DRAFT

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

February 16, 1999

MEMORANDUM

SUBJECT: Revised Preliminary HED Risk Assessment for Dichlorvos
DP Barcode D252804

FROM: Susan V. Hummel, Branch Senior Scientist
Chemistry and Exposure Branch 2
Health Effects Division (7509C)

Susan V. Hummel

TO: Pam Noyes, Chemical Review Manager
Special Review Branch
Special Review and Reregistration Division (7508W)

and

Robert McNally , Chief
Special Review Branch
Special Review and Reregistration Division (7508W)

Attached please find the Revised Preliminary Risk Assessment for Dichlorvos (Case No. 084001). This chapter incorporates information from the toxicology assessment from Ghazi Dannan and Joycelyn Stewart, the assessments of human incidence data from Jerry Blondell and Monica Spann, the residue chemistry assessment from Sue Hummel, the occupational and residential exposure assessments from Dave Jaquith, and the dietary risk analyses from Brian Steinwand. Bill Sette, Jess Rowland, Ray Kent, and Steve Knizner also contributed to this risk assessment. The preliminary risk assessment has been revised in response to error correction comments from Amvac.

cc: Jack Housenger, Jacqueline McQueen, Ray Kent, Dave Jaquith, Sue Hummel, Ghazi Dannan, Joycelyn Stewart, Bill Sette, Jess Rowland, RCAB Files

PRELIMINARY RISK ASSESSMENT

for

DICHLORVOS

February 12, 1999

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency

Table Of Contents

I. EXECUTIVE SUMMARY

A. Use and Major Formulations

Dichlorvos (2,2-dichlorovinyl dimethyl phosphate; DDVP) is an organophosphate insecticide and fumigant registered for use in controlling flies, mosquitos, gnats, cockroaches, fleas, and other insect pests. At present, there are 154 product registrations for formulations containing Dichlorvos. Formulations of Dichlorvos include pressurized liquids, granulars, emulsifiable concentrates, total release aerosols, and impregnated materials. Dichlorvos is applied with aerosols and fogging equipment, with ground spray equipment, and through slow release from impregnated materials, such as resin strips and pet collars.

Dichlorvos is registered to control insect pests on agricultural sites; commercial, institutional and industrial sites; and for domestic use in and around homes and on pets. Dichlorvos is used in mushroom houses, storage areas for bulk, packaged and bagged raw and processed agricultural commodities, food manufacturing/processing plants, animal premises, and non-food areas of food-handling establishments. It is also registered for direct dermal treatment of cattle and poultry.

The mechanism of pesticidal action of Dichlorvos is inhibition of cholinesterase. The Agency has determined that the adverse effects caused by Dichlorvos that are of primary concern to human health are carcinogenicity and neurological effects related to inhibition of cholinesterase activity.

B. Regulatory History

The Agency initiated a Special Review (PD 1) for pesticide products containing Dichlorvos on February 24, 1988. At that time, the Agency was concerned that exposure to Dichlorvos from registered uses posed an unreasonable carcinogenic risk and that there were inadequate margins of exposure for cholinesterase inhibition and liver effects to exposed individuals. After evaluation of information submitted through the Special Review Process, the Agency conducted another risk assessment for Dichlorvos. In 1995, the Agency concluded that Dichlorvos posed carcinogenic risks of concern to the general population from dietary exposure. The Agency also concluded in 1995 that Dichlorvos posed risks of concern for cholinesterase inhibition to residents and to individuals mixing, loading, and applying this pesticide, as well as to those reentering treated areas. Subsequently, the Agency issued a proposal to cancel the registrations of the Dichlorvos uses which posed the greatest risks (Draft Notice, Federal Register of September 28, 1995). In its 1995 Notice of Intent to Cancel (NOIC, PD 2/3), the Agency concluded that the risks outweighed the benefits for most uses of Dichlorvos and, therefore, recommended a variety of measures to reduce those risks. The Agency proposed cancellation of certain uses of Dichlorvos and cancellation of other uses unless certain labeling modifications were made to reduce risk.

The Federal Register Notice provided for a formal comment period, which closed on December 28, 1995. Comments were received, and are contained in a public docket identified as "OPP-30000/56." Major comments were submitted to the Agency by Amvac Chemical Corporation, the Japanese Resin Strip Manufacturer's Association, grower groups, and the general public. Some of the comments contained additional data pertaining to the risks posed by Dichlorvos.

The Agency has also identified newer exposure and toxicity data pertaining to Dichlorvos that have become available since publication of the Draft Notice of Intent to Cancel (PD 2/3). In addition to the newer data and information described above, the Food Quality Protection Act of 1996 has effectively modified the considerations the Agency uses to assess the risks of pesticides. Therefore, the Agency has recently re-evaluated the toxicology database for Dichlorvos to make a determination of potential special susceptibility of infants and children, as mandated by FQPA. In addition, the Agency has reviewed new information pertaining to dietary exposure and performed a refined dietary exposure assessment. The Agency has also refined the occupational and residential exposure assessment for Dichlorvos with new information and new methodologies that were previously unavailable.

The following issues pertaining to the ongoing Dichlorvos risk assessment were presented to the FIFRA Science Advisory Panel (SAP) on July 28, 1998: (1) the selection of a 3X FQPA safety factor for Dichlorvos and (2) the resin strip exposure assessment.

The Agency has revised the Dichlorvos risk assessment to incorporate new information received to date, to the extent feasible. This preliminary risk assessment has been conducted for Dichlorvos in conjunction with the public review and comment process for all of the organophosphate pesticides.

C. Hazard Identification and Dose-Response Assessment

The toxicology database for Dichlorvos is complete and fulfills the OPPTS Guideline requirements. For acute toxicity, technical Dichlorvos was placed in Toxicity Categories II, I and II, respectively for the oral, dermal and inhalation routes and in Toxicity Category III and IV for eye and dermal irritation, respectively. Dichlorvos did not cause organophosphate induced delayed neurotoxicity (OPIDN) in the hen following single or multiple (28 days) exposures. Following a single oral dose to rats, Dichlorvos was associated with a variety of neurological and physiological changes as well as inhibition of cholinesterase activity. Subchronic and chronic oral exposures in rats and dogs as well as chronic inhalation exposure in rats resulted in significant decreases in plasma, red blood cell and/or brain cholinesterase activity. Dichlorvos is classified as a Group C, possible human carcinogen, with a linear low dose extrapolation based on mononuclear cell leukemia in male rats. The cancer potency value (Q_1*) for Dichlorvos was calculated to be 2.72×10^{-1} $(mg/kg/day)^{-1}$ in human equivalents. Dichlorvos has been shown to be a direct acting mutagen by common *in vitro* bacterial genetic toxicity assays. In addition, Dichlorvos is a direct acting mutagen in *in vitro* mammalian test systems. Dichlorvos seems to

also have clastogenic activity in CHO cells *in vitro* with or without metabolic activation. On the other hand, some studies showed that Dichlorvos was not clastogenic in *in vivo* micronucleus tests. There was no evidence of increased susceptibility following *in utero* exposures to rats and rabbits as well as pre/post natal exposure to rats. Also, there was no evidence of abnormalities in the development of the fetal nervous system in the studies submitted to the Agency. However, a study in the open literature (Mehl et al. 1994), which reported decreased total brain weight in two litters of guinea pig pups produced by dams which had been exposed to Dichlorvos twice daily, raised the concern for potential increased susceptibility of infants and children. Because of this concern, a developmental toxicity study in guinea pigs is recommended with protocol modifications (to include examination of brain weight) to substantiate or dismiss this concern.

