopathological changes were observed other than those of the skin. The NOEL was 1 mg/kg/day for dermal irritation, systemic toxicity, and cholinesterase inhibition. The LOEL was 20 mg/kg/day based on the findings of dermal irritation, reduced weight gain, and cholinesterase inhibition. (MRID 00160750)

A 28-day feeding study with rats and a 90-day study with dogs were supplementary. In the feeding study, the doses tested were 0, 0.25, 1, 10, or 100 mg/kg/day naled. The LOEL was 10 mg/kg/day and the NOEL was 1 mg/kg/day based on cholinergic effects. The 28-day study was graded Core Supplementary because it was a range finding study designed to provide the rationale for dose selection (MRID 00088871). The 90-day dog study which was conducted in 1958, did not meet current Agency guideline requirements. The subchronic feeding study requirements are satisfied by the two-year rat and one-year dog studies.

c. Chronic Toxicity and Carcinogenicity

A dietary stability study of naled incorporated into standard rodent feed indicated that the test material rapidly degraded at room temperature (half-life of 1.5 days at 21 C). Consequently, gavage administration was used in most long-term studies of naled. The dosage preparations were generally suspensions of the test material in aqueous carboxymethylcellulose (0.5% w/w). Acute oral studies indicated that carboxymethylcellulose (CMC) preparations of naled were more toxic than corn oil preparations.

A one-year study was conducted with male and female beagle dogs. Naled was administered at dose levels of 0, 0.2, 2, or 20 mg/kg/day by gavage (vehicle, CMC). Clinical signs of emesis and diarrhea were associated with doses of 2 and 20 mg/kg/day, as well as statistically significant increases in mineralization of the lumbar spinal cord in both sexes. Plasma, RBC, and brain cholinesterase activities were depressed at these same dose levels (brain was depressed at 2 mg/kg/day in females only) relative to the control group. Anemia was also evident at 2 and 20 mg/kg/day. Erythrocyte count, hemoglobin, and hematocrit were reduced. At the high dose only, liver and kidney weights were increased but unaccompanied by histopathological changes. The NOEL was 0.2 mg/kg/day for cholinesterase inhibition and systemic toxicity. The LOEL was 2 mg/kg/day based on depressed cholinesterase activity, anemia and mineralization of the lumbar spinal cord. (MRID 00160751)

In a two-year chronic toxicity/carcinogenicity study, male and female Sprague-Dawley CD rats were administered naled at doses of 0, 0.2, 2, or 10 mg/kg/day by gavage (vehicle, CMC). Plasma, RBC, and brain cholinesterase activities were statistically significantly depressed at dose levels of 2 and 10 mg/kg/day relative to base levels. The NOEL for cholinesterase inhibition was 0.2 mg/kg/day, and the LOEL was 2 mg/kg/day. The NOEL for systemic toxicity was the highest dose tested, 10 mg/kg/day. No neoplastic lesions were related to treatment. Dose selection was supported by the results of a 28-day pilot study demonstrating mortality at 100 mg/kg/day and mild cholinergic signs (lethargy and muscle weakness) accompanying 50% reductions in plasma and

activities at 10 mg/kg/day. Therefore, the high dose of 10 mg/kg/day was considered adequate to test for carcinogenic potential. (MRID 00141784)

An 89-week carcinogenicity study was conducted with male and female CD-1 mice. Naled was administered at doses of 0, 3, 15, or 75 mg/kg/day by gavage (vehicle, CMC). The high dose of 75 mg/kg/day was reduced to 50 mg/kg/day after 26 weeks due to high mortality. Mortality was 10 and 13% for high dose males and females, respectively, compared to 2% mortality of control after 26 weeks. Tremors were observed in 3 of 8 high dose females that died during the first 26 weeks. The only other treatment-related finding was a slight reduction (3-5%) in weight gain by males showing a dose-related trend at the middle and high dose levels. Cholinesterase activity was not determined. No neoplastic findings were related to treatment. The dose selection was supported by the results of a pilot study, which indicated the use of a high dose between 50 and 100 mg/kg/day in the carcinogenicity study to avoid excessive toxicity and mortality. In the pilot study, a dose level of 300 mg/kg/day for two weeks produced mortality (60 to 80%), 150 mg/kg/day for two weeks produced cholinergic signs, and 50 mg/kg/day for four weeks produced a slight decrease in body weight gain and a significant reduction in food consumption. The mortality rate associated with the 75 mg/kg/day dose level after 26 weeks justified reduction of the high dose to 50 mg/kg/day. (MRID 00148569)

d. Developmental Toxicity

A developmental toxicity study was conducted with pregnant Sprague-Dawley rats. Naled was administered at doses of 0, 2, 10, or 40 mg/kg/day by gavage (vehicle, CMC) on days 6 through 19 of gestation. Dams were sacrificed on day 20 of gestation. The high dose of 40 mg/kg/day was maternally toxic producing clinical signs and reducing weight gain. The clinical signs included tremors, hypoactivity, discharge from the mouth and eyes, and dyspnea. No developmental toxicity was related to treatment. There may have been a marginal effect on resorptions at the high dose because there were 6 litters with 2 or more resorptions. However, because these were observed at a dose that was maternally toxic, they were not considered significant enough to change the NOEL for developmental toxicity. The NOEL for maternal toxicity was 10 mg/kg/day, and the LOEL was 40 mg/kg/day based on clinical signs and reduced weight gain. The developmental toxicity NOEL was 40 mg/kg/day, the highest dose tested. (MRID's 00138682, 00144026)

A developmental toxicity study was conducted with artificially inseminated New Zealand rabbits given doses of 0, 0.2, 2, or 8 mg/kg/day of naled by gavage (vehicle, CMC) on days 7 through 19 of gestation. Does were sacrificed on day 29 of gestation. No maternal or developmental toxicity was related to treatment. Although no maternal toxicity was elicited by the highest dose, dose selection was supported by the results of a pilot study (MRID 146495) with inseminated animals. In the pilot study, dose levels of 20 mg/kg/day and higher produced mortality, 10 mg/kg/day and above produced marked cholinergic signs, and 2 mg/kg/day was associated with clinical signs consistent with mild cholinergic effects. The clinical effects at 10 mg/kg/day indicated that the high dose of 8 mg/kg/day in the definitive study was sufficient for testing developmental toxicity. The NOEL for maternal toxicity and developmental toxicity was 8 mg/kg/day, the highest dose tested. (MRID 00146496)

e. Reproduction

A two-generation reproduction study was conducted with Sprague-Dawley-derived Charles River CD rats. Naled was administered at doses of 0, 2, 6, or 18 mg/kg/day by gavage (vehicle, CMC). Systemic effects were observed in adult male rats of both generations. Body weight gain was depressed at 18 mg/kg/day for F_0 males and at all dose levels for F_1 males. Reproductive

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indices were unaffected in both generations. Survival of pups was reduced at 18 mg/kg/day in the F_1 and F_{2b} generations. A consistent decrease in pup weight was also noted during lactation in both generations. The NOEL for parental systemic effects was 6 mg/kg/day, and the LOEL was 18 mg/kg/day based on decreased body weight gain by both generations. The reproductive toxicity NOEL was the highest dose tested, 18 mg/kg/day. (MRID 00146498)

f. Mutagenicity

An in vivo gene mutation study (mouse spot test) was conducted with pregnant C57BL/6 mice given 0, 3, 20, or 150 mg/kg/day of naled by gavage (vehicle, CMC) for 4 days of gestation (days 8-12). Litters were scored for coat color mutations ("spots") on post-partum days 12 and 28. The test was conducted to detect mutation events consisting of intragenic base-pair changes, deletions, and somatic crossing-over. The high dose of naled was very toxic producing maternal mortality, decreased maternal body weight, and decreased pup survival. Naled exhibited no potential to induce coat color spots. (MRID 00141571)

Naled was tested for gene mutation in the Salmonella typhimurium reverse mutation assay (Ames assay) using tester strain TA 100 with and without metabolic activation (PCB-induced mouse liver S9 fraction). Naled was tested at concentrations of 0.5, 1, and 2 μM. The highest concentration was toxic in the absence of metabolic activation but was mutagenic with metabolic activation. The middle concentration of 1 μM was positive both with and without metabolic activation. The low concentration of 0.5 μM was marginally positive (<2-fold DMSO control). (MRID 00142662)

Naled was tested for DNA damage in Proteus mirabilis strains PG273 (wild type) and PG713 (thr^-, rec^-, hcr^-). Naled was negative in both strains at inhibitory concentrations of 10 and 40 μM. (MRID 00142662)

Naled was tested for cytogenetic effects in vivo in the mouse bone marrow micronucleus assay. Naled was administered to male and female Swiss mice (Crl: CD-1, 1CR, BR) as a single oral dose by gavage (vehicle, CMC). Dose levels were 0, 55, 110, or 220 mg/kg for males and 0, 55, 110, or 290 mg/kg for females. Dose selection was based on preliminary studies indicating oral LD_{50} values of 257 mg/kg for males and 336 mg/kg for females. Bone marrow cells were harvested 24, 48, and 72 hours after treatment. The highest dose produced mortality (16-24%) and clinical signs of toxicity. Naled had no cytotoxic effect on bone marrow at these dose levels, and produced no nuclear anomalies. (MRID 00146497)

In another in vivo cytogenetics study, male and female Sprague Dawley rats were administered naled as a single oral dose by gavage (vehicle, CMC). Dose levels were 0, 3.88, 12.93, or 38.80 mg/kg for males and 0, 6.17, 20.57, or 61.70 mg/kg for females. Dose selection was based on preliminary studies conducted at the same laboratory indicating oral LD_{50} values of 85.1 mg/kg for males and 81.2 mg/kg for females. Bone marrow cells were harvested 6, 24, and 48 hours after treatment. High dose females showed signs of toxicity including ataxia, dyspnea, and oral exudate. Cytotoxicity in bone marrow was not evident at any dose level. Naled had no clastogenic effect. The highest dose was considered to be near a maximum tolerated dose based on the clinical signs observed in females and the results of preliminary studies indicating the high dose for males was approximately one-half the oral LD_{50}. (MRID 00142665)

g. Metabolism

A general metabolism study is a data gap. Two submitted studies, singly or combined, do not meet the data requirement.

O,O-Dimethyl-2,2-dichlorovinyl phosphate (dichlorvos) is an expected metabolite of naled. Limited data have shown metabolites to include dichlorvos and hydrolysis products. In a study with a single cow, some metabolites were tentatively identified: methyl phosphates (mono- and di-), O-methyl 2,2-dichlorovinyl phosphate (desmethyl dichlorvos), and inorganic phosphate. (Naled Registration Standard, 1983; MRID 00013546)

Three metabolites were identified in a in vitro study using rat liver homogenates: dichlorvos, dichloroacetaldehyde, and bromodichloroacetaldehyde. (Naled Registration Standard, 1983; MRID 00074857)

h. Neurotoxicity

Naled was tested for acute delayed neurotoxicity. Adult domestic hens (set 1) were given an acutely toxic dose of naled (42 mg/kg, LD_{50}) preceded by treatment with atropine sulfate and 2-PAM to protect from acute cholinergic effects. The hens were observed for neurotoxic signs for 21 days, re-dosed, observed an additional 21 days, then sacrificed for histopathological examination of central and peripheral nervous tissue. A second set of hens was administered a single dose of 8 or 42 mg/kg and sacrificed 24 hours later for determination of brain cholinesterase and neurotoxic esterase activities. Two of 10 controls and 4/40 treated hens (set 1) died during the study. All treated hens (set 1) showed clinical signs of neurotoxicity (i.e., "subdued", unsteady). None displayed locomotor ataxia characteristic of delayed neurotoxicity. Axonal degeneration in the spinal cord was increased in naled treated hens compared to controls (concurrent and historical), but it was less severe than that produced by the positive control, TOCP. Brain cholinesterase was markedly depressed (50%, 42 mg/kg) in naled treated hens. Neurotoxic esterase activity was unaffected. Naled did not produce frank delayed neurotoxicity, but a degenerative neuronal effect was manifest in the spinal cord. (MRID 41630701)

Because of the findings in the acute study, EPA requires a 28-day or 90-day repeated dose delayed neurotoxicity study in hens.

An acute neurotoxicity study was conducted with rats given a single dose of 0, 25, 100, or 400 mg/kg of naled by gavage (vehicle, CMC). Functional observational battery and motor activity evaluations were made pre-treatment, 30 minutes after treatment (time of peak effect), and 7 and 14 days after treatment. The high dose of 400 mg/kg produced mortality and overt clinical signs of toxicity (e.g., orange/yellow material on body surfaces; red material around mouth/nose/eyes). Body weight gain by the high dose group was transiently decreased (days 0-7). Animals given 100 and 400 mg/kg showed marked effects in the functional observational battery on the day of treatment. Observed changes included convulsions, tremors, increased secretions, exophthalmus, respiratory changes, reduced muscle strength, and slowed response to stimuli. Total motor activity also was reduced. A few treatment-related effects were observed on the day of treatment in one to two females given the low dose of 25 mg/kg. One female had tremors, two displayed exophthalmus during handling, and one exhibited reduced hindlimb grip strength. These changes were not observed in concurrent controls or historical controls (from 3 studies). No treatment-related neurological effects were observed 7 or 14 days after treatment at any dose level. The NOEL for acute neurotoxicity was 25 mg/kg in males, the lowest dose tested. The LOEL for males was therefore 100 mg/kg. A NOEL for females was not identified in this study. However, an estimate of this parameter can be reasonably set for females at 5 mg/kg, based upon minimal neurological compromise at 25 mg/kg in the main study, coupled with no toxicity at 5 or 25 mg/kg in the preliminary range-finding study. Therefore, the NOEL for females was 5 mg/kg and the LOEL for females was 25 mg/kg. (MRID 42861301)

Naled was tested in a subchronic (90-day) neurotoxicity study in Sprague-Dawley Crl:CD®BR

rats. The test article (94.35%) was administered by gavage in carboxymethylcellulose (CMC) at dose levels of 0, 0.4, 2.0 or 10.0 mg/kg/day. Neurological parameters were measured by both the functional observational battery (FOB) and locomotor activity (LA). Minimal neurological effects were observed in 3/10 high dose females, but no other clinical effects were observed in either sex at any other dose level. The observed effects included sporadic occurrences of tremors (forelimb, hindlimb and/or whole body). The NOEL for neurotoxicity was 2.0 mg/kg/day for females and 10.0 mg/kg/day for males (MRID 432239-01).

i. Domestic Animal Safety

Subchronic (16-week) dermal toxicity studies were conducted with dog and cat antiflea collars containing naled (7%, cat collar; 15%, dog collar) and propoxur (Tradename Baygon; 2.4%, cat collar; 4.2%, dog collar) as the active ingredients. Endpoints evaluated in each study included clinical signs, dermal irritation, body weight, urinalysis, blood chemistry (glucose, BUN, SGOT, SAP), hematology, and histopathology (including brain and spinal cord). Plasma and RBC cholinesterase activities were determined on days 3 and 7 and weeks 2, 3, 4, 5, 6, 7, 8, 12, and 16.

Male and female mixed breed cats wore a placebo, 1, 2, or 4 collar(s) for 16 weeks. Cats wearing 4 collars exhibited more extensive flaking of the skin on the neck than controls or other treatment groups. A slight, transient decrease in plasma cholinesterase was observed for the group wearing 1 (days 3 & 7), 2 (day 7), or 4 (through week 5) treated collars. RBC cholinesterase was unaffected. No other treatment-related effects were observed. (MRID 00079549)

Male and female mixed breed dogs wore a placebo, 1, 2, or 4 collar(s) for 16 weeks. Two dogs wearing 4 collars showed dry flaky skin on the neck during week 10. Plasma cholinesterase was lower for dogs wearing 4 collars through the first 4 weeks of the study. No other treatment-related effects were observed. (MRID 00060430)

j. Toxicology Data Requirements

There is one data gap for toxicology, Guideline 85-1, General Metabolism. Two submitted studies, an in vitro study and a study conducted with a single cow, do not meet the data requirement.

II. DOSE-RESPONSE ASSESSMENT

a. Toxicity Endpoints Identified for Risk Assessment

NALED

Acute dietary exposure (1 day):

The endpoint for acute dietary risk assessment is the NOEL of 1 mg/kg/day from a 28-day oral study with rats. In the study, the doses tested were 0, 0.25, 1, 10, or 100 mg/kg/day naled by gavage. The LOEL is 10 mg/kg/day based on cholinergic signs of toxicity (muscular tremors, salivation, ocular discharge, increased urination, weight loss and soft, moist feces) and cholinesterase inhibition (plasma, RBC, brain). The study was graded Core Supplementary because it was a range finding study designed to provide the rationale for dose selection (MRID 00088871).

Short term occupational exposure (1-7 days):

The endpoint for short term occupational or residential risk assessment is the NOEL of 1 mg/kg/day from a 28-day dermal study with rats. In the study, the doses tested were 0, 1, 20, or 80 mg/kg/day for 6 hrs/day, 5 days/week. The two highest doses were extremely irritating to the skin producing severe erythema and edema, necrosis, and exfoliation. The NOEL was 1 mg/kg/day for dermal irritation, systemic toxicity, and cholinesterase inhibition (MRID 00160750). The LOEL is 20 mg/kg/day based on the findings of dermal irritation, reduced weight gain and cholinesterase inhibition (plasma, RBC, brain).

Intermediate term occupational or residential exposure (1 week-several months):

The endpoint for intermediate term occupational or residential risk assessment is the NOEL of 1 mg/kg/day from a 28-day dermal study with rats. The NOEL was 1 mg/kg/day for dermal irritation, systemic toxicity, and cholinesterase inhibition (MRID 00160750). The LOEL is 20 mg/kg/day based on reduced weight gain and cholinesterase inhibition (plasma, RBC, brain).

Chronic exposure - Reference Dose (RfD)

The RfD was established as 0.002 mg/kg/day based on a NOEL of 0.2 mg/kg/day and an uncertainty factor of 100. The NOEL was obtained from a 2-year gavage study in the rat. The 1-year gavage study in the dog was considered to be co-critical with a NOEL of 0.2 mg/kg/day as well. The RfD was approved by the HED (8/18/94) Reference Dose Committee. The Committee concluded that naled is classified as a "Group E" chemical (e.g. evidence of non-carcinogenicity for humans). Naled has not been reviewed by the World Health Organization (WHO) and an acceptable daily intake (ADI) has not been developed.

Dermal Penetration

According to the Toxicology Endpoint Selection Document (8/4/94) for Naled, dermal penetration should be considered 100%, based on a NOEL of 1 mg/kg/day in both dermal and oral 28-day studies in rats for cholinesterase inhibition with LOELs of 20 mg/kg/day.

DICHLORVOS

Results from acute, subchronic and chronic toxicity studies have shown DDVP to be a potent inhibitor of plasma, red blood cell and brain cholinesterases.

Acute Dietary

Acute dietary exposure in the DRES acute analysis was compared to a NOEL of 0.5 mg/kg/day for signs associated with cholinesterase inhibition, taken from an acute neurotoxicity study in rats (M.Beringer memorandum to D.Utterback, 9/8/93). Dichlorvos has not yet been evaluated by OPP's Less than Lifetime Committee. This endpoint was informally acknowledged as the most appropriate endpoint for acute dietary risk by Toxicology Branch 1 (personal communication with Joycelyn Stewart, 7/11/95) and Elizabeth Doyle, secretary of the Less than Lifetime Committee (personal communication with E. Doyle, 11/28/94).

Chronic exposure - Reference Dose (RfD)

Chronic exposure was compared to a Reference Dose (RfD) of 0.0005 mg/kg/day, based on a No Observed Effect Level (NOEL) of 0.05 mg/kg/day and an uncertainty factor of 100. The NOEL was taken from a 1 year feeding study in dogs in which plasma and red blood cell cholinesterase inhibition (ChE) were the effects observed in males and females (G.Ghali memorandum to

G.LaRocca and L.Rossi dated 6/10/92).

Carcinogenicity

Dichlorvos has been classified as a Group C possible human carcinogen by the HED Carcinogenicity Peer Review Committee (G.Ghali to G.LaRocca, 9/18/89). The upper bound potency factor (Q_1*) was revised to incorporate the 3/4 interspecies scaling factor. The revised Q_1* is 1.22 x 10^{-1} $(mg/kg/day)^{-1}$ (B.Fisher and H.Pettigrew memo to D. Edwards, 9/20/94).

III. EXPOSURE ASSESSMENT

a. Dietary Exposure

According to the Agency's Reference Files System (REFS), in a search conducted 3/15/94, naled is presently registered for use on a variety of food and feed crops including alfalfa, almonds, beans (dry and succulent), broccoli, brussel sprouts, cabbage, cauliflower, celery, collards, cotton, eggplant, grapefruit, grapes, grasses (pasture and rangeland), kale, lemons, melons, oranges, peas (succulent), peaches, peppers, safflower, squash (summer), strawberries, sugar beets, tangerines, tobacco, and walnut. Naled is also presently registered for mosquito abatement and fly control in terrestrial non-food areas such as residential areas, municipalities, tidal marshes, swamps, woodlands, livestock pastures, feed lots, farm buildings, dairy barns, and feed and forage areas. Other registered uses of naled include greenhouse/ornamental pest control, outside residential areas/lawns, rangeland grasshopper control, miscellaneous non-food indoor uses, and pet flea collars.

SUMMARY OF SCIENCE FINDINGS

GLN 171-3: Directions for use

A REFS search conducted 3/15/94 indicated that there are nine naled end-use products (EPs) with food/feed uses registered to Valent U.S.A Corporation. These EPs are presented below.

EPA Reg. No.	Acceptance Date	Formulation Class	Product Name
59639-14	5/27/93	4% D	Dibrom 4 Dust
59639-15 [a]	3/21/94	7.2 lb/gal EC	Dibrom 8 Emulsive
59639-18	5/5/92	3.6 lb/gal EC	Valent Fly Killer D.
59639-19 [b]	2/28/94	12.6 lb/gal EC	Dibrom Concentrate
59639-21	5/25/92	1% RTU	Dibrom Fly & Mosquito Spray
59639-25	10/11/89	1.26 lb/gal RTU	Dibrom LVC 10
59639-46	9/30/91	4% D	Dibrom Sevin 4-5 Dust
59639-72	2/27/90	7.2 lb/gal EC	Naled 8 Insecticide
59639-74	8/1/91	12.6 lb/gal EC	Naled 85 Concentrate Insecticide

[a]Including OR900020 and WA890019. [b]Including FL890003 and GA770011. [Note: MD8100023 has expired; NY920002 is a non-food use label.]

A comprehensive summary of the registered food/feed use patterns of naled, based on these product labels, is presented in Table A within Attachment 2. An examination of Valent's naled end-use products indicates that these labels do not specify the maximum number of applications per growing season (or maximum seasonal rate) allowed for registered crops. For reregistration purposes, the registrant is required to specify the maximum number of applications per growing season that may be allowed for each registered crop. The required label revisions must be supported by adequate residue data; refer to "GLN 171-4 (k): Magnitude of the Residue in Plants" section for a discussion of seasonal application rates which are currently supported by field residue data.

A tabular summary of the residue chemistry science assessments for reregistration of naled is presented in Table B within Attachment 2. The conclusions regarding the reregistration eligibility of naled on the crops listed in Table B within Attachment 2 are based on the use patterns registered by the basic producer, Valent U.S.A. Corporation. 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 adequately understood. Naled is generally considered to be non-systemic based on studies with a variety of plants including cucumbers, cotton, and Swiss chard. Metabolism studies with oranges and tomato processed fractions have also been conducted to investigate the nature and magnitude of organic brominated components of the residue derived from naled *per se* or from its bromine-containing impurities. These studies indicated that the only residues of organic bromine compounds are naled, the parent, and metabolite bromodichloroacetaldehyde (BCDA), both of which are rapidly debrominated by sulfhydryl compounds or by hydrolysis.

The results of the submitted plant metabolism studies are consistent with the scientific literature on pesticide metabolism. The major pathway is debromination to form dichlorvos. A minor pathway is hydrolysis to dimethylphosphate and BCDA. Dichlorvos may be lost by two routes, evaporation from leaf surfaces under field conditions and/or hydrolysis to form dimethylphosphate and dichloroacetaldehyde (DCA). The latter is converted to 2,2-dichloroethanol which is then conjugated and/or incorporated into naturally occurring plant components. The dimethylphosphate component of hydrolyzed naled is sequentially degraded to monomethyl phosphate and inorganic phosphates. The chemical structures of the terminal residues of concern, naled and dichlorvos, are presented in Figure A of the chemistry chapter (Attachment 2). The metabolic pathway is shown in Figure B of the chemistry chapter (Attachment 2).