Inhibition of cholinesterase activity was the toxicity endpoint selected for acute and chronic dietary, as well as occupational, risk assessments. The Uncertainty Factor(s) ranged from 10 to 300 depending on the use of (1) a NOEL vs. a LOEL, (2) human vs. animal study, (3) the FQPA Safety Factor, and (4) the type of exposure assessment (occupational vs. residential). The 10x Safety Factor for the protection of infants and children as required by the Food Quality Protection Act (FQPA) of 1996 was reduced to 3x based on the following factors: 1) the toxicology database is complete with regard to the standard Subdivision F guideline requirements and 2) the standard developmental and reproductive toxicity studies submitted to the Agency showed no indication of increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure to Dichlorvos. The Agency is confident that the methods used to estimate dietary and residential exposure to Dichlorvos do not underestimate risks to children. The Agency has requested a prenatal developmental toxicity study in guinea pigs to replicate/confirm the findings of a literature study by Mehl et al. (1994).

D. Exposure Assessment

Dietary exposure to Dichlorvos residues may occur as a result of use on or at a variety of sites, including mushroom houses, bulk-stored and packaged or bagged nonperishable processed and raw food, commercial food processing plants, direct animal treatment, and livestock premise treatment. Two other pesticides, Naled and Trichlorfon, degrade to Dichlorvos through plant metabolism. The Agency does not expect measurable Dichlorvos residues from Trichlorfon because all Trichlorfon food uses have been canceled and associated tolerances revoked. Therefore, no Dichlorvos residues are expected to occur in food as a result of Trichlorfon use.

Most product and residue chemistry data requirements for Dichlorvos have been fulfilled. However, the Reregistration data requirements for storage stability (Guideline 860.1380), for meat, milk, poultry, and eggs (Guideline 860.1480), and directions for use (Guideline 860.1200) have not been fulfilled.

Dietary exposure estimates for Dichlorvos have been refined with residue data from USDA's PDP monitoring program, FDA surveillance data and FDA Total Diet Study (TDS) data. Anticipated residues for Dichlorvos have been revised to incorporate these residue data.

Dichlorvos residues may be present in water as a result of use of three pesticides: Dichlorvos (DDVP), Naled, and Trichlorfon. Dichlorvos is a degradate of Naled and Trichlorfon. The environmental fate and Effects Division (EFED) evaluated the potential for Dichlorvos to contaminate water from these sources. The environmental fate properties of Dichlorvos, Naled, and Trichlorfon are an indicator of the potential of these compounds to migrate to ground or surface water. EFED has limited monitoring data on the concentrations of Dichlorvos, Naled, or Trichlorfon in groundwater. Validated monitoring data for Dichlorvos, Naled, and Trichlorfon are available for the states of California and Hawaii from the Pesticides in Groundwater Database. These data indicated that Naled, Dichlorvos, or Trichlorfon have not been detected in groundwater; however, these data were not targeted to the pesticide use area. OPP does not have any surface water monitoring data on the concentrations of Dichlorvos, Naled, or Trichlorfon at the present time. Therefore, the Tier I screening model GENEEC was used to estimate surface water concentrations for Naled, Trichlorfon and Dichlorvos.

Exposure assessments for a number of occupational and residential scenarios were derived from limited data from the scientific literature, textbooks, and knowledge of cultural practices. Other estimates, particularly in the residential environment, were derived from chemical specific monitoring data, including biomonitoring, in combination with models and literature studies. The Agency considers the occupational and residential exposure estimates to be the best available with current methodologies.

E. Risk Assessment/Characterization

Dietary (food source). The Agency has refined the dietary risk estimates using new anticipated residues, a new acute dietary endpoint, a revised Reference Dose (RfD), and a revised cancer potency estimate (Q_1*).

Acute Dietary (Food). The acute dietary analysis was conducted using the new Dietary Exposure Evaluation Model (DEEM) software. Results are reported as Margin of Exposure (MOE) for the 95th percentile of the population. The MOE is a measure of how closely the calculated exposure comes to the NOEL (the highest dose at which no effects were observed in the laboratory test), and is calculated as the ratio of the NOEL to the exposure (MOE = NOEL/exposure). A NOEL of 0.5 mg/kg/day (based on an acute human study) was used for acute dietary risk assessment. All MOEs for the acute dietary analysis were above the target MOE of 30. Therefore, the Agency does not have a risk concern for acute dietary exposure to Dichlorvos in food.

Chronic Dietary (Food). The chronic dietary analysis for Dichlorvos was conducted using the Dietary Risk Evaluation System (DRES) software. Chronic dietary exposure to Dichlorvos was compared to the chronic RfD. Chronic dietary exposure was less than 5% of the RfD for all subpopulations, which is below the Agency's level of concern.

Lifetime Dietary Cancer Risk (Food). The Agency estimated dietary cancer risks for Dichlorvos using the low-dose extrapolation model and the Q_1^* of 0.272 $(mg/kg/day)^{-1}$. The total estimated cancer risk from all dietary sources of Dichlorvos is 5.2×10^{-7}, which is below the Agency's level of concern. Therefore, the Agency does not have a risk concern for chronic dietary exposure to Dichlorvos in food. **In summary, the Agency has concluded that lifetime dietary exposure and cancer risk estimates from food are not of concern at this time.**

Dietary (Water). Monitoring data were not available for drinking water risk assessment. Therefore, estimated concentrations of Dichlorvos in water were compared with Drinking Water Levels of Comparison (DWLOCs) for acute or chronic systemic toxicity or cancer. Estimated concentrations of Dichlorvos in ground and surface water were derived from models.

Acute Drinking Water. For acute drinking water exposure, both the modeled groundwater concentrations of 0.0002 to 0.015 µg/L and the modeled surface water concentrations of 0.4 to 194 µg/L are less than the $DWLOC_{acute}$ of 485 µg/L for adults. However, the modeled surface water concentration of 194 µg/L exceeds the $DWLOC_{acute}$ value of 119 µg/L for children age 1-6 , indicating a potential concern and a need to refine the surface water estimate.

Chronic Drinking Water. For chronic drinking water exposure, the modeled groundwater concentrations of 0.0002 to 0.015 ug/L exceed the $DWLOC_{chronic}$ of 0 µg/L. The modeled surface water concentrations of Naled and Trichlorfon-derived Dichlorvos (2.2 and 26 ug/L, respectively) also exceed the $DWLOC_{chronic}$ of 0 µg/L. The $DWLOC_{chronic}$ value is driven by the chronic residential inhalation exposure to Dichlorvos from resin strips. Food and water exposure to Dichlorvos is negligible compared with residential exposure. Therefore, any water exposure will add to exposures and risks of concern.

Lifetime Drinking Water Cancer Risk Estimate. For lifetime drinking water exposure, the modeled ground water concentration of 0.015 ug/L is below the $DWLOC_{cancer}$ of 0.062 µg/L, but the modeled surface water concentration of 0.06 to 26 µg/L are equal to or greater than the $DWLOC_{cancer}$ of 0.062 µg/L.

Residential Risk Estimates. The Agency has refined residential risk estimates using new information, including the Pesticide Handlers Exposure Database (PHED, version 1.1), additional information on cultural practices in mushrooms and greenhouses, and the toxicological endpoints chosen by OPP's Hazard Identification Assessment Committee. The FQPA uncertainty factor of 3x was incorporated into residential, but not occupational, risk assessments. Resulting risk estimates are reported as Margins of Exposure (MOEs).

Application with Pressurized Aerosol Spray Can. The Agency estimated the risk to residents applying insecticide as a aerosol spray for different clothing scenarios. Pressurized aerosol products containing Dichlorvos do not list any clothing requirements, therefore the Agency is assuming that Dichlorvos is applied during hot weather when an individual will be wearing the least amount of clothing (i.e., shorts and shoes). Neither inhalation nor dermal

MOEs exceed the Agency's level of concern. The total MOE of 128 does not exceed the Agency's level of concern.