GLN 171-4 (b): Animal Metabolism

The qualitative nature of the residue in animals is adequately understood based on acceptable poultry and ruminant metabolism studies reflecting oral exposure. The residues of concern in animal commodities, naled and dichlorvos, are also those which are currently included in the tolerance expression. The HED's Greybeard Committee waived the requirements for an additional poultry metabolism study reflecting direct dermal treatment because the registrant does not intend to support this use; Valent has subsequently deleted direct dermal treatment of poultry with naled from its product labels. The salient features of the available animal metabolism studies are described below. A discussion of the livestock metabolism studies and metabolic pathways of naled in poultry and ruminants can be found within the chemistry chapter (Attachment 2).

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

Adequate residue analytical methods are available for the purposes of reregistration. Two GC methods, Method I and A, are listed in the Pesticide Analytical Manual (PAM, Vol. II, Section 180.215) for tolerance enforcement. Other GC methods (RM-3G-3 and the method of Boone) for separate determination of naled and dichlorvos are adequate for tolerance enforcement purposes. In addition, a GC method (RM-3G-4 revision of Method RM-3G-3) is adequate for enforcement of tolerances for residues in almonds, broccoli, oranges, and alfalfa. The limit of detection for both compounds is 0.01 ppm. A revised version of the residue analytical method RM-3G-4 has been reviewed; additional revisions to this method are required before it can be forwarded to FDA for inclusion in PAM, Vol. II.

Residue data submitted for tolerance reassessment were collected using the current or proposed enforcement methods. The registrant provided adequate method validation data to verify the suitability of these methods for data collection.

The FDA PESTDATA database dated 1/94 (PAM Vol. I, Appendix II) indicates that naled and dichlorvos are completely recovered (>80%) using multiresidue method PAM Vol. I Section 302 (Luke method) and not recovered using Sections 303 (Mills, Onley, Gaither method) and 304 (Mills fatty food method). However, dichlorvos has a short relative retention time and is detected only using low GC column temperatures ("early eluter" conditions).

GLN 171-4 (e): Storage Stability

The requirements for storage stability data are not fully satisfied for the purposes of reregistration. Information concerning the storage intervals and conditions of some residue data previously submitted in support of tolerance establishment remains outstanding: this includes eggplant, winter squash, and alfalfa forage/hay. The registrant has, however, submitted adequate storage and interval data for all other crops.

Storage stability studies have been conducted using fortified samples of beans, celery, citrus fruits, peas, and strawberries. Residues of naled and dichlorvos are stable in hexane extracts of treated beans, peas, and citrus fruits stored at 4 C for approximately 9 months. Residues of naled remained stable in/on oranges and strawberries stored frozen (-20 C) for 1 month, but by the end of 6 months, naled residues can convert to dichlorvos. Method I of PAM and method RM-3G-4 specify that samples should be extracted within 24 hours of sample receipt (and within 48 hours of sample collection) and that extracts should be stored frozen at -20 C until analysis.

Additional dichlorvos storage stability studies are reported in the Dichlorvos Registration Standard dated 1/86. No significant reduction of residues were reported in samples of sorghum, figs, and swine tissues following fortification of these commodities with dichlorvos at 0.005 to 5.0 ppm and storage of fortified samples under frozen conditions (temperature unspecified) for up to 12 weeks. In addition, flour and pinto beans were fortified with dichlorvos at 6.25 and 2.5 ppm and stored under ambient conditions for up to 28 days. The data indicate that the dichlorvos residues decline rapidly under ambient storage conditions.

Data which depict the decline in levels of naled and its metabolite dichlorvos in commodities stored under the range of conditions and for the range of intervals specified are required for any remaining registered crops or for any crops for which the registrant wishes to establish or re-establish tolerances/registration. Finally, the outstanding field trials and processing studies are required to be validated by adequate storage stability data.

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

The reregistration requirements for magnitude of the residue in plants are fulfilled for the following commodities: almond hulls; almond nutmeat; beans (dry and succulent); bean vines; broccoli; brussel sprouts; celery; cottonseed; eggplant; grapefruit; grapes; grass forage; lemons; melons; oranges; peaches; peas (succulent); pea vines; peppers; safflower seed; spinach (and chard); squash, summer; strawberries; sugar beet roots; sugar beet tops; tangerines; and walnuts. Adequate field trial data depicting the combined residues of naled and dichlorvos (expressed as naled) following treatments according to the maximum registered use patterns have been submitted for these commodities. The reregistration requirements for magnitude of the residue in wide area and general outdoor treatments for area pest (mosquito and fly) are also fulfilled.

Additional data are required for the following commodities: bean hay; cabbage; cauliflower; collards; cucumbers; grass hay; hops; lettuce; mushrooms; pea hay; rice grain and straw; safflower; soybeans; soybean forage and hay; squash, winter; tobacco; tomatoes; and turnip roots and tops. The required data for collards will be translated to kale. The required data for winter squash will be translated to pumpkins.

The Naled Reregistration Standard Guidance Document dated 7/83 and the Naled Reregistration Standard Update Residue Chemistry Chapter dated 6/8/90 previously required data reflecting use of the dust (D) formulation according to the maximum registered use patterns on a number of crops. Valent responded to these requirements by amending its product labels for the 4% D formulation (EPA Reg. Nos. 59639-14 and 59639-46) to delete all food/feed uses, except on grapes. Although the Agency no longer requires data for dust formulations when there are data available for a wetting spray at the same rate, a much higher application rate is allowed for the 4% D on grapes. As a consequence, residue data reflecting application of a D formulation are required on grapes.

Valent has requested the reinstatement of the following use sites that were voluntarily canceled by Chevron (previous registrant): eggplant, hops, melons, peaches, peppers, pumpkins, spinach, squash, and Swiss chard. The Chemistry Branch has considered this request (CB No. 12128, 12/16/93, D. McNeilly). A summary of the available data, reinstatement request, and reregistration requirement status by crop group is presented in the Naled Residue Chemistry Chapter for the RED.

Wide Area and General Outdoor Treatments

The combined residues of naled and dichlorvos (expressed as naled) were below the established 0.5-ppm tolerance from use of naled for area pest control in/on representative raw agricultural commodities (listed in 40 CFR §180.34) harvested one hour following one aerial application the EC formulation at 0.25 lb ai/A (~1.1x the maximum registered rate). The submitted data from 17 field trials indicate that measurable residues up to 0.04 ppm naled (cranberries, wheat) and up to 0.27 ppm dichlorvos (mustard greens) occurred. The highest combined residue value, when expressed in terms of naled was 0.46 ppm (mustard greens). The current tolerance expression listed in 40 CFR §180.215 for area pest control covers only residues of naled *per se* and should be revised to reflect the combined residues of naled and its conversion product dichlorvos.

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

The reregistration requirements for magnitude of the residue in processed food/feed commodities are fulfilled for cottonseed, grapes, oranges, and soybeans. Processing studies involving rice, soybeans, and tomatoes will not be required provided all registered uses of naled on these crops are canceled. It should be noted that because of revisions in the livestock feeds table for Subdivision O, data on cannery waste of beans are no longer required.

The combined residues of naled and dichlorvos are not expected to concentrate in the processed commodities of grapes, oranges, and soybeans, except for orange oil. An acceptable orange processing study indicates that residues of dichlorvos concentrated in oil 13x during processing of oranges treated with naled. Residues of naled were non-detectable in both unprocessed oranges and all orange processed commodities. The study also indicates that residues of dichlorvos did not concentrate in the citrus processed commodities wet pulp, dried pulp, molasses, and juice. HED previously concluded that for the purposes of establishing food additive tolerances, if appropriate, the combined residues of naled and dichlorvos will be assumed to concentrate 13x during processing of citrus treated with naled. [Note: See Tolerance Reassessment regarding § 701 tolerance under FFDCA, Appendix 1]

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

The reregistration requirements for magnitude of the residue in animals are fulfilled. There are presently no registered direct application uses of naled on livestock animals; the only indirect uses of naled on animals involve animal premise treatment. HED has reconsidered the available information for naled and has determined that additional animal feeding studies are not required. This decision was based on a goat feeding study wherein the test animals were fed radiolabeled naled at 107 ppm (~20x the expected maximum dietary burden for goats) in 3 equal daily doses and sacrifices on day-4; no naled or dichlorvos residues were detected in goat tissues or milk. In another study, residues were nondetectable (<0.01 ppm) in milk from Holstein cows subjected to body and premise sprays for 14 days at 2 oz ai/2.5 gal (~10x the registered maximum use rate). The registrant has voluntarily canceled the previously registered dermal uses of naled on poultry; consequently a poultry dermal study is no longer required for reregistration.

The established tolerances of 0.05 ppm for the combined residues of naled and dichlorvos (expressed as naled) in the eggs, milk, and tissues of animals are adequate. These tolerances mainly reflect residues resulting from dietary sources. The contribution of the combined residues of naled and dichlorvos to eggs, milk, and meat from the indirect uses of naled in livestock premises is not expected to be significant in relation to the levels which result from dietary sources.

According to the Residue Chemistry Science Chapter of the Naled Reregistration Standard Guidance Document, the calculated maximum dietary burden of naled for poultry and livestock animals were: 10 ppm (horses), 8 ppm (dairy cattle), 5 ppm (beef cattle), 5 ppm (sheep), 0.6 ppm (swine), and 0.1 ppm (poultry). As a result of tolerance reassessment as well as Valent's intent not to support naled uses on rice, soybeans, tomatoes, and turnips which are considered feed commodities, the maximum dietary burdens are expected to be even lower.

GLN 171-5: Reduction of Residues

Data reflecting residue decline studies are available. These data include common practices such as special processing and cooking that could reduce dietary exposure to naled. A summary of naled residue reduction data is presented within Attachment 2.

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

Confined rotational studies (GLN 165-1) have been reviewed and deemed adequate by the Environmental Fate and Effects Division provided that an application rate higher than 2 lb ai/A is not registered for crops which may be rotated or intercropped; EFED concluded that if an application rate >2 lb ai/A is registered, then an additional confined rotational crop study at the higher rate is required. According to Table A within Attachment 2, the maximum rate presently registered for naled on rotational crops (e.g., collard and eggplant) is 1.8 lb ai/A. Up to 3.6 lb ai/A may be applied on peach; however, peach is not considered a rotational crop.

The confined rotational crop study indicated that the total radioactive residues (expressed as naled equivalents) were ≤0.03 ppm in/on mature lettuce (tops and roots), wheat (grain, bran, and straw), and carrots (tops) and roots) harvested at 30-day plantback interval from pots of loam soil that had been surface-treated with [ethyl 1-^{14}C]naled at a nominal application rate of 2 lb ai/A. The rapid degradation of naled and dichlorvos and the fact these materials can be readily metabolized to CO_2 indicate that there is not a large potential for naled residues to accumulate in rotational crops in soil treated with naled. Limited or extensive field rotational crop studies (GLN 165-2) are not required. Furthermore, rotational crop tolerances and plantback interval restrictions are not needed.

TOLERANCE REASSESSMENT SUMMARY

Tolerances Listed Under 40 CFR §180.215

The tolerances listed in 40 CFR §180.215 are for the residues of naled and its conversion product dichlorvos (2,2-dichlorovinyl dimethyl phosphate), expressed as naled. A summary of naled tolerance reassessments is presented in Appendix 1.

Sufficient data are available to ascertain the adequacy of the established tolerances listed in 40 CFR §180.215 for the following commodities: almonds, hulls; almonds, nutmeat; beans, dry; beans, succulent; broccoli; brussel sprouts; celery; cottonseed; eggplant; grapefruit; grapes; grass forage; lemons; melons; oranges; peaches; peas, succulent; peppers; spinach (and chard); squash, summer; strawberries; sugar beet roots; sugar beet tops; tangerines; and walnuts. Sufficient data are also available to support the established tolerances for eggs, milk, and tissues of animals resulting from dietary sources or through exposure via animal premise treatment.

The available data indicate that the established tolerances for the following commodities are too high and that the tolerance levels may be reduced: beans, dry; beans, succulent; beets, sugar, roots; broccoli; brussel sprouts; celery; cottonseed; grapes; and peas, succulent.

Additional field residue data are required for the following commodities before a complete tolerance reassessment can be made: cabbage; cauliflower; collards; hops; mushrooms; and squash, winter. The required data for collards will be translated to kale. The required data for winter squash will be translated to pumpkins.

The established tolerances on cucumbers, lettuce, mushrooms, rice, tomatoes, and turnip tops should be revoked since Valent does not have registered uses of naled on these commodities and it is unlikely that other registrant will support these uses. If registrants other than Valent intend to retain the use of naled on these commodities, then residue data reflecting the maximum registered use patterns are required.

The established 10-ppm crop group tolerance for "legumes, forage" is inappropriate because Valent does not intend to support naled uses on soybeans which is the third representative crop of

(17)

the foliage of legume vegetables group. Therefore, this crop group tolerance should be revoked concomitant with the establishment of individual tolerances for beans, forage; beans, hay; peas, vines; and peas, hay.

The available data for grapefruit, lemons, and oranges suggest that a crop group tolerance of 3.0 ppm for the citrus fruits group is appropriate. The individual tolerances for grapefruit, lemons, oranges, and tangerines should be deleted and replaced concomitant with the establishment of a crop group tolerance for citrus fruits.

The Agency classifies the registered Section 24(c) use of naled on alfalfa grown for seed to be a non-food use, because of adequate Oregon State regulatory controls. Therefore, no residue data are required and no tolerance proposals are needed for alfalfa forage, hay, seed, and seed screenings.

The established 0.5-ppm tolerance on all raw agricultural commodities (except those listed above in 40 CFR section 180.215) from use of naled for area pest control is adequate. The current tolerance for area pest control should be revised to include residues of dichlorvos as follows:

> " A tolerance of 0.5 part per million is established for the pesticide naled and its conversion product 2,2-dichlorovinyl dimethyl phosphate, expressed as naled equivalents, in or on all raw agricultural commodities, except those otherwise listed in this section, from use of the pesticide for area pest (mosquito and fly) control."

Tolerances That Need To Be Proposed Under 40 CFR §180.215

The livestock feeds table for Subdivision O (June 1994) indicates that data on cotton gin byproducts (commonly called gin trash) are required. The registrant must propose a tolerance for this commodity.

The registrant must also propose a tolerance for grass hay supported by adequate data.

Food/Feed Additive Tolerance Issues

Residues of naled and dichlorvos in citrus oil are assumed to concentrate 13X. However, citrus oil is not considered ready to eat and its dilution in food is expected to be less than 13X concentration. Therefore, a section 409 tolerance under FFDCA is not needed; a section 701 tolerance under FFDCA is needed.

Dietary Exposure Analysis

Dichlorvos, a metabolite of naled, is also a List A active ingredient and is currently in Special Review. Dichlorvos has been found to induce cancer in animals. A decision document ending an earlier Special Review (or RPAR) for Dichlorvos was published in 47 FR 45075 on 10/13/82, PD 1 initiating Special Review was published in 53 FR 5542 on 2/24/88, and a PD 2/3 will be issued by EPA shortly. EPA has published a final rule, revoking the food additive tolerances for residues of dichlorvos in packaged or bagged nonperishable processed food as of 3/10/94 because these tolerances violate the Delaney clause in Section 409 of the FFDCA. However, the revocation has been stayed.

Naled per se has not been determined to be an animal carcinogen. A reasonable reliable dietary risk assessment of naled uses can be performed using the available residue data. Anticipated residue data are available for naled uses. A dietary exposure assessment for dichlorvos

residues including those resulting from the use of naled is in preparation in support of the Special Review of naled.

DRES chronic and acute exposure analyses included in this RED chapter evaluated residues of naled and dichlorvos resulting from the uses of naled (Attachment 3). Food uses evaluated were those uses listed in the Tolerance Reassessment Summary for naled (Appendix 1). An addendum to the Chemistry Assessment (D. Miller memo to B. Lowery, 9/19/94) includes reassessed tolerance levels for spinach and Swiss chard. Published food use tolerances for naled are listed in 40 CFR 180.215 and in the Tolerance Index System (TIS). Where a tolerance level recommended through reregistration differed from the existing published tolerance, the recommended tolerance level was used in the analyses. If submitted residue data were inadequate to reassess a tolerance for a commodity, the existing tolerance was assumed in the DRES analysis.

A tolerance of 0.5 ppm is established in 180.215 for all raw agricultural commodities (RACs) not listed as having specific tolerances in that section, from use of naled for area pest (mosquito and fly) control. Uses recommended for revocation (within Attachment 2) are included in the analyses but assigned the pest control tolerance instead of their respective RAC-specific tolerances. Where a published or recommended tolerance for a commodity was lower than the pest control tolerance, that lower RAC-specific tolerance was assumed in the analyses instead of the area pest control tolerance. Since mosquito/fly control use of naled is primarily used on non-agricultural land (J.Faulkner/D.Sutherland memorandum to D. Edwards, 10/26/94), it is assumed that residues of naled are much more likely to occur on a RAC through its agricultural use than through area pest control use.

Percent of crop treated refinements:

Percent of crop treated information supplied by BEAD was used in the chronic exposure analyses for naled and dichlorvos and in the carcinogenic risk assessment for dichlorvos. Percent of crop treated estimates for naled food uses and direct animal treatments are described in the Faulkner/Sutherland memorandum to D. Edwards dated 10/26/94. Refinements in percent crop treated information for direct treatments to dairy cattle and laying hens are described in Faulkner's 2/15/95 memorandum to Schaible. Discussion of the rationale behind these refinements is found in S. Schaible's memorandum to D. Utterback, dated 3/6/95. Where a range of percent crop treated values were supplied, the upper end of the range was assumed.

Naled percent crop treated estimates were assumed for both the naled and dichlorvos analyses. Where both a RAC-specific percent crop treated estimate and a crop group percent crop treated estimate were supplied for a given RAC, the RAC-specific estimate was used.

For all food items in DRES not having specific RAC or crop group percent crop treated estimates, it was assumed that less than one percent of the crop would contain residues resulting from naled use to control mosquitoes and flies. For certain crops grown in water-filled areas (e.g., sugarcane) this may be an underestimate, but across all crops, 1% is considered a conservative estimate of percent of agricultural crops containing residues through this use.

Anticipated residues:

Chronic anticipated residues (ARs) used in the DRES chronic and cancer analyses were supplied by Chemistry Branch II- Reregistration Support (CBRS) (Attachment 3A). In this table, residues were supplied for naled, dichlorvos from use of naled, and total residues of naled and dichlorvos (expressed in naled equivalents). This memo updates ARs for naled and dichlorvos previously supplied in D. McNeilly memo dated 2/27/92 by incorporating information from additional

processing, cooking and field trial studies.

There are numerous commodities for which chronic ARs were not supplied. One half the limit of detection (LOD) was assumed in generating ARs if residues were not detectable and the detection limit for the RAC was supplied in the 9/12/94 memo (Attachment 3A). If no anticipated residues and no detection limits were supplied, total residues expressed in naled equivalents were apportioned between naled and dichlorvos by extrapolating from data for another RAC. ARs for cucumbers, melons, pumpkins, peppers, eggplants, and mushrooms were generated by extrapolating from tomato data; ARs for collards, kale and Swiss chard were generated by extrapolating from spinach data. The assumptions made above were recommended by CBRS (personal communication, Hummel, 3/21/95). [Note: dichlorvos ARs supplied in the table at the front of Hummel's 9/12/94 memo for these commodities are inappropriate for use in the RED chronic analysis for dichlorvos as they assume 100% conversion of naled to dichlorvos; these ARs were generated for the dichlorvos special review] and were not used to assess chronic naled dietary risk in the current assessment.

Reduction factors for celery, collards, oranges, strawberries and grapes were supplied for both naled and dichlorvos on p. 22 of Hummel's 9/12/94 memo. Where naled reduction factors were not available, reduction factors for dichlorvos were assumed in generating naled ARs (Hummel, 9/12/94). The reduction factors for strawberries were not used in generating ARs, at the recommendation of CBRS (personal communication, S. Hummel, 3/14/95). A reduction factor of 0.1X was also applied to all cooked forms of DRES items in both the naled and dichlorvos analyses (with the exception of collards and grape juice, where cooking factors supplied on p. 22 were used instead).

High-end anticipated residues for use in acute dietary exposure analyses were not supplied by CBRS as part of the Residue Chemistry Chapter. Unlike in the dietary risk evaluation for the dichlorvos special review (S. Schaible memorandum to D. Utterback/M. Beringer, 12/2/94) where 100% conversion of naled residues to dichlorvos was assumed, more realistic assumptions of conversion are reflected in the acute ARs DRES generated for these analyses.

The tolerance is generally the high end residue estimate recommended for acute risk assessment by CBRS. DRES calculated acute ARs by using the ratios observed in the chronic ARs of naled and dichlorvos residues to total residues in naled equivalents to apportion the tolerance level residue for each RAC into separate "tolerances" for naled and dichlorvos (the tolerance expression for naled food uses is for naled <u>and</u> its conversion product dichlorvos, expressed as naled). Residues based on the ratio of the naled tolerances apportioned to dichlorvos were converted to dichlorvos equivalents by multiplying the residues by 0.58, the ratio of dichlorvos's molecular weight to that of naled. The reduction factor of 0.1X was applied to all cooked forms of DRES items in the acute analyses as well as the chronic analyses. As field trial data were used in generating the chronic ARs, it is reasonable to assume that the ratios between naled and dichlorvos residues observed in chronic ARs would be also be appropriate for use in generating acute ARs. More specific discussion of how acute ARs were calculated is included in Appendix A (within Attachment 3).

Following a DRES policy relating to the use of food handling establishment tolerances in acute dietary exposure analyses, residues on food crops resulting from the pest control use of naled were not considered in the naled or dichlorvos acute analyses. High end anticipated residues used in the acute analyses for naled and dichlorvos are included below in Table 1.

Table 1: High End Residues used in DRES Acute Exposure Analyses		
Commodity	**Naled (ppm)**	**dichlorvos (ppm)**
Almond	0.25	0.145
Beans	0.0165	0.019
Broccoli	0.006	0.055
Brussel Sprouts	0.005	0.055
Cabbage	0.05	0.55
Cauliflower	0.05	0.55
Celery		
- trimmed	0.0075	0.14
- cooked	0.003	0.056
Citrus		
- whole	0.405	0.16
- peel	1.62	0.8
- juice	0.06	0.03
Collards	0.06 (0.004)	1.71 (0.12)
Cottonseed	0.0165	0.019
Cucumber	0.165	0.19
Eggplant	0.165	0.19
Grapes		
- whole	0.025	0.0145
- juice, raisins	0.0165	0.0096
Hops	0.25	0.145
Kale	0.06	1.71
Lettuce	0.005	0.29
Melon	0.165	0.19
Mushroom	0.165	0.19
Peach	0.115	0.22
Peas- succulent	0.0165	0.019
Pepper	0.165	0.19
Pumpkin	0.165	0.19
Rice	0.025	0.28
Safflower	0.25	0.145
Spinach	0.1	2.84
Squash	0.07	0.25
Strawberries	0.02	0.57
Sugar beets		
- tops	0.25	0.145
- roots	0.025	0.0145
Swiss chard	0.1	2.84

Table 1: High End Residues used in DRES Acute Exposure Analyses		
Commodity	Naled (ppm)	dichlorvos (ppm)
Tomatoes	0.165	0.19
Turnips	0.25	0.145
Walnuts	0.25	0.145
RACs not already listed in 180.215	0.09	0.24
Red meat	0.0185	0.018
Milk	0.018	0.019
Poultry	0.0165	0.019
Eggs	0.0165	0.019

B. OCCUPATIONAL AND RESIDENTIAL EXPOSURE

1. Use Patterns

Naled, 1,2-dibromo-2,2,-dichloroethyl dimethyl phosphate, is a short residual contact insecticide used to control insects on vegetables, cotton, grapes, some citrus, strawberries, sugar beets, tobacco, ornamental and shade trees, ornamental herbaceous plants, forests, dogs, cats, animals used as food, and in greenhouses. Naled is currently registered for a wide variety of food and non-food uses. The insecticide is formulated as a soluble concentrate/liquid (20 percent a.i. to 85 percent a.i.), an emulsifiable concentrate (36 percent a.i. to 58 percent a.i.), liquid ready to use (1 percent a.i. to 35 percent a.i.), ultra low volume (1 percent a.i. to 35 percent a.i), dust (4 percent a.i.), and impregnated collar/tag (7 percent a.i. and 15 percent a.i.). Dichlorvos or dichlorvos (2,2,-dichlorovinyl dimethyl phosphate) is a potential metabolite and/or contaminant of Naled.

Naled is applied by the following methods: aerial equipment/helicopter; tractor-drawn groundbooms; airblast (mist blower); backpack sprayer; low pressure hand wand; thermal fog generator; sewage system injection; dog/cat collar or tags; dust by hand; hand pump sprayer; hand held sprinkler can; ultra low volume cold fog; thermal fog generators; paint on heating/steam pipe; and by hot plate/pan.