Residential Post-application: All Products. Indoor post application exposures for all scenarios were obtained from a single study measuring the exposures of individuals performing defined activity patterns following the activation of of a total release fogger. This study was intended to be used as a conservative estimate for all types of indoor applications. The total exposure from the biomonitoring phase, plus amount of Dichlorvos measured on the hands in the dosimetry phase, was compared to the oral NOEL. The resulting MOE for short term exposure was 33, which does not exceed the level of concern. The Agency considers this to be a conservative estimate for other Dichlorvos uses such as directed applications (crack and crevice treatments).

Resin Strips. Respiratory exposures resulting from the use of resin pest strips were estimated using a study found in the scientific literature. Exposure estimates have recently been revised to incorporate the recommendations of the July 30, 1998 FIFRA Science Advisory Panel. Exposure estimates and MOEs were calculated for 4 population groups; adult males, adult females, children, age 1-4 years; and children, age 5-11 years. The MOEs ranged from 0.4 to 1.2, all well below the required MOE of 300. Therefore, these MOEs are all of concern.

Pet Flea Collars. The assessment for flea collar exposure was derived from a study submitted by a previous registrant. There are no data with which to estimate dermal exposure from contact with pets. Respiratory exposures were estimated for 7 population groups; adult males; adult females; children, age 1-2; children, age 3-5; children, age 6-8; males, age 9-11; and females, age 9-11. The MOEs ranged from 15 to 33 and were all less than the required MOE of 300. Therefore, the MOEs are all of concern.

Ornamental Lawns, Turf and Plants - Post-Application Exposure. The assessment was obtained by using dislodgeable foliar residue information from a study found in the scientific literature and a registrant submitted study measuring the exposures of individuals performing defined activities on carpets following the activation of a total release fogger. The estimated MOE for a scenario where activity occurs for 20 minutes was 250. If the activity pattern is extrapolated to 1 hour of activity, which is conservative, the MOE becomes 83. The MOEs, which include both dermal and hand-to-mouth exposures, do not exceed the Agency's level of concern.

Occupational Risk Estimates. The Agency has refined occupational and residential risk estimates using new information, including the Pesticide Handlers Exposure Database (PHED, version 1.1), additional information on cultural practices in mushrooms and greenhouses, and the toxicological endpoints chosen by OPP's Hazard Identification Assessment Committee. The FQPA uncertainty factor of 3x was incorporated into residential, but not occupational, risk assessments. Resulting risk estimates are reported as Margins of Exposure (MOEs).

Crack and Crevice Treatment. Occupational exposure estimates for certified pesticide applicators conducting crack and crevice treatment with Dichlorvos were obtained from PHED (V1.1). All MOEs for crack and crevice treatment in homes (by certified pest control operators) are considered to be acceptable.

Mushroom House Application and Re-entry. The Agency has a risk concern for application scenarios involving use of a backpack sprayer and a portable sprayer on a cart. All MOEs for re-entry are considered to be below the Agency's level of concern.

Greenhouse Application and Re-entry. Application of Dichlorvos to greenhouse plants was previously allowed by hand-held foggers and by smoke generators. The Registrant has recently submitted a request for voluntary deletion of the hand-held fogger use under FIFRA Section 6(f). Total release foggers and smoke generators are considered to result in negligible exposure since the applicator vacates the premises immediately upon activation of the foggers. For re-entry to Dichlorvos treated greenhouses, all MOEs are below the level of concern at 10 hours after treatment. The MOE for total exposure (with re-entry at 10 hours) is 208, which is considered to be below the level of concern.

Animal Premises Treatment, Direct Animal Sprays, Feedlots, Manure Treatment, Garbage Dumps, and Baits. Exposure assessments for direct application to dairy cattle using handheld sprayers were conducted using PHED V1.1. Both inhalation and dermal MOEs are considered to be below the Agency's level of concern. MOEs for total exposure are also considered to be below the Agency's level of concern (MOE = 27 to 1600). There are no data addressing potential reentry into animal facilities.

Application to Lawns, Turf, and Ornamentals. There are no chemical specific usage data addressing the potential exposures of commercial lawn care operators to Dichlorvos. There are no registered homeowner uses. The material is applied only in tank mixtures with Chlorpyrifos. The types of equipment used and clothing worn by lawn care operators is likely to be similar to that used/worn by workers applying the material to dairy barns. Because of the enclosed nature of a barn versus an open lawn area, this would probably be conservative. The exposures and risks are considered to be similar to those for dairy barn treatments.

Warehouse Treatment and Re-entry. Dichlorvos can be applied to warehouses with wall-mounted automatic foggers. Exposure to mixer/loaders through automatic application is expected to be negligible; however, there would still be reentry exposure. EPA assumed 6 hours elapsed before reentry is allowed, as required on labels; and that workers spend 8 hours per day in the treated area for the next 3 days. The dermal MOE does not exceed the level of concern, but the inhalation MOE of 2.8 is of concern.

Insect Traps. Exposure is believed to be negligible since the pesticide is in the form of an impregnated strip and the traps are placed in outdoor areas (such as forests) where there is no human exposure.

Aggregate Exposure and Risk. The Agency considered aggregate exposure and risk estimates for residents who might be exposed to Dichlorvos from multiple sources, such as residential use, food, and water. This was taken into consideration in calculating DWLOCs. As noted below, the exposures from food and water are negligible compared to the exposure from residential use. Nonetheless, the aggregate exposure and risk estimates suggest the need to further refine the drinking water exposure estimates.

Aggregate Acute Dietary (Food and Water) Exposure and Risk. Acute dietary risk estimates for food do not exceed the Agency's level of concern. The aggregate acute dietary risk estimate for food and water does not exceed the Agency's level of concern for adults. However, the aggregate acute risk estimate for food and water slightly exceeds the Agency's level of concern for children. This indicates a need to refine the Agency's Tier I drinking water exposure estimates.

The $DWLOC_{acute}$ value is 485 µg/L for the total US Population and 119 µg/L for children age 1-6. These $DWLOC_{acute}$ values reflect the allowable drinking water exposure after food is subtracted. Both the modeled Tier I acute groundwater concentrations of 0.0002 to 0.015 µg/L and the modeled Tier I acute surface water concentrations of 0.4 to 194 µg/L are less than the $DWLOC_{acute}$ of 485 µg/L for adults. However, the modeled Tier I acute surface water concentration of 194 µg/L exceeds the $DWLOC_{acute}$ of 119 µg/L for children age 1-6, indicating a potential concern and a need to refine the surface water estimate.

Aggregate Short and Intermediate Term Dietary and Residential Exposure and Risk. DWLOCs were not calculated for short or intermediate term exposure. Because the short and intermediate term residential exposure scenarios are associated with risks of concern, the DWLOCs would effectively be zero. Further, food and water exposure are negligible compared to the residential exposure.

Aggregate Chronic Dietary (Food and Water) and Residential Exposure and Risk. Chronic dietary exposure and risk estimates from food do not exceed the Agency's level of concern. However, the chronic residential inhalation exposure estimates from resin strips exceed the Agency's level of concern. Therefore, the $DWLOC_{chronic}$ value is effectively 0 µg/L. Food and water exposure to Dichlorvos is negligible compared with residential exposure. Therefore, any water exposure will only add to exposures and risks already of concern.

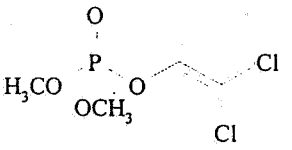
The Agency did not aggregate exposure from multiple uses in the residential environment because it is unlikely that a resident would be using multiple Dichlorvos products at the same time. Further, no data addressing this issue are available.