Home-use products

Currently registered products containing naled include some intended primarily for homeowner use including backpack and low pressure hand wand application, dog and cat collars or tags, dust application by hand, and hand held sprayer and sprinkler can.

2. Potential Occupational and Residential Exposures

Handler Exposures and Assumptions

EPA has determined that there is a potential for exposure to mixers, loaders, applicators, or other handlers resulting from the use-patterns associated with naled.

Mixer/loader/applicator (M/L/A) exposure data for naled were not required in the Guidance for the Reregistration of Pesticide Products Containing Naled issued in June 1983. PHED, Version 1.1, was used in this document to determine potential exposures to M/L/A resulting from registered uses of naled.

Based on the registered use-patterns for naled, 20 major exposure scenarios for handlers (M/L/A) were identified for naled: (1) mixing/loading liquids, (2) mixing/loading dusts, (3) applying with aerial equipment (liquid), (4) applying with aerial equipment (dust), (5) applying with groundboom equipment (liquid), (6) applying with groundboom equipment (dust), (7) applying with airblast equipment, (8) applying with thermal fog generator, (9) applying with ultra low volume cold fog generator, (10) applying dog/cat collars or tags, (11) applying ready-to-use liquid, (12) applying liquid by hand (as bait), (13) applying by painting on heating/steam pipe in greenhouses, (14) applying by evaporating liquid using a hot plate and pan, (15) applying with backpack sprayer, (16) flagger (liquids), (17) flagger (dusts), (18) mixing/loading/applying with low pressure hand wand, (19) mixing/loading/applying to sewage systems by injection, and (20) mixing/loading/applying by hand-held sprinkler can.

Post-Application Exposures

EPA has determined that there is a potential for exposure to persons entering treated sites after application is complete. The potential for exposure exists in a variety of post-application scenarios, including agricultural and residential settings. In agricultural settings, post-application exposure to workers is of concern for (1) vine crops (grapes), (2) low- and medium- height crops (e.g. strawberries, cotton), (3) orchard-type tree crops (e.g., citrus, peaches), (4) outdoor ornamentals and turfgrass, (5) greenhouse-grown ornamentals and vegetable crops, (6) forestry uses, and (7) livestock sites. A significant potential for both dermal and inhalation post-application exposure exists for greenhouse use scenarios because workers routinely enter greenhouses to perform a variety of cultural tasks. The Agency is particularly concerned about dermal and inhalation exposures in greenhouses following applications of naled by painting heat/steam pipes and by boiling naled in hot plates/pans, as well as post-application exposures resulting from foliar applications in greenhouses. In residential settings, post-application exposure to residents (children and adults) is of concern following applications (1) outdoors on turfgrass, fruits, vegetables, and ornamentals and (2) indoors when naled is applied as a crack-and-crevice treatment and on pets and ornamentals (houseplants). In addition, naled can be used in industrial-premise treatments and refuse sites, and as a mosquito control agent.

III. RISK CHARACTERIZATION

A. DIETARY

Acute Risk

Acute dietary exposure analyses were performed assessing risk from both naled and naled-derived dichlorvos. As mentioned before, only the agricultural uses of naled were considered, and not the tolerance for area pest control. The acute dietary risk analyses estimated the distribution of single-day exposures for consumers only in the overall U.S. population, infants less than 1 year, children aged one through 6 years, females 13 years and above, and males 13 and above. These analyses evaluated individual food consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS), assuming uniform distribution of naled and dichlorvos in the commodity supply. Because neurotoxicity is the endpoint of concern being evaluated, exposure and risk estimates were calculated for all of the standard DRES subgroups listed above.

The Margin of Exposure (MOE) is an estimate of how closely the calculated exposure comes to the NOEL (the highest dose at which no effect was observed in the most sensitive study), and is calculated as the ratio of the NOEL to the exposure. The Agency is not generally concerned with MOEs of 100 or greater when the NOEL is taken from an animal study. In these analyses, MOEs were calculated for the high end (approximately 99th percentile) and if necessary, 95th percentile exposed individuals. Tables illustrating the distribution of exposures and calculated MOEs for all five population groups for both naled and dichlorvos are provided within Attachment 3. MOEs for naled for each of the DRES standard population groups are included in Table 2 below; MOEs for dichlorvos are listed in Table 3, with 95th percentile MOEs listed where necessary.

Table 2: Acute Dietary Margins of Exposure for Naled	
DRES subgroup	High end MOE
U.S. population	250
Infants < 1 yr	167
Children 1 through 6	125
Females 13+	250
Males 13+	250

In Table 2 above, it is seen that MOEs are above 100 for all DRES population subgroups in the acute analysis. Acute dietary risk from residues of naled does not appear to be of concern.

Table 3: Acute Dietary Margins of Exposure for Naled derived dichlorvos		
DRES subgroup	High end MOE	95th %ile
U.S. population	100	-
Infants < 1 yr	71	167
Children 1 through 6	71	167
Females 13+	125	-
Males 13+	125	-

In Table 3 above, it is seen that two DRES subgroups, "Infants < 1 yr" and "Children aged 1 through 6 years", have MOEs below 100 when the "highest exposed individual" (roughly, the 99th percentile exposed individual) is considered. However, MOEs based on the 95th percentile exposed individual are both above 100, and MOEs are acceptable at even the 98th percentile of the consumers for these population subgroups.

Chronic Dietary Risk

The DRES chronic exposure analysis for naled assumed tolerance level residues and 100 percent of crop treated to estimate the Theoretical Maximum Residue Concentration (TMRC) for the overall U.S. population and 22 population subgroups. Anticipated residues and refined percent of crop treated information were used to calculate the Anticipated Residue Contributions (ARCs) from naled and dichlorvos for those same population groups. The ARC is considered the more accurate estimate of dietary exposure. These exposure estimates were then compared to the RfDs for naled and dichlorvos to derive estimates of chronic dietary risk from naled and naled-derived dichlorvos. Summaries of the TMRCs, the ARCs, and their associated percentages of the RfD for naled and ARCs and their representations as percentages of the RfD for naled-derived dichlorvos are provided as attachments within Attachment 3 (TMRC estimates for naled-derived dichlorvos should be disregarded since there are no separate tolerance levels for dichlorvos resulting from application of naled).

The ARC for naled is 0.000004 mg/kg bwt/day, which represents 0.2% of the RfD. The subgroup most highly exposed, "Children aged 6 through 12 years", has an ARC of 0.000008 mg/kg bwt/day, or 0.4% of the RfD.

The ARC for dichlorvos resulting from the recommended uses of naled is 0.000006 mg/kg

bwt/day, or 1.2% of the RfD; the ARC for "Children aged 6 through 12 years" is 0.000012 mg/kg bwt/day, or 2.4% of the RfD.

Given the chronic risk estimates arrived at in these analyses, it appears that chronic dietary risk from naled and naled-derived dichlorvos is minimal.

Cancer Risk for Naled Derived dichlorvos

The upper bound excess lifetime cancer risk from naled-derived dichlorvos was calculated for the overall U.S. population using the following relationship:

$$\text{Upper Bound Cancer Risk} = \text{Dietary Exposure (ARC)} \times Q_1^*$$

An upper bound cancer potency factor (Q_1^*) of 1.22×10^{-1} $(mg/kg/day)^{-1}$ and a 70 year lifetime exposure were assumed in this calculation. Based on these assumptions, **the upper bound cancer risk from naled derived dichlorvos was calculated to be 7.2×10^{-7}.** This upper bound risk does not exceed the level that the Agency generally considers to be of concern.

B. OCCUPATIONAL AND RESIDENTIAL RISK

There are no engineering control requirements, such as closed mixing systems or closed tractor cabs, currently required on labeling for naled products. Exposure scenarios and corresponding exposure/risk assessments for naled are presented in Table 4 (agricultural uses) and Table 5 (non-agricultural uses) which follow. Dermal and inhalation exposure values and corresponding risks were estimated for individuals according to the current label requirements for PPE which include long pants, long-sleeve shirts, and chemical resistant gloves (first column of Tables 4 and 5). This includes the flagger exposure/risk assessment which is based on workers wearing long pants, long-sleeve shirts, and no gloves. Exposure and risk values are also estimated for handlers using maximum "engineering controls" and PPE, such as chemical resistant clothing, closed cab application equipment, and closed mixing/loading systems (second column of Tables 4 and 5). Exposure via the inhalation route for all use scenarios was insignificant compared to that via the dermal route and therefore was not included in the estimated MOEs.

Estimated daily exposure to handlers was calculated using the following formula:

Daily exposure (mg ai/kg bw/day) =

$$\frac{\text{Unit exposure (mg ai/lb ai)} \times \text{use (lb ai/A)} \times \text{daily acres treated (A/day)}}{\text{body wt (kg)}}$$

The actual clothing and equipment worn by all persons being monitored in the exposure studies are also described in the Occupational and Residential Exposure Branch Assessment (Attachment 4).

Risks from Handler (Mixer/Loader/Applicator) Exposures

The risk estimates indicate that all but one exposure scenario have MOEs of concern (under 100); several scenarios have MOEs less than 5 for mixing/loading and application of naled using both current label and maximum PPE/engineering controls. Thus, even when maximum engineering controls and PPE are simulated, the MOEs for mixer/loaders and applicators are still below 100 for most exposure scenarios. Risk mitigation measures for handlers of naled will be required for uses of

naled with MOE's of concern (below 100).

HED recommends that immediate risk mitigation negotiations between the Agency and registrant be initiated. Specifics regarding the mitigation measures will be recommended by the registrant at an upcoming meeting. HED also strongly recommends that the registrant submit data for the following use scenarios (Pesticide Assessment Guidelines, Subdivision U Mixer/Loader and Applicator Data Requirements: 231 Dermal Exposure, 232 Respiratory Exposure, 233, 234) which pose concern:

> [AGRICULTURAL USES] loading dusts for aerial and groundboom application, aerial application of dusts, groundboom application of dusts, thermal fog and ultra low volume cold fog generator application, hot plate/pan application, the dust flagger use;
>
> [NON-AGRICULTURAL USES] dog/cat collars and tags, pump sprayer (ready-to-use-liquid), bait (liquid) by hand, sewage system by injection, hand-held sprinkler can, and high volume/low pressure lawn sprayer (residential uses of naled represent the combined exposure from mixing/loading and applying naled since mixing,loading and application are normally done by the same person for non-agricultural uses) and the occupational pest control operator (PCO) uses.

Table 4. Summary Exposure/Risk Values for Agricultural Uses of Naled

Exposure Scenario (Number)	Dermal Exposure (mg/lb ai)		Inhalation Exposure (ug/lb ai)		Maximum Label Application Rate[c] (lb ai/acre)	Daily Max. Treated[d] (acres)	Daily Dermal Dose[e] (mg/kg/day)		MOE[f] (dermal)	
	Current Label PPE[a]	Max Mitigation Controls[g]	Current Label PPE[b]	Max Mitigation Controls[h]			Current Label PPE	Max Mitigation Controls	Current Label PPE	Max Mitigation Controls
Mixer/Loader Exposure										
Mixing All Liquids for Aerial Application (1a)	0.02	0.009	0.12	0.08	1.875	800	5.0×10^{-1}	1.9×10^{-1}	2	5.2
Mixing All Liquids for Groundboom Application (1b)	0.02	0.009	0.12	0.08	1.875	80	5.0×10^{-2}	1.9×10^{-2}	20	52
Mixing of Liquids for Backpack Sprayer (1c)	0.02	0.009	0.12	0.08	4.69×10^{-2} lb ai/ gal	200 gal	3.2×10^{-3}	1.2×10^{-3}	320	830
Loading Dusts for Aerial Application (2a)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Loading Dusts for Groundboom Application (2b)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Applicator Exposure										
Aerial equipment (liquids) (3a)	0.02	0.005	0.09	0.07	1.875	800	4.3×10^{-1}	1.1×10^{-1}	2.3	9.1
Aerial equipment (dusts) (3b)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Groundboom (liquids) (4a)	0.013	0.007	0.07	0.04	1.875	80	2.8×10^{-2}	1.5×10^{-2}	36	67
Groundboom (dusts) (4b)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Airblast equipment (5)	0.15	0.1	0.5	0.4	3.75	40	3.2×10^{-1}	2.1×10^{-1}	3.1	4.7
Thermal fog generator (6)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Ultra low volume cold fog generator (7)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Painting heat/steam pipe (8)	75	N/A	57	N/A	7.5	1	8.0	N/A	0.1	N/A
Hot plate/pan (9)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data

Table 4. Summary Exposure/Risk Values for Agricultural Uses of Naled

Exposure Scenario (Number)	Dermal Exposure (mg/lb ai)		Inhalation Exposure (ug/lb ai)		Maximum Label Application Rate[c] (lb ai/acre)	Daily Max. Treated[d] (acres)	Daily Dermal Dose[e] (mg/kg/day)		MOE[f](dermal)	
	Current Label PPE[a]	Max Mitigation Controls[g]	Current Label PPE[b]	Max Mitigation Controls[h]			Current Label PPE	Max Mitigation Controls	Current Label PPE	Max Mitigation Controls
Backpack Sprayer (10)	148	N/A	38	N/A	4.69×10^{-2} lb ai/gal	40 gal	4.0	N/A	0.3	N/A
Flagger										
Liquids (11)	0.01	0.0002	0.03	0.0006	1.8	800	3.1×10^{-1}	4.1×10^{-3}	3.2	240
Dusts (12)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data

[a] The current label PPE represents coveralls over long pants, long sleeve shirt, chemical resistant gloves using open systems.
[b] PPE Inhalation Exposure Values are for workers wearing a respirator with organic vapor removing cartridge (10 fold PF used).
[c] Dibrom 8 Emulsive Label, Reg. No. 59639-15; LUIS Reports for Naled dated 08/30/94 and 08/31/94.
[d] Values represent the maximum area or the maximum volume of spray solution which can be used in a single day to complete treatments for each exposure scenario of concern.
[e] Daily Dermal Dose (mg/kg/day) = $\frac{\text{Exposure (mg/lb ai)} * \text{Max. Appl. Rate (lb ai/acre)} * \text{Max. Treated}}{70 \text{ kg}}$

[f] MOE = NOEL / Daily Dermal Dose (mg/kg/day). NOEL = 1 mg/kg/day, 28-day dermal study.
[g] The max mitigation controls includes long pants, long-sleeve shirt, chemical resistant gloves, and closed systems (i.e., closed mixing/loading or enclosed cockpit/cabs).
[h] The max mitigation controls values include workers wearing no respirators, but mixing/loading and applying the pesticide within enclosed systems (e.g., enclosed cab, closed mixing/loading system).

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Table 5. Summary Exposure/Risk Values for Non-Agricultural Uses of Naled

Exposure Scenario (Number)[a]	Dermal Exposure[b] (mg/lb ai)		Inhalation Exposure[c] (ug/lb ai)		Maximum Label Application Rate[d] (lb ai/gal)	Daily Max. Treated[e] (gallons)	Daily Dermal Dose[f] (mg/kg/day)		MOE[g](dermal)	
	Homeowner	Occupational	Homeowner	Occupational			Homeowner	Occupational	Homeowner	Occupational
Applicator Exposure										
Dog/cat collars and tags (10)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Pump Sprayer (Ready-to-use liquid) (11)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Bait (liquid) by hand (12)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Mixer/Loader/Applicator										
Backpack Sprayer (15)	3.4	1.3	30	6.0	4.69×10^{-2}	10 gal 40 gal	2.9×10^{-2}	3.5×10^{-2}	34	29
Low pressure hand wand (18)	103	1.5	31	6.2	4.69×10^{-1}	4 gal 10 gal	2.8×10^{-2}	1.1×10^{-2}	3.6	91
Sewage system by injection (19)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Hand-held sprinkler can (20)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
High Volume\Low Pressure Lawn Sprayer (21)	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data

[a] For residential/non-agricultural exposure includes mixing/loading/application activities combined.

[b] Dermal unit exposures are reported as the best fit mean for handlers wearing: Homeowner = long pants and long-sleeved shirts and no gloves; Occupational = Coveralls over long pants, long-sleeved shirts, and chemical resistant gloves. Occupational handlers include commercial lawn applicators/pest control operators.

[c] Inhalation Exposure Values are reported as geometric means (lognormal distributions). No respirators for homeowners. A ten fold protection factor for occupational workers was used to simulate workers wearing organic vapor removing respirators.

[d] Dibrom 8 Emulsive Label, Reg. No. 59639-15; LUIS Reports for Naled dated 08/30/94 and 08/31/94.

[e] Values represent the maximum area or the maximum volume of spray solution which can be used in a single day to complete treatments for each exposure scenario of concern.

[f] Daily Dermal Dose (mg/kg/day) = $\frac{\text{Exposure (mg/lb ai)} * \text{Max. Appl. Rate (lb ai/acre)} * \text{Max. Treated}}{70 \text{ kg}}$

[g] MOE = NOEL / Daily Dermal Dose (mg/kg/day). NOEL = 1 mg/kg/day, 28 day dermal study.

The non-agricultural uses of naled include homeowner/residential uses and the occupational pest control operator (PCO) uses. For the home uses, mitigation measures, such as engineering controls and chemical resistant PPE are unfeasible. For the non-agriculture use scenarios, exposure was not separated out according to mixing/loading and application; estimated exposure values for these activities are combined into one since mixing,loading and application are normally done by the same person for non-agricultural uses.

Handler Exposure Risk Summary

Table 6 summarizes exposure risk for naled use scenarios for which data are available. For many uses of naled, no exposure data are available, including loading dusts for aerial and groundboom application, aerial and groundboom dust application, thermal fog generator application, ultra low volume cold fog generator, hot plate/pan application, flagger exposure to dusts, dog/cat collars and tags, pump sprayer, hand bait use, sewage system injection, hand-held sprinkler can, and high volume/low pressure lawn sprayer. Exposure data requirements for uses for which no data are available needs to be addressed at the time of Agency-registrant negotiations.

The Exposure Risk Summary below indicates the margins of exposure for naled uses. Table 6 is meant to be a tool for better understanding the exposure-risk relationship for naled, and the degree of impact for potential mitigation measures.

Table 6. Summary of Exposure Risk for Use Scenarios (Agricultural and Non-Agricultural)

EXPOSURE RISK SUMMARY				
AGRICULTURE USE EXPOSURE SCENARIO	AMOUNT AI HANDLED (lbs)	LEVEL OF CONFIDENCE[1]	MARGIN OF EXPOSURE	
			LABEL PPE[2]	MITIGATION CONTROLS[3]
Mixer/Loaders-Liquids for Aerial Application	1500	dermal and inhal data:high	2	5.2
Mixer/Loaders-Liquids for Groundboom Application	150	all data:high	20	52
Mixer/Loaders-Liquids for Backpack Application	9.38	dermal and inhal data:high	320	830
Airblast Application-Liquids	150	dermal and inhal data:high	3.1	4.7
Backpack Application-Liquids	1.88	dermal and inhal data:high	0.3	N/A
Aerial Application-Liquids	1500	dermal:med-high inhal:med	2.3	9.1
Groundboom Application-Liquids	150	dermal:med inhal:high	36	67
Painting Application to Steam/Heat Pipes	7.5	dermal and inhal data:med	0.1	N/A
Flagger-Liquids	1440	dermal:low inhal:med	3.2	240
NON-AGRICULTURE USE SCENARIOS[4]	(Res,Occ)		Residential	Occupational
Backpack Sprayer	0.47, 1.88	dermal and inhal data:low	34	29
Low Pressure Hand Wand	0.19, 0.47	dermal and inhal data:low	3.6	91

[1] Level of Confidence in PHED data: "High" is defined as acceptable grades (i.e. A and B) and 15+ replicates; "Medium" is defined as data graded A,B, or C and 15+ replicates; "Low" is defined as All grades, acceptable gareds and less than 15 replicates or grades A,B,C and less than 15 replicates. See Tables 2 and 4 within Attachment 4.

[2] Label PPE: Current Label PPE based on the Dibrom 8 Emulsive label.

[3] Mitigation Controls: PPE: Includes long pants, long sleeved shirt, chemical-resistant gloves; Engineering controls: closed systems (i.e. closed mixing/loading or enclosed cab/cock pit).

[4] For residential/non-agricultural exposure includes mixing/loading/application activities combined.

Risks From Post-Application Exposures

Based on the foliar dissipation and post-application/reentry exposure data submitted for grapes, the Agency calculated a Restricted Entry Interval (REI) for grapes as well as interim REIs for all other agricultural crops and WPS uses for which naled is registered. The interim REIs established for crops other than grapes were calculated by the Agency using data submitted for grapes in conjunction with assumptions pertaining to foliar residue and post-application exposure levels that would be expected on crops treated at rates up to the maximum label application rate (3.6 lbs ai/A). The Agency is establishing the following REIs at this time:

Crop/Crop Group	Restricted Entry Interval (REI)
Grapes/vine crops	3 days postapplication
All other WPS uses*	4 days postapplication **(interim REI)**

*THESE REIs ARE BASED ON DERMAL EXPOSURE DATA FOR OUTDOOR SETTINGS. INHALATION EXPOSURE DATA FOR GREENHOUSE/INDOOR SETTINGS ARE NOT AVAILABLE. THE REGISTRANT MUST ADDRESS THE ISSUE OF INHALATION EXPOSURE WHEN DEVELOPING AND CONDUCTING ADDITIONAL POST-APPLICATION EXPOSURE STUDIES FOR GREENHOUSE EXPOSURE SCENARIOS.

POST-APPLICATION EXPOSURE DATA ARE NOT AVAILABLE FOR HOMEOWNER/RESIDENTIAL USES OR FOR NUISANCE-INSECT CONTROL USES. THE REGISTRANT MUST ADDRESS THE ISSUES RELATIVE TO HOMEOWNER/RESIDENTIAL RISKS AND RISKS FROM MOSQUITO AND OTHER INSECT CONTROL PROGRAMS.

OPTIONS PERTAINING TO THE ABOVE ISSUES SHOULD BE IDENTIFIED BY THE REGISTRANT AND SUBMITTED TO THE AGENCY.

Post-application Studies

Post-application/reentry exposure studies are required as confirmatory data to determine definitive REIs for all crop groups/use sites on which naled is registered for use. The interim REIs established in this document will be adjusted accordingly upon submission of the additional data. Data requirements for grapes have been satisfied; however, confirmatory data are still required to support the use of naled on the following crop groups/use sites:

- **Tree crops (orchard-type, i.e. citrus, peaches)**
- **Medium-height crops (such as cotton, tobacco)**
- **Low crops (such as strawberries, broccoli, cauliflower)**
- **Greenhouse-grown crops (roses and other ornamental plants)**
- **Residential sites (turfgrass)**

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

Guidelines:

132-1(a) Foliar Residue Dissipation
*133-3 Post-application Dermal Passive Dosimetry Exposure
*133-4 Post-application 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 post-application/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.

C. RECOMMENDATIONS

PRODUCT CHEMISTRY CONFIRMATORY DATA REQUIREMENTS

Additional information must be provided by Valent concerning the composition of the two technical products and the manufacturing process and location before the Agency can determine whether the data submitted previously by Chevron are applicable to the Valent 90% technicals.

RESIDUE CHEMISTRY CONFIRMATORY DATA REQUIREMENTS

Additional Residue Chemistry data are required. Changes to the analytical method RM-3G-4 for naled are required before the method can be forwarded to FDA for publication in PAM II. There are many outstanding data requirements for storage stability, residue, and processing data.

CONFIRMATORY TOXICOLOGY DATA REQUIREMENTS

There is one data gap for toxicology, Guideline 85-1, General Metabolism.

OCCUPATIONAL DATA REQUIREMENTS/RISK MITIGATION

The risk estimates for occupational and residential handler exposure indicate that all but one exposure scenario have MOEs of concern (under 100). Even when maximum PPE (engineering controls - closed loading system and enclosed cab with respiratory filtration system) are simulated, the MOEs for mixer/loaders and applicators are still below 100 for most exposure scenarios. Risk mitigation measures are necessary for handlers of naled for uses of naled with MOE's of concern (below 100) such as reduced application rates and/or reducing the amount of product handled per day, and/or the requirement for closed mixing/loading or application from enclosed cabs .

HED recommends that immediate risk mitigation negotiations between the Agency and registrant be initiated. Specifics regarding possible mitigation measures will be discussed in an upcoming meeting with the registrant. HED also strongly recommends that the registrant submit data for those use scenarios for which no data are available.

Handler (M/L/A) Studies

HED RECOMMENDS THAT HANDLER (M/L/A) EXPOSURE STUDIES (GUIDELINES 231, 232, 233, AND 234) BE REQUIRED AS CONFIRMATORY DATA; HOWEVER, THE DETERMINATION OF THE SPECIFIC EXPOSURE SCENARIOS TO BE ADDRESSED HAS BEEN POSTPONED PENDING THE OUTCOME OF THE HANDLER RISK-MITIGATION NEGOTIATIONS AND FINAL DECISION.