Lifetime Exposure (Cancer) Food and Water. The cancer endpoint for Dichlorvos is considered relevant to oral exposures only. Therefore, the $DWLOC_{cancer}$ value for Dichlorvos reflects the allowable drinking water exposure after food is subtracted. For lifetime drinking

water exposure, the modeled Tier I ground water concentration of 0.015 µg/L is below the $DWLOC_{cancer}$ of 0.062 µg/L, but the modeled Tier I surface water concentrations of 0.06 to 26 µg/L are equal to or greater than the $DWLOC_{cancer}$ of 0.062 µg/L. This suggests the need for a more refined Tier II drinking water exposure assessment.

II. Physical and Chemical Properties

The chemical structure and physical properties of Dichlorvos are given below.



CAS Registry No.:	62-73-7
PC Code No.:	084001
Empirical Formula:	$C_4H_7Cl_2O_4P$
Molecular Weight:	221.0
Physical State	liquid
Water Solubility	slightly soluble
Vapor Pressure	0.032 mm Hg at 32°C
Specific Gravity	1.42 at 25°C

III. Hazard assessment

A. Toxicology Assessment

1. Overview

Based on available information to date, the Agency has determined that the adverse effects of primary concern for Dichlorvos are those related to inhibition of cholinesterase activity and cancer.

Organophosphate pesticides, such as Dichlorvos, are known to inhibit cholinesterase activity and some cause delayed neurotoxic effects. Inhibition of cholinesterase activity can result in a number of clinical signs and symptoms, including headaches, dizziness, nausea, vomiting, diarrhea and increased urination, blurred vision, pinpoint pupils, increased salivation, labored breathing, muscle paralysis, slow heart rate, respiratory depression, convulsions, coma and even death. Numerous toxicological studies using laboratory animals are available addressing most of these toxicological endpoints for Dichlorvos.

Dichlorvos is classified as a Group C, possible human carcinogen, with a linear low dose extrapolation based on mononuclear cell leukemia in male rats. The cancer potency value (Q_1*) for Dichlorvos was calculated to be 2.72 x 10^{-1} $(mg/kg/day)^{-1}$ in human equivalents, based on the incidence of mononuclear cell leukemias seen in male rats. Dichlorvos has been shown to be a direct acting mutagen by common *in vitro* bacterial genetic toxicity assays. In addition, Dichlorvos is a direct acting mutagen in *in vitro* mammalian test systems. Dichlorvos seems to also have clastogenic activity in CHO cell *in vivo* with or without metabolic activation. Some studies showed that Dichlorvos was not clastogenic in *in vivo* micronucleus tests.

2. FIFRA Guideline Studies

The acute toxicity studies for Dichlorvos are presented in Table 1, and the non-acute toxicology profile for Dichlorvos is summarized in Table 2. The toxicology database required to support the Reregistration of Dichlorvos is essentially complete. All required toxicology studies have been submitted and reviewed by Agency scientists. In addition, the registrant recently conducted a voluntary (non-guideline) study in human volunteers. This is summarized below.

Table 1. Acute Toxicity Studies for Dichlorvos

Study Type	MRID No.	Results	Toxicity Category
Acute Oral - Rat	00005467	LD_{50} = 80 mg/kg (M) 56 mg/kg (F)	II
Acute Dermal - Rat	00005467	LD_{50} = 107 mg/kg (M) 75 mg/kg (F)	I
Acute Inhalation - Rat	00137239	LC_{50} = > 0.198 mg/L	II
Primary Eye Irritation	00146921	Mild irritant	III
Primary Skin Irritation	00146920	Mild-irritant	IV
Dermal Sensitization	none	No study available	NA
Acute Delayed Neurotoxicity - Hen	41004702	Negative for acute delayed neurotoxicity; axonal degeneration seen in 1 of 10 animals	NA
Acute Neurotoxicity - Rat	42655301	NOEL = 0.5 mg/kg; LOEL = 35 mg/kg (Changes in FOB, motor activity) No neuropathology	NA

Table 2. Toxicology Studies for Dichlorvos

Study Type	MRID No.	Results
28-Day Delayed Neurotoxicity- Hen	43433501	Cholinesterase inhibition (ChE_i) NOEL = 0.1 mg/kg/day LOEL = 0.3 mg/kg/day (brain ChEi) No neuropathology
90-Day Subchronic Toxicity - Rat	41004701	NOEL = 0.1 mg/kg/day LOEL = 1.5 mg/kg/day (plasma and RBC ChEi)
90-Day Neurotoxicity - Rat	42958101	NOEL = 0.1 mg/day LOEL = 7.5 mg/kg/day (plasma, red blood cell (RBC) and brain ChE_i).
Chronic-Feeding-Dog	41593101	NOEL = 0.05 mg/kg/day LOEL = 1.0 mg/kg/day (plasma and RBC ChE_i in both sexes and brain ChE_i in males).
Chronic toxicity/ Carcinogenicity-F344 Rats (NTP study)	40299401	NOEL = Not established LOEL = 4.0mg/kg/day (plasma and RBC ChE_i) **Evidence of carcinogenicity (mononuclear cell leukemia in male rats)**
Carcinogenicity-Mouse	40299401	NOEL = Not established LOEL = 10 mg/kg/day (plasma and RBC ChE_i in males) **Evidence of carcinogenicity (forestomach tumors in female mice)**
Developmental Toxicity-Rat	41951501	Maternal toxicity NOEL = 3 mg/kg/day LOEL = 21 mg/kg/day (clinical signs, decreased body weight gain and reductions in food consumption and efficiency) Developmental toxicity NOEL = $\geq$ 21 mg/kg/day (HDT)
Developmental Toxicity-Rabbit	41802401	Maternal toxicity NOEL = 2.5 mg/kg/day LOEL = 7.0 mg/kg/day (mortality, clinical signs, decreased body weight gain) Developmental toxicity NOEL= $\geq$ 7 mg/kg/day (HDT)

Study Type	MRID No.	Results
Reproductive Toxicity - Rat	42483901	Parental/Systemic NOEL = 2.3 mg/kg/day LOEL = 8.3 mg/kg/day (decreased % of females with estrous cycle and increased % of females with abnormal cycling. Offspring NOEL= 2.3 mg/kg/day; LOEL = 8.3 mg/kg/day (reduced dams bearing litter, fertility index, pregnancy index and pup weight).
Mutagenicity		Dichlorvos has been shown to be a direct acting mutagen by common *in vitro* bacterial genetic toxicity assays and in *in vitro* mammalian test systems. Conflicting evidence was seen for clastogenic activity *in vivo*.
Metabolism-Rat	41228701 41839901	The overall metabolic profile suggests the involvement of the one-carbon pool biosynthetic pathway as evidenced by the presence of a relatively large amount of radioactivity in the form of expired $^{14}CO_2$ and the presence of dehalogenated metabolites as well as urea and hippuric acid.

3. Literature Studies (Non-guideline)

In addition to the developmental and reproduction studies submitted to the Agency to fulfill the OPPTS Guidelines, HED's Hazard Identification Assessment Review Committee (HIARC) evaluated a prenatal developmental toxicity study in guinea pigs that was published in the open literature (Mehl et al. 1994). In this study Trichlorfon (125 mg/kg), Dichlorvos (15 mg/kg, once or twice/day) and several other organophosphates (Dimethoate, TOCP, Soman, and Ethyl Trichlorfon) were administered (route unspecified) to pregnant outbred albino guinea pigs (Ssc: AL, MOI:DHF) between day 42 and 46 of gestation. A dose of 15 mg/kg Dichlorvos was considered the largest dose that could be given without causing cholinergic symptoms in the pregnant dams, but it was noted that the mother of the litter that received 15 mg/kg once in 24 hours had slight symptoms. Offspring were born between day 69 and 72 of gestation. Brain weights of pups were determined within 24 hours of birth. Brain regions dissected and weighed were: medulla oblongata, cerebellum, superior and inferior colliculi, hippocampus; and thalamus and hypothalamus. The brain regions were homogenized and analyzed for choline acetyltransferase, acetyl cholinesterase, and glutamate decarboxylase.