Post-application Studies

Post-application/reentry exposure studies are required as confirmatory data to determine definitive REIs for all crop groups/use sites on which naled is registered for use. The interim REIs established in this document will be adjusted accordingly upon submission of the additional data. Data requirements for grapes have been satisfied; however, confirmatory data are still required to support the use of naled on the following crop groups/use sites:

- **Tree crops (orchard-type, i.e. citrus, peaches)**
- **Medium-height crops (such as cotton, tobacco)**
- **Low crops (such as strawberries, broccoli, cauliflower)**
- **Greenhouse-grown crops (roses and other ornamental plants)**
- **Residential sites (turfgrass)**

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

Guidelines:

132-1(a) Foliar Residue Dissipation
*133-3 Post-application Dermal Passive Dosimetry Exposure
*133-4 Post-application 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 post-application/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.

POST-APPLICATION EXPOSURE DATA ARE NOT AVAILABLE FOR HOMEOWNER/RESIDENTIAL USES OR FOR NUISANCE-INSECT CONTROL USES. THE REGISTRANT MUST ADDRESS THE ISSUES RELATIVE HOMEOWNER/RESIDENTIAL RISKS AND RISKS FROM MOSQUITO AND OTHER INSECT CONTROL PROGRAMS.

OPTIONS PERTAINING TO THE ABOVE ISSUES SHOULD BE IDENTIFIED BY THE REGISTRANT AND SUBMITTED TO THE AGENCY.

Labeling Recommendations

TWO SECTIONS OF THE OREB CHAPTER (SUGGESTED LANGUAGE FOR INSERTION INTO SECTIONS IV AND V OF THE RED) HAVE BEEN COMPLETED TO THE EXTENT POSSIBLE (Appendix 3). SOME SEGMENTS WILL NEED TO BE FINALIZED PENDING THE OUTCOME OF THE RISK-MITIGATION DISCUSSIONS WITH THE REGISTRANT.

Index of Appendices:
Appendix 1-Tolerance Reassessment Summary
Appendix 2-Product Chemistry Data Summary
Appendix 3-Occupational and Residential Labeling Recommendations and rationale

REFERENCES

Bibliographic citations include only MRIDs containing data which fulfill data requirements.

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Case No. 0092
Chemical No. 034401

Case Name: Naled
Registrant: Valent U.S.A. Corporation
Product(s): 90% T (EPA Reg. No. 59639-43)

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APPENDIX 1

Tolerance Reassessment Summary for Naled.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	[*Correct Commodity Definition*]/ Comment
Tolerances Listed Under 40 CFR §180.215			
Almonds (hulls)	0.5	0.5	[*Almonds, hulls*]
Almonds (nuts)	0.5	0.5	[*Almonds, nutmeats*]
Beans (dry)	0.5	0.05	[*Beans, dry*]
Beans (succulent)	0.5	0.05	[*Beans, succulent*]
Beets, sugar, roots	0.5	0.05	[*Sugar beets, roots*]
Beets, sugar, tops	0.5	0.5	[*Sugar beets, tops*]
Broccoli	1	0.1	
Brussels sprouts	1	0.1	
Cabbage	1	TBD *	
Cattle, fat	0.05	0.05	
Cattle, mbyp	0.05	0.05	
Cattle, meat	0.05	0.05	
Cauliflower	1	TBD *	
Celery	3	1	
Citrus, fruits group	-	3	This tolerance should be established concomitant with the revocation of the tolerances on grapefruit, lemons and oranges.
Collards	3	TBD *	
Cottonseed	0.5	0.05	[*Cotton, undelinted seed*]
Cucumbers	0.5	Revoke	The tolerance should be revoked unless registrants other than Valent intend to support the use of naled on cucumbers and submit additional data.
Eggplant	0.5	0.5	
Eggs	0.05	0.05	
Goats, fat	0.05	0.05	
Goats, mbyp	0.05	0.05	
Goats, meat	0.05	0.05	
Grapefruit	3	Revoke	The tolerance should be revoked concomitant with the establishment of a crop group tolerance for citrus fruits group.
Grapes	0.5	0.05	
Grasses, forage	10	10	[*Grass, forage*]

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	[*Correct Commodity Definition*]/ Comment
Hogs, fat	0.05	0.05	
Hogs, mbyp	0.05	0.05	
Hogs, meat	0.05	0.05	
Hops	0.5	TBD *	[*Hops, dried*]
Horses, fat	0.05	0.05	
Horses, mbyp	0.05	0.05	
Horses, meat	0.05	0.05	
Kale	3	TBD *	
Legumes, forage	10	Revoke	This crop group tolerance should be revoked concomitant with the establishment of individual tolerances for beans, forage; beans, hay; peas, vines; and peas, hay.
Lemons	3	Revoke	The tolerance should be revoked concomitant with the establishment of a crop group tolerance for citrus fruits group.
Lettuce	1	Revoke	The tolerance should be revoked unless registrants other than Valent intend to support the use of naled on lettuce and submit additional data.
Melons	0.5	0.5	
Milk	0.05	0.05	
Mushrooms	0.5	Revoke	The tolerance should be revoked unless registrants other than Valent intend to support the use of naled on mushrooms and submit additional data.
Oranges	3	Revoke	The tolerance should be revoked concomitant with the establishment of a crop group tolerance for citrus fruits group.
Peaches	0.5	0.5	
Peas (succulent)	0.5	0.05	[*Peas, succulent*]
Peppers	0.5	0.5	
Poultry, fat	0.05	0.05	
Poultry, mbyp	0.05	0.05	
Poultry, meat	0.05	0.05	
Pumpkins	0.5	TBD *	

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	[*Correct Commodity Definition*]/ Comment
Rice	0.5	Revoke	The tolerance should be revoked unless registrants other than Valent intend to support the use of naled on rice and submit additional data.
Safflower, seed	0.5	0.5	
Sheep, fat	0.05	0.05	
Sheep, mbyp	0.05	0.05	
Sheep, meat	0.05	0.05	
Spinach	3	3	
Squash, summer	0.5	0.5	
Squash, winter	0.5	TBD *	
Strawberries	1	1	
Swiss chard	3	3	
Tangerines	3	3	
Tomatoes	0.5	Revoke	The tolerance should be revoked unless registrants other than Valent intend to support the use of naled on tomatoes and submit additional data.
Turnips, tops	3	Revoke	The tolerance should be revoked unless registrants other than Valent intend to support the use of naled on turnips and submit additional data.
Walnuts	0.5	0.5	
All Raw Agricultural Commodities except those listed above (Area Pest Control Use)	0.5	0.5	
Tolerances That Need To Be Proposed Under 40 CFR §180.215			
Beans, forage	None	1	
Beans, hay	None	TBD *	
Citrus fruits group	None	3	
Cotton, gin byproducts	None	0.05	
Grass, hay	None	TBD *	
Peas, hay	None	1	

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	[*Correct Commodity Definition*]/ Comment
Peas, vines	None	TBD *	
Tolerances That Need To Be Proposed Under 40 CFR §701 FFDCA			
Citrus, oil, refined	none	40	

* TBD = To be determined. Reassessment of tolerance(s) cannot be made at this time because additional data are required.

APPENDIX 2

Case No. 0092
Chemical No. 034401

Case Name: Naled
Registrant: Valent U.S.A. Corporation
Product(s): 90% T (EPA Reg. No. 59639-73) should be -43

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	N	
61-2	Starting Materials and Manufacturing Process	N	
61-3	Discussion of Formation of Impurities	N	
62-1	Preliminary Analysis	N	
62-2	Certification of Ingredient Limits	N	
62-3	Analytical Methods to Verify the Certified Limits	N	
63-2	Color	N	
63-3	Physical State	Y	No MRID No.
63-4	Odor	N	
63-5	Melting Point	N	
63-6	Boiling Point	N	
63-7	Density, Bulk Density or Specific Gravity	N	
63-8	Solubility	N	
63-9	Vapor Pressure	N	
63-10	Dissociation Constant	N	
63-11	Octanol/Water Partition Coefficient	N	
63-12	pH	N	
63-13	Stability	N	
63-14	Oxidizing of 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. If Valent confirms that the two Valent technicals now registered have the same composition and manufacturing process, submitted data may be applicable to both products.

[b] The single reference was reviewed under CBRS No. 11588, D189133, dated 3/29/93, by R. Perfetti.

Case No. 0092
Chemical No. 034401

Case Name: Naled
Registrant: Valent U.S.A. Corporation
Product(s): 90% T (EPA Reg. No. 59639-73)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	N [c]	00074653 00074724 CSF (date not specified)
61-2	Starting Materials and Manufacturing Process	Y	**00138602 00138846**
61-3	Discussion of Formation of Impurities	N [d]	**00138846**
62-1	Preliminary Analysis	N [e]	**00138846**
62-2	Certification of Ingredient Limits	N [c]	CSF (date not specified) **00138846**
62-3	Analytical Methods to Verify the Certified Limits	Y	**00138602 00138846**
63-2	Color	Y	00074790
63-3	Physical State	Y	00074790 *No MRID No.*
63-4	Odor	Y	00074790
63-5	Melting Point	N/A [f]	
63-6	Boiling Point	Y	00074653 00074724 00074790
63-7	Density, Bulk Density or Specific Gravity	Y	**00138602**
63-8	Solubility	Y	00074653 00074790
63-9	Vapor Pressure	Y	00074653 00074790.
63-10	Dissociation Constant	N	
63-11	Octanol/Water Partition Coefficient	Y	**00138602**
63-12	pH	Y	**00138602**
63-13	Stability	Y	00074653 00074724 00074790
63-14	Oxidizing of Reducing Action	Y	00074790
63-15	Flammability	N [g]	00074790
63-16	Explodability	Y	00074790
63-17	Storage Stability	Y	00074653
63-18	Viscosity	Y	00074790
63-19	Miscibility	Y	00074790
63-20	Corrosion Characteristics	Y	00074790 00144887

[a] Y = Yes; N = No; N/A = Not Applicable. The status of the data requirements reflected in this table is predicated on Valent's confirmation that the manufacturing process and location have not changed since the product transfer from Amvac (EPA Reg. No. 5481-198); if the manufacturing process or location has changed since the transfer, updated product chemistry data will be required for all GLNs except 63-3.

[b] Unbolded references were reviewed in the Naled Guidance Document dated 6/83; **bolded** references were reviewed in the Naled Reregistration Standard Update dated 6/8/90; underlined references were reviewed under CBRS No. 1197, dated 10/16/85, by J. Garbus; and the *italicized* reference was reviewed under CBRS No. 11588, D189133, dated 3/29/93, by R. Perfetti.

[c] These data do not satisfy the requirements of 40 CFR §158.155 and §158.175 (Guideline Reference Nos. 61-1 and 62-2) concerning product composition and certified limits because a Confidential Statement of Formula (CSF) reflecting the current registrant and EPA

Registry Number must be submitted on EPA Form 8570-4 (Rev. 12/90).

[d]These data do not satisfy the requirements of 40 CFR §158.167(Guideline Reference No. 61-3) concerning discussion of formation of impurities because additional information must be submitted regarding the possible degradation of ingredients after production, post-production reactions between ingredients, possible contamination from packaging materials or production equipment, and process control, purification, and quality control measures.

[e]These data do not satisfy the requirements of 40 CFR §158.170(Guideline Reference No. 62-1) concerning preliminary analysis because data based on five or more representative samples from a single supplier must be submitted. Complete and detailed descriptions including statements of precision and accuracy of the methods used for sample analysis must be included.

[f]Data are not required because the TGAI is a liquid at room temperature.

[g]These data do not satisfy the requirements of 40 CFR §158.190(Guideline Reference No. 63-15) concerning flammability because the submitted data are unclear; the registrant must submit new data for the flammability of the MP.

APPENDIX 3

THE FOLLOWING TWO SECTIONS OF THE OREB CHAPTER (SUGGESTED LANGUAGE FOR INSERTION INTO SECTIONS IV AND V OF THE RED) HAVE BEEN COMPLETED TO THE EXTENT POSSIBLE. SOME SEGMENTS WILL NEED TO ALTERED PENDING THE OUTCOME OF THE RISK-MITIGATION DISCUSSIONS WITH THE REGISTRANT.

(SECTION IV - REGULATORY POSITION AND LABELING RATIONALE)

Occupational/Residential Labeling Rationale/Risk Mitigation

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, 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 the plants are (or will be) grown in.

Currently registered uses of naled include some uses within the scope of the Worker Protection Standard for Agricultural Pesticides (WPS) as well as some uses outside the scope of the WPS. Those that are outside the scope of the WPS include:

- on pastures or rangelands,
- on livestock or other animals (including collars and tags), or in or around animal premises,
- on plants grown for other than commercial or research purposes, which may include plants in habitations, home fruit and vegetable gardens, and home greenhouses;
- 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; and
- 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 and structural pest control, such as termite control and wood preservation.
- for mosquito abatement or nuisance-insect control that is part of a government-sponsored wide-area public pest control program,
- on the portions of agricultural plants that have been harvested, such as in cull piles of discarded vegetables.

Compliance With The WPS

Any product whose labeling reasonably permits 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, all products within the scope of those notices must bear WPS PR Notice complying labeling when they 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, all products within the scope of those notices must bear WPS PR Notice complying labeling when they are distributed or sold by any person.

Personal Protective Equipment/Engineering Controls for Handlers

Occupational-Use Products (WPS and NonWPS Uses)

For each end-use product, PPE/engineering control requirements for pesticide handlers will be set during reregistration in one of two ways:

1. If EPA has no special concerns about the acute 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 will be established using the process described in PR Notice 93-7 or more recent EPA guidelines.

2. If EPA has special concerns about an active ingredient due to 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 or engineering-control requirements that pertain to all or most occupational 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 each 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.

There are special toxicological concerns about naled that warrant the establishment of active-ingredient-based handler PPE/engineering-control requirements.

THE SPECIFIC LABEL REQUIREMENTS FOR HANDLER PPE/ENGINEERING CONTROLS WILL BE DETERMINED UPON COMPLETION OF THE HANDLER RISK-MITIGATION DECISION.

Post-Application/Entry Restrictions

Occupational-Use Products (WPS Uses)

Restricted Entry Interval:

Under the Worker Protection Standard (WPS), interim restricted entry intervals (REIs) 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.

For occupational end-use products containing naled as an active ingredient, EPA is establishing a 3-day restricted-entry interval for uses on grapes and a 4-day restricted-entry interval for each other use of the product that is within the scope of the Worker Protection Standard for Agricultural Pesticides (WPS). The basis for this decision is the post-application data on grapes, the range-finder estimate for non-grape crops, the lack of crop-specific data (other than grape data) pertaining to post-application exposures, and low MOE's for certain applications of naled.

In addition, due to concerns about post-application exposures to naled/DDVP in greenhouses following applications where naled is painted on heating/steam pipe or applied by heating in a hot plate/pan, EPA is establishing additional entry restrictions following those uses. For those uses, EPA is prohibiting entry by any person -- other than a correctly trained and equipped handler who is performing a WPS-defined handler task -- into the entire enclosed treated area from the start of application until one of the WPS ventilation criteria has been met. After ventilation is completed, workers are not allowed into the entire enclosed area during the remainder of the restricted-entry interval, except for worker entry as allowed by the WPS.

EPA notes that the WPS places very specific restrictions on entry during restricted-entry intervals when that entry involves contact with treated surfaces. EPA believes that these existing WPS protections are sufficient to mitigate post-application exposures of workers who contact surfaces treated with naled.

The WPS REI in effect until now was 24 hours. A 24-hour reentry interval was established by the June 1983 Registration Standard for naled. That reentry interval was converted into a 24-hour restricted-entry interval through labeling modifications specified in PR Notice 93-7, which implemented the labeling requirements of the 1992 Worker Protection Standard for Agricultural Pesticides. EPA found no reason to retain the 24-hour interim REI placed on naled products by PR Notice 93-7.

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 the requirement that personal protective equipment be worn. Personal protective equipment requirements for persons who must enter areas that remain under a restricted-entry interval are based on the toxicity concerns about the active ingredient. The requirements are set in one of two ways.

1. If EPA has no special concerns about the acute or other adverse effects of an active ingredient, it establishes the early-entry PPE requirements based on the acute dermal toxicity, skin irritation potential, and eye irritation potential of the active ingredient.

2. If EPA has special concerns about an active ingredient due to very high acute toxicity or to certain other adverse effects, such as allergic effects, cancer, developmental toxicity, or reproductive effects, it may establish early-entry PPE requirements that are more stringent than would be established otherwise.

Since naled is classified as category II for acute oral toxicity, category II for acute dermal

toxicity, category II for acute inhalation toxicity, category I for eye irritation potential, and category I for dermal irritation, and EPA has special concerns about other adverse effects, the PPE required for early entry is: coveralls over long-sleeve shirt and pants, chemical-resistant footwear plus socks, chemical resistant headgear for overhead exposures, protective eyewear, and chemical resistant gloves. PPE for entry by handlers into vapor-treated greenhouses before the WPS ventilation criteria have been met is the PPE required for handlers.

The Agency will not require a respirator for early-entry workers, since the WPS places very specific restrictions on early entry and these existing WPS protection are sufficient to mitigate post-application inhalation exposures of workers. EPA notes that following vapor treatments in greenhouses, entry by anyone other than a correctly trained and PPE-equipped (including organic-vapor-removing respirator) handler, is prohibited until one of the WPS ventilation criteria has been met.

WPS Notification Statement:

Since the sufficient post-application data are not available to establish permanent restricted-entry intervals (REIs) and the available post-application data indicate that fairly lengthy REIs may be necessary (at least 3-4 days) and EPA has concerns about inadvertent exposures to naled, EPA is specifying that a statement requiring such "double" notification be placed on the labeling of all naled end-use products which contain uses within the scope of the WPS.

Entry Restrictions for Occupational-Use Products (Non-WPS Uses)

Since EPA has concerns about post-application exposures to persons following nonWPS occupational applications of naled, it is establishing entry restrictions for all nonWPS occupational uses of naled end-use products. For specific language refer to Section V of this document.

Homeowner-Use Products (NonWPS Uses)

Since EPA has concerns about post-application exposures to persons following homeowner applications of naled, it is establishing entry restrictions for all homeowner uses of naled end-use products. For specific language refer to Section V of this document.

Other Labeling Requirements

The Agency is requiring additional labeling statements to be located on all end-use products containing naled. For the specific labeling statements, refer to Section V of this document.

(RED SECTION V - LABELING REQUIREMENTS)

LABELING REQUIREMENTS FOR END-USE PRODUCTS

Occupational/Residential Labeling

PPE Requirements for Pesticide Handlers

Sole-active-ingredient end-use products that contain {active ingredient} must be revised to adopt the handler personal protective equipment requirements set forth in this section. Any conflicting PPE requirements on their current labeling must be removed.

Multiple-active-ingredient end-use products that contain {active ingredient} must compare the handler personal protective equipment requirements set forth in this section to the PPE requirements on their current labeling and retain the more protective. For guidance on which PPE is considered more protective, see PR Notice 93-7.

Products Intended Primarily for Occupational Use

WPS and nonWPS uses

Minimum (baseline) PPE requirements -- TO BE DETERMINED BASED ON OUTCOME OF RISK-MITIGATION DISCUSSIONS WITH THE REGISTRANT

Exception: When applying to hot pipes in greenhouses or entering vapor-treated greenhouses during application or before ventilation is complete, the protective eyewear must be goggles, unless a full-face respirator is worn..

* The glove statement for naled is the statement established through the instructions in Supplement Three of PR Notice 93-7.
** The word "mixing" may be removed if the product is formulated as "ready-to-use."

Actual end-use product PPE requirements -- The PPE that would otherwise be established based on the acute toxicity of each end-use product must be compared to the 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 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

Minimum (baseline) PPE requirements -- TO BE DETERMINED BASED ON OUTCOME OF RISK-MITIGATION DISCUSSIONS WITH THE REGISTRANT

Actual end-use product PPE requirements -- TO BE DETERMINED BASED ON OUTCOME OF RISK-MITIGATION DISCUSSIONS WITH THE REGISTRANT

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

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

Multiple-active-ingredient end-use products that contain naled must compare the entry restrictions set forth in this section to the entry restrictions on their current labeling and retain the more protective. A specific time-period in hours or days is considered more protective than "sprays have dried" or "dusts have settled."

<u>Products Intended Primarily for Occupational Use</u>

WPS uses

Restricted-entry interval --

Entry Restrictions for End-Use Products That Do NOT Contain Greenhouse Vapor Treatments --

Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 4 days. Exception: the restricted-entry interval for uses on grapes is 3 days.

Entry Restrictions for End-Use Products That Contain Greenhouse Vapor Treatments -- The following is the entry-restriction statement for naled end-use products that contain directions for use as a vapor-treatments in greenhouses (i.e., directions for painting naled on heat/steam pipes or heating naled in a hot plate/pan):

Entry Restrictions:
Outdoors and NonVapor Treatments in Greenhouses: Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 4 days. Exception: the restricted-entry interval for uses on grapes is 3 days.

Vapor Treatment in Greenhouses: Entry by any person -- other than a correctly trained and equipped handler who is performing a WPS-defined handling task -- is PROHIBITED in the entire enclosed area from the start of application until one of the WPS ventilation criteria has been met. After ventilation is completed, do not enter or allow worker entry into the entire enclosed area during the restricted-entry interval (REI) of 24 hours, except as allowed by the WPS.

Early-entry personal protective equipment (PPE)

Early-Entry PPE Requirements for End-Use Products That Do NOT Contain Greenhouse Vapor Treatments --

PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, is:
-Coveralls over long-sleeved shirt and long pants
-Chemical-resistant gloves*
-Chemical-resistant footwear plus socks

-Protective eyewear
-Chemical-resistant headgear for overhead exposure
-Chemical-resistant apron when cleaning equipment, mixing, or loading

* The glove statement for naled is the statement established through the instructions in Supplement Three of PR Notice 93-7.

Early-Entry PPE Requirements for End-Use Products That Contain Greenhouse Vapor Treatments -- The following are the early-entry PPE requirements for naled end-use products that contain directions for use as a vapor-treatments in greenhouses (i.e., directions for painting naled on heat/steam pipes or heating naled in a hot plate/pan):

PPE for early entry to treated areas (1) outdoors, (2) in non-vapor treated greenhouses, or (3) in vapor-treated greenhouses after ventilation is complete -- that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, is:
-Coveralls over long-sleeved shirt and long pants
-Chemical-resistant gloves,
-Chemical-resistant footwear plus socks
-Protective eyewear
-Chemical-resistant headgear for overhead exposure

PPE for entry by handlers into vapor-treated greenhouses before WPS ventilation criteria have been met is listed in the "Hazards to Humans and Domestic Animals" section of this labeling.

* The glove statement for naled is the statement established through the instructions in Supplement Three of PR Notice 93-7.

Placement in labeling -- The entry restrictions and early-entry PPE requirements must be inserted into the Agricultural Use Requirements box as shown in Supplement Three of PR Notice 93-7.

NonWPS uses

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

--For spray applications, other than applications to livestock:

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

--For spray applications to livestock:

"Avoid contact with treated animals until sprays have dried."

--For dust applications:

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

--For impregnated tags and livestock/pet collars:

EPA is not establishing an entry restriction for this use.

--For mosquito/nuisance-insect control applications:

EPA is not establishing an entry restriction for this use.

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 restriction in that box.

If no WPS uses are on label: Add the appropriate nonWPS entry restriction to the labels of all end-use products, except products primarily intended for homeowner use, in a section in the Directions For Use with the heading: "Entry Restrictions:"

Products Intended Primarily for Homeowner Use

Entry restrictions --

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

--For spray applications, other than applications to pets:

"Do not allow people or pets to touch treated plants, soil, or other surfaces until the sprays have dried."

--For dust applications, other than applications to pets:

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

--For impregnated tags and pet collars and other applications to pets:

EPA is not establishing an entry restriction for this use.

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 naled that are intended primarily for occupational use.

Application Restrictions: (except wide-area government-sponsored pest control programs, such as for mosquito or nuisance-insect control):

Respirator Type:

The following type of respirator is appropriate to mitigate naled inhalation concerns:

"A respirator with either an organic-vapor-removing cartridge with a prefilter approved for pesticides (MSHA/NIOSH approval number prefix TC-23C), or a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G)."

<u>Products Intended Primarily for Home Use</u>

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 requirements

"Follow manufacturer's instructions for cleaning/maintaining protective clothing and equipment. If no such instructions for washables, use detergent and hot water. Keep and wash protective clothing and equipment 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 protective clothing and equipment immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."

Skin sensitizer statement

"This product may cause skin sensitization reactions in some people."