Dosing of the dams resulted in the exposure of: 19 pups receiving saline on days 42-45; 10 pups receiving Trichlorfon on days 42-44 (125 mg/kg); and 4 pups each receiving Dichlorvos at either 15 mg/kg/day on days 42-44 (3 pups), 15 mg/kg/12 hours on days 42-44, or 15 mg/kg/12 hours on days 44-46. No effects on body weight were found. Trichlorfon caused

significant decreases in total brain weight (29%), and significant weight decreases of the cerebellum; medulla; thalamus/hypothalamus; colliculi; and the cerebral cortex.

In both litters of guinea pigs produced by dams dosed twice daily with Dichlorvos, significant decreases in total brain weight (12-14%) and significant decreases in cerebellum, medulla, thalamus/hypothalamus, and the colliculi were observed. In the group given 15 mg/kg Dichlorvos once daily, total brain weight decreases (6%) were not statistically significantly decreased, and only the thalamus/hypothalamus (19%) was significantly decreased. For dams given Trichlorfon, RBC cholinesterase inhibition was 64% at 1 hour, with recovery at 24 hours. There were no significant decreases in brain levels of ChE, glutamate decarboxylase, or choline acetyltransferase. Neither soman, a much more potent ChE inhibitor, nor TOCP, a potent neurotoxic esterase (NTE) inhibitor, caused any affect on brain weight. Ethyl Trichlorfon, a more potent ChE inhibitor and analogue of Trichlorfon, caused a slight decrease in brain weights of offspring, and atropine given with Trichlorfon did not prevent the decrease in brain weights (data not shown). The article mentions seven articles by a variety of labs in several countries in which decreases in brain weights of pups from Trichlorfon have been noted in guinea pigs and pigs, but not rats. It has been shown that 1-10% of Trichlorfon is metabolized to Dichlorvos, which is generally regarded as the active moiety in its anthelminthic and ChE inhibitory properties.

After reviewing the open literature studies, the Agency concluded that the open literature findings could not be dismissed and that additional data in the guinea pig are needed to further assess the developmental toxicity potential of Dichlorvos. It should be noted that the developmental effects reported in the open literature and discussed above for the neonatal guinea pig and piglet where not seen in developmental (test species rat and rabbit) or reproduction (test species rat) toxicity studies submitted to the Agency for Dichlorvos. Also, at least one literature article (Arch. Toxicol. 1986, 59:30-35) indicates that the effects on brain weight and size seen in guinea pig pups following administration of Trichlorfon during gestation could not be reproduced in the offspring of rats. However, based upon the results from the literature studies, the HIARC concluded that a standard developmental toxicity study in guinea pigs be submitted with certain protocol modifications to further assess the findings reported in the Mehl et al. study.

4. Human Studies (Non-guideline)

In addition to the animal studies discussed above, the registrant submitted results from three studies conducted in human volunteers. In the first study (MRID 44317901), fasted Caucasian male subjects were administered a single oral dose of 35 mg Dichlorvos, followed by a placebo dose of corn oil capsules then a second dose of 35 mg Dichlorvos (Phase I). All doses were in a volume of 0.5 mL. Prior to dosing, all individuals were given thorough medical examinations and three baseline cholinesterase measurements were taken. A symptom form was kept for each volunteer to record any adverse physical signs or symptoms. RBC cholinesterase activity was monitored immediately prior to dosing, and on study days 1, 3, 5/6, and 7. Under the

study conditions, RBC cholinesterase was not inhibited in phase I. The NOEL was 35 mg, equivalent to 0.5 mg/kg based on the absence of reduction of cholinesterase activity. When the same volunteers were administered 21 mg of Dichlorvos daily for twelve or 15 days (Phase II), the LOEL was 21 mg, equivalent to 0.3 mg/kg/day, based on significant and persistent reduction of cholinesterase activity. A NOEL was not determined in this study (Stewart 1998).

The second study (MRID 44248801) was a single blind oral study in which fasted male volunteers were administered Dichlorvos in capsules daily at a dosage of 7 mg (equivalent to approximately 0.1 mg/kg/day) in corn oil for 21 days. Control subjects received corn oil as a placebo. Any adverse events suffered by the participants were recorded on "adverse events" forms. Baseline values for RBC cholinesterase activity for each participant were determined on days -14, -12, -10, -7, -5, -3, and immediately prior to dosing, and RBC cholinesterase activity was monitored on days 2, 4, 7, 9, 11, 14, 16, and 18. No toxicity was reported which could be attributed to Dichlorvos administration. While there were significant decrements in RBC cholinesterase activity in Dichlorvos treated subjects at some reporting periods, the overall mean reduction from pretreatment values did not exceed 16 percent at any time. The cholinesterase activity values used to calculate the individual means varied by up to 21 percent. From this study The LOEL for RBC cholinesterase inhibition was determined to be 0.1 mg/kg/day (Stewart 1998).

In the third study (MRID 44248802), Dichlorvos was administered in a single oral dose of 70 mg (equivalent to 1 mg/kg) to fasted young healthy male volunteers. Prior to dosing, baseline RBC cholinesterase activity was measured on study days -22, -20, -18, -15, -13, -11, -8, -6, -4, and immediately prior to dosing. The study subjects were medically supervised for clinical signs and body temperature changes for twenty four hours and for RBC cholinesterase inhibition for up to fourteen days post Dichlorvos administration. Under the study conditions, no adverse clinical signs and no body temperature variations were reported. Mean RBC cholinesterase activity was statistically significantly inhibited, but the percent decrement was 12 percent or less on days 5/6, day 7, and day 14. No reduction in RBC cholinesterase activity was apparent at days 1 and 3. The reduction in RBC cholinesterase is considered to be biologically meaningful (Stewart 1998). Under the study conditions, the LOEL for this study is 70 mg (equivalent to 1 mg/kg).

B. Dose Response Assessment

1. Determination of Susceptibility

The HIARC evaluated the toxicology database with regard to increased susceptibility to infants and children and concluded that there was no indication of increased susceptibility to rat or rabbit fetuses following *in utero* exposure or to the offspring after pre/post natal exposures to Dichlorvos (Ghali 1997, Rowland 1998). In all these studies, maternal or parental NOELs were less than or equivalent to the developmental or offspring NOELs.

However, as discussed above, an open literature study (Mehl et al., 1994) which reported decreased brain weight in pups whose dam had been exposed to Dichlorvos again raised the concern for potential increased susceptibility of infants and children. The HIARC recommended that a developmental toxicity study in guinea pigs should be conducted with protocol modifications which included examination of brain weight.

The FQPA Safety Factor Committee, reviewed both the hazard (toxicity data including the literature study by Mehl et al) and exposure data to determine if the retention of the additional 10x factor is warranted (Rowland and Tarplee 1998). The discussion focused on the weight that should be given the guinea pig study found in the open literature. The study had several obvious deficiencies: it did not meet Agency guidelines, the route of exposure was not reported, the number of dams exposed was small, the number of pups was small, the relevance of guinea pigs to humans is uncertain, and none of the required guideline studies submitted to OPP reported or suggested this effect. On the other hand, the study did report significant decreases in brain weights of guinea pig pups whose dams were exposed to Dichlorvos during gestation.

After carefully considering all the factors, the decision was made that an FQPA Safety Factor was required but the factor should be reduced to 3x. The reduction of the FQPA Safety Factor was made based on the following factors: 1) the toxicology database is complete with regard to the standard Subdivision F guideline requirements and 2) the standard developmental and reproductive toxicity studies submitted to the Agency showed no indication of increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure to Dichlorvos. The Agency is confident that the methods used to estimate residential exposure to Dichlorvos do not underestimate risks to children. The Agency has requested a prenatal developmental toxicity study in guinea pigs to replicate/confirm the findings of a literature study by Mehl et al. (1994).

The Agency's position was presented to the FIFRA Scientific Advisory Panel on July 30, 1998, The SAP concluded that *"Flaws in the Mehl et al. Study limit its significance and do not permit the Agency to reach any conclusions regarding developmental toxicity. However, the study suggests the possibility of a developmental effect on the brain--despite its flaws-- and the Panel believes that the Agency should further investigate 1) if the study were conducted according to an acceptable experimental design, would the effects be replicated ? And 2) is the guinea pig an acceptable test species to predict the risk of human developmental effects?"* (Lewis 1998). The Agency has not received any additional clarifying information on the issue of increased susceptibility to date.

2. Cancer Classification

Dichlorvos has been the subject of several cancer peer reviews by the OPP Carcinogenicity Peer Review Committee, the Agency Cancer Review and Verification Effort (CRAVE) Workgroup, and the FIFRA Science Advisory Panel (SAP). In the 5th and final review by the OPP Carcinogenicity Peer Review Committee on March 27, 1996, the Committee

recommended maintaining a "C" carcinogen classification based on statistically significant increased incidence of mononuclear cell leukemias (MCL) in male Fisher 344 rats at 4, and 8 mg/kg/day (MRID No. 40299401); and, based on mononuclear cell leukemias, the Committee recommended a low dose linear extrapolation (Stewart and Burnam 1996). The Committee considered new mechanistic information in their deliberations.

The Agency's concern for carcinogenicity is limited to the oral route of exposure. Although the Agency often extrapolates results from oral studies to other routes of exposure, the Agency has determined that extrapolation from the gavage studies to the dermal or inhalation routes of exposure is not appropriate for Dichlorvos for purposes of cancer risk assessment (Ghali 1993). A 2-year rat inhalation study was negative for cancer. Also, because the dermal absorption efficiency of Dichlorvos is only 11%, it is not expected that topically applied doses would reach the target organ(s) in sufficient quantity to produce a carcinogenic response. Therefore, extrapolation from oral cancer data to dermal or inhalation routes is not appropriate for estimation of excess individual cancer risk following dermal or inhalation exposure to Dichlorvos.

The Agency received oral comments from the public and the FIFRA Science Advisory Panel Meeting of July 30, 1998 regarding the carcinogenicity of Dichlorvos (Lewis 1998). Also, the Registrant has recently submitted a lengthy Blue Ribbon Panel Report on the carcinogenicity of Dichlorvos. The Agency has recently concluded that dietary cancer risk estimates for Dichlorvos from food exposure alone are no longer of concern. Dietary exposures and risks are further described in section IIIC of this report. The Agency has not yet had an opportunity to review the Blue Ribbon Panel Report but does not expect this report to alter the conclusion regarding carcinogenic risk.

3. Toxicology Endpoint Selection

The Hazard Identification Committee (HIARC) met on November 13 and 18, 1997 and May 7, 1998 to evaluate the existing toxicology database for Dichlorvos, identify toxicological endpoints and dose levels of concern appropriate for use in risk assessments for different exposure routes and durations, and assess/reassess the reference dose (RfD). A group of HED Branch Chiefs and Toxicologists met on November 19, 1998 to revisit the inhalation endpoints for Dichlorvos. Reports on Dichlorvos (Ghali 1997, Rowland 1998, Kent 1998) discussed issues relating to acute and chronic dietary exposures and Reference Dose (RfD), dermal and inhalation exposures, susceptibility (FQPA) issues, and the selection of uncertainty factors (UF). The conclusions and toxicology endpoints selected for dietary and non-dietary risk assessments are presented in Table 3 below.

Subsequent to the HIARC discussions of Dichlorvos, the Agency received oral comments regarding the cholinesterase inhibition endpoint at the July 1998 FIFRA SAP Meeting. The Registrant convened a Blue Ribbon Panel on cholinesterase inhibition, and presented the findings

of that panel at the July SAP meeting. The Agency has not yet had an opportunity to review the Blue Ribbon Panel Report.

Table 3. Doses and Toxicological Endpoints Selected for Risk Assessment of Dichlorvos

EXPOSURE SCENARIO	DOSE (mg/kg/day) UF /MOE	ENDPOINT	STUDY
Acute Dietary	NOEL =0.5	RBC cholinesterase inhibition	Acute-Human
	UF=30 [a]		
Chronic Dietary	NOEL = 0.05	Plasma and RBC cholinesterase inhibition in both sexes and brain cholinesterase inhibition in males	1-Year Dog
	UF = 300 [b]	**Chronic RfD = 0.00017 mg/kg/day**	
Cancer Oral Route Only	oral Q_1* = 0.272	Leukemia in male rats (Applies only to dietary and drinking water risk assessment)	2-year Rat Oral Bioassay
Short-Term Inhalation and Dermal[e]	Oral NOEL= 0.5	Red blood cell cholinesterase inhibition	Acute - Human
	UF = 10 for occupational and 30 for residential exposure[c]		
Intermediate-Term Inhalation and Dermal[e]	Oral LOEL= 0.1	Red blood cell cholinesterase inhibition	Repeated Dose Human
	UF = 30 for occupational exposure[d]		
Chronic Dermal	None	Use pattern indicates no potential Long-Term dermal exposure; risk assessment not required	None
Chronic Inhalation	0.05 (0.00005 mg/L)	Plasma, RBC and Brain cholinesterase inhibition in chronic rat inhalation study with NOEL of 0.00005 mg/L and 23 h/day of exposure. Conversion to mg/kg/day assumes rat body wt of 0.236 kg, respiratory volume of 10.3L/hr, and exposure of 23 hr/day .	2-Year Rat Inhalation Study
	UF=300 [b]		

[a]The uncertainty factor (UF) includes the 10x for inter-species extrapolation and the 3x FQPA Safety Factor. [b]The UF includes the 10x for inter-species extrapolation, 10x for intra-species variation and the 3x FQPA Safety Factor. [c]The UF includes 10x for intraspecies variation (occupational and residential) and the 3X FQPA Safety Factor (residential only). [d]The UF includes 10x for intraspecies variation and 3x for use of a LOEL. [e]Since an oral

NOEL was selected for these exposure periods, a dermal absorption factor of 11% (determined from a dermal absorption study, MRID No. 41435201) should be used for these exposure risk assessments.

The critical toxicology study for acute dietary risk assessment was the acute oral human study (non-guideline, MRID No. 44317901). Study details have been described in the previous section of this document. It should be noted, however, that in this study plasma cholinesterase inhibition was not measured. The NOEL for Phase 1 was 35 mg/subject (equivalent to 0.5 mg/kg) and a NOEL was not established for Phase 2. The NOEL of 0.5 mg/kg for RBC cholinesterase inhibition was the dose and endpoint selected for acute dietary risk assessment. Because the study was conducted in human subjects, there was no need to account for the interspecies extrapolation. Therefore, an uncertainty factor of 30 is required to account for intraspecies variation (10x) and the FQPA safety factor (3x).

The critical toxicology study for chronic noncancer dietary risk assessment is the one-year feeding study in dogs (Guideline 83-1b, MRID No. 41593101). Groups of beagle dogs were administered Dichlorvos by capsule for 52 weeks at dose levels of 0, 0.1, 1.0 and 3.0 mg/kg/day. The 1.0 mg/kg/day dose was lowered to 0.05 mg/kg/day on day 22 due to the inhibition of plasma cholinesterase noted after 12 days. Plasma cholinesterase was decreased in males (21.1%) and females (25.7%) at week 2 in the 0.1 mg/kg/day which was then reduced to 0.05 mg/kg/day. After week 2, plasma cholinesterase activity was only significantly reduced in males (39.1 to 59.2%) and females (41.0 to 56.7%) in the mid-dose group and in males (65.1 to 74.3%) and females (61.1 to 74.2%)in the high dose group at all other later time intervals. RBC cholinesterase activity was reduced in males (23.6%) and females (50.1%) at week 6 in the low-dose group. This was believed to be residual effect on RBC cholinesterase of the higher dose of 0.1 mg/kg/day. Much lower levels were observed in this group after week 6. After week 6, RBC cholinesterase activity was only significantly decreased in males (43.0 to 53.9) and females (38.0 to 51.9) in the mid-dose group and in males (81.2 to 86.9%) and females 79.2 to 82.5%) in the high-dose groups at all other later time intervals. Brain cholinesterase activity was significantly reduced in males (22%) in the mid-dose group and in males (47%) and females (29%) in the high dose group. The NOEL/LOEL are 0.05 and 0.1 mg/kg/day, respectively, based on plasma and RBC cholinesterase inhibition in males and females as early as 1st time point measure and brain cholinesterase in males. The NOEL of 0.05 mg/kg/day based on plasma and RBC cholinesterase inhibition in males and females and brain cholinesterase inhibition in males observed at 0.1 mg/kg/day was selected for chronic dietary risk assessment. An uncertainty factor of 300 is required to account for interspecies extrapolation (10x), intraspecies variation (10x), and the FQPA safety factor (3x). **Therefore, the Reference Dose (RfD) was determined to be 0.00017 mg/kg/day (NOEL of 0.05 mg/kg/day ÷ UF of 300).** Although a human repeated dose study was available, the Committee did not use it because of the short duration of the study and the fact that cholinesterase inhibition did not demonstrate a steady state (equilibrium) by the end of the study at three weeks, i.e., the inhibition of cholinesterase was progressive in this case. Furthermore, the human repeated dose study did not include plasma cholinesterase measurements and failed to demonstrate a NOEL.

For occupational and residential risk assessment, the dermal absorption rate for Dichlorvos was estimated to be approximately 11% in 10 hours of exposure. This was based on the findings of a dermal absorption study in rats (85-2), MRID No. 41435201.

The critical study selected for short term dermal risk assessment was the acute oral (non-guideline) human study, MRID No. 44317901, which is summarized above. The NOEL of 0.5 mg/kg for RBC cholinesterase inhibition was selected for risk assessment. Because the study was conducted in human subjects, there was no need to account for the interspecies extrapolation. Therefore, for short-term dermal risk assessments for occupational exposure, an MOE of 10 is adequate (10x for intraspecies variation). For short term dermal risk assessments for residential exposure, an MOE of 30 is required (10x for intraspecies variation and 3x for FQPA).

The HIARC used the acute oral toxicity study conducted on human volunteers since no dermal toxicity study was available for this purpose. The test chemical is volatile and the requirement for the 21-day dermal toxicity study for this chemical has been waived by the Agency. Since a NOEL generated from an oral toxicity study will be used in the dermal risk assessment, the dermal absorption rate of 11% should be taken into consideration.

The critical study selected for risk assessment for intermediate-term dermal exposure was the repeated dose oral toxicity study in human subjects (21-day non-guideline, MRID No. 44248801). In a single blind oral study, 6 fasted male volunteers were administered 7 mg of Dichlorvos in corn oil (equivalent to approximately 0.1 mg/kg/day) via capsule daily for 21 days. Three control subjects received corn oil as a placebo. Baseline values for RBC cholinesterase activity for each study participant were determined. After dosing started, RBC cholinesterase activity was monitored on days 2, 4, 7, 9, 11, 14, 16, and 18, then on day 25 or 28 post dosing. No toxicity attributable to administration of Dichlorvos was reported. Mean RBC cholinesterase activity was significantly reduced in treated subjects on days 7, 11, 14, 16, and 18. These values were 8, 10, 14, 14, and 16 percent below the pre-dose mean. Under the study conditions, a LOEL for RBC cholinesterase inhibition was established at 0.1 mg/kg/day, the lowest dose tested. The LOEL of 0.1 mg/kg/day for RBC cholinesterase inhibition was chosen as selected for risk assessment. An uncertainty factor of 10 was recommended to account for intraspecies variability. Since the study was conducted in human subjects, there was no need to account for the interspecies extrapolation. For intermediate term dermal risk assessments for occupational exposure, an MOE of 30 is required (10x for intraspecies variation and 3x for use of a LOEL because a NOEL was not established in the critical study). For intermediate term dermal risk assessments for residential exposure, an MOE of 100 is required (10x for intraspecies variation, ~3x for use of a LOEL, and 3x for the FQPA safety factor).

The HIARC used the oral toxicity study conducted on human volunteers since no dermal toxicity study was available for this purpose. The test chemical is volatile and the requirement for the 21-day dermal toxicity study for this chemical has been waived by the Agency. Since a

NOEL generated from an oral toxicity study will be used in this dermal risk assessment, the dermal absorption rate of 11% should be taken into consideration.

The HIARC did not select a toxicology endpoint for long term dermal exposure to Dichlorvos. The available information on the Dichlorvos use pattern and exposure profile indicate that long term dermal exposure will not occur. Therefore, the HIARC determined that this type of risk assessment is not required.

The critical study for inhalation risk assessment for Dichlorvos is an inhalation carcinogenicity study in rats (83-2a), MRID No. 0057695, 00632569). Groups of 50/sex/group Carworth rats were exposed to atmospheres containing Dichlorvos vapor for 23 hours/day, 7 days/week at concentrations of 0, 0.05, 0.5, and 5 mg/m^3 equivalent to 0.055, 0.5, and 5.0 mg/kg/day for 2 years. Animals were observed for clinical signs of toxicity, hematology, clinical chemistry and plasma and RBC cholinesterase activity. Brain cholinesterase activity was monitored at study termination. There were no toxic signs, and no organ weight or organ to body weight changes, or hematological changes attributable to administration of Dichlorvos. Body weights were significantly decreased in mid and high dose males up to study termination, and in high dose females throughout the study. Plasma, RBC, and brain cholinesterase activity were significantly reduced in the mid and high dose groups (76, 72, and 90 and 83, 68, and 90 percent of control in mid dose males and females, and to 38, 4, and 21, and 22, 5, and 16 percent of control in the high dose male and female groups, respectively). RBC cholinesterase activity was reduced to 88 percent of control in the low dose females. The NOEL for cholinesterase inhibition was 0.055 mg/kg/day and the LOEL was 0.5 mg/kg/day. This is the same inhalation study which has been used by the Agency RfD/RfC Work Group in deriving the RfC for Dichlorvos. An Agency RfC document is available on IRIS.

The study NOEL of 0.05 mg/m^3 (or 0.00005 mg/L) was selected for chronic inhalation risk assessment scenarios. Plasma, RBC, and brain cholinesterase inhibition were observed at the next higher dose level of 0.48 mg/m^3. For inhalation risk assessments for occupational exposure, an MOE of 100 is adequate (10x for interspecies variation and 10x for intraspecies variation). For inhalation risk assessments for residential exposure, an MOE of 300 is adequate (10x for interspecies variation, 10x for intraspecies variation, and 3x for the FQPA safety factor).

4. Incident Reports

The Agency has conducted a review of reported poisoning incidents associated with human exposure to Dichlorvos. The Agency has consulted the following data bases for the poisoning incident data on the active ingredient Dichlorvos: (1) the OPP Incident Data System, which contains anecdotal reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992, (2) Poison Control Center Data for 28 organophosphate and carbamate chemicals for the years 1985 through 1992, (3) California Department of Food and Agriculture reports

(superceded by the Department of Pesticide Regulation), which contain uniform data on suspected pesticide poisonings collected since 1982, and (4) National Pesticide Telecommunications Network (NPTN), which is a toll-free information service supported by OPP. In addition, the Agency has received public comments regarding poisoning incidences associated with Dichlorvos as comments to the Proposed Notice of Intent to Cancel (PD 2/3). Specific comments on incidences were received from Amvac Chemical Corporation, the Japanese Resin Strip Manufacturer's association, and two private citizens, Arturo Haran and Philip Levine.

Exposure to Dichlorvos has resulted in poisoning incidents. Dichlorvos has widespread use patterns in the home and agricultural environments. Many of these uses (e.g., poultry houses) are atypical of most organophosphates, which makes it difficult to compare the risk. According to California data, it appears that a majority of cases involved illnesses to workers indoors that entered a previously Dichlorvos fumigated facility. Often exposure results from inadequate ventilation before persons are allowed in or near the treated area or lack of proper personal protective equipment (PPE).

Dichlorvos can cause systemic illness, including respiratory effects, to individuals who are exposed after fumigation.

I. Agency Review of Incidence Reports

Incident Data System. The Agency's incident data system has 6 reports of poisoning incidences associated with Dichlorvos use between 1992 and 1998; the majority of these incidences were associated with misuse. These cases do not have documentation confirming exposure or health effects unless otherwise noted.

Poison Control Center Data. Dichlorvos was one of 28 organophosphate chemicals for which Poison Control Center (PCC) data were requested. There were a total of 19,666 Dichlorvos cases in the Poison Control Center (PCC) data base from 1985 to 1992. Of these, 316 cases were occupational exposure; 259 (82.0%) involved exposure to Dichlorvos alone and 57 (18.0%) involved exposure to multiple chemical products including Dichlorvos. There were a total of 9043 adult non-occupational exposures; 8575 (94.8%) involved this chemical alone and 468 (5.2%) were attributed to multiple chemical products. Workers who were indirectly exposed (not handlers) were usually classified as non-occupational cases. In this analysis, four measures of hazard were developed based on the Poison Control Center data, as listed below:

1. Percent of all accidental cases that were seen in or referred to a health care facility (HCF).

2. Percent of these cases (seen in or referred to HCF) that were admitted for medical care.

3. Percent of cases reporting symptoms based on just those cases where the medical outcome could be determined.

4. Percent of those cases that had a major medical outcome which could be defined as life-threatening or resulting in permanent disability.

Exposure to Dichlorvos alone or in combination with other chemicals was evaluated for each of these categories, giving a total of 8 measures. A ranking of the 28 chemicals was done based on these measures with the lowest number being the most frequently implicated in adverse effects. Dichlorvos did not rank in the top 7 for any category. Table 4 presents the analyses for occupational and non-occupational exposures.

Dichlorvos had average or below average evidence of effects compared to other organophosphate insecticides (Blondell 1994). For non-occupational exposure, six life-threatening cases were reported for exposure to Dichlorvos alone and eight life-threatening cases were reported which involved exposure to Dichlorvos and other products (Table 5 below). Among cases seen in a health care facility, Dichlorvos cases were much less likely to be hospitalized than the other insecticides. On other measures of hazard (percent seen in a health care facility or percent with symptoms), Dichlorvos had percents similar to the median for other cholinesterase inhibitors (Blondell 1994).

A separate analysis of the number of exposures in children five years of age and under from 1985-1992 was conducted. For Dichlorvos, there were 10307 incidents; 10070 involved exposure to Dichlorvos alone and 237 involved other pesticide products as well. Compared to 14 other organophosphates and carbamates that 25 or more children were exposed to, Dichlorvos cases were less than half as likely to be seen in a health care facility or require hospitalization. Symptoms, however, occurred just as often for Dichlorvos and there were four life-threatening cases reported in children under age six.

Table 4. Measures of Risk From Occupational and Non-occupational Exposure to Dichlorvos Using Poison Control Center Data from 1985-1992[a]

	Occupational Exposure	Non-occupational Exposure
Percent Seen in HCF		
Single chemical exposure	51.4 (68.2)	24.0 (44.0)
Multiple chemical exposure	50.3 (69.8)	24.9 (46.1)
Percent Hospitalized		
Single chemical exposure	9.8 (12.2)	5.4 (9.9)
Multiple chemical exposure	10.7 (14.3)	6.0 (12.6)
Percent with Symptoms		
Single chemical exposure	81.8 (85.8)	69.5 (74.0)
Multiple chemical exposure	84.4 (85.8)	70.3 (75.2)
Percent with Life-threatening Symptoms		
Single chemical exposure	0.6[b] (0.0)	0.1[b] (0.0)
Multiple chemical exposure	0.5[b](0.5)	0.1[b] (0.05)

[a] Extracted from Blondell 1994: number in parentheses is median score for that category.
[b] The percent calculated here is based on a single case for a single chemical exposure. The percent calculated here is based on between 6 to 8 cases for multiple chemical exposures.

California Pesticide Illness Surveillance Data (1982 to 1995). Detailed descriptions of 227 cases submitted to the California Pesticide Illness Surveillance Program (1982-1995) were reviewed. In 62 of these cases, Dichlorvos alone was judged to be responsible for the health effects. Only cases with a definite, probable or possible relationship were reviewed. Dichlorvos ranked 27th as a cause of systemic poisoning in California. One individual was hospitalized between 1982 and 1995. Table 5 presents the types of illnesses reported by year. A total of 51 of 62 people had systemic illnesses (82.3%).
Table 6 gives the total number of workers who took time off work as a result of their illness, the total number of these workers who were hospitalized, and the length of hospitalization. A variety of worker activities were associated with exposure to Dichlorvos as illustrated in Table 7 below.

Table 5. Cases Due to Dichlorvos Exposure in California , 1982-1995.

	Illness Type					
Year	Systemic[a]	Eye	Skin	Respiratory	Combination[b]	Total
1982	8	1	2	-	-	11
1983	6	1	2	-	-	9
1984	2	-	-	-	-	2
1985	6	1	-	-	-	7
1986	2	-	-	-	-	2
1987	-	-	-	-	-	-
1988	2	-	-	-	-	2
1989	1	-	-	-	-	1
1990	2	-	-	1	-	3
1991	1	-	-	-	-	1
1992	5	-	-	-	-	5
1993	4	-	-	-	-	4
1994	11	-	-	2	1	14
1995	1	-	-	-	-	1
Total	51	3	4	3	1	62

[a] Category includes cases where skin, eye, or respiratory effects were also reported. [b] Category includes combined irritative effects to eye, skin, and respiratory system

Table 6. Number of Persons Disabled (taking time off work) or Hospitalized for Indicated Number of Days After Dichlorvos Exposure in California, 1982-1995.

	Number of Persons Disabled	Number of Persons Hospitalized
1 day	5	-
2 days	2	1
3-5 days	4	-
6-10 days	-	-
> 10 days	2	-
Unknown	4	2

Table 7. Illnesses by Activity Categories for Dichlorvos Exposure in California, 1982-1995

Activity Category[a]	Illness Category					
	Systemic[b]	Eye	Skin	Respiratory	Combination[c]	Total
Applicator	6	1	1	-	-	8
Mixer/loader	1	-	-	-	-	1
Clean/Fix	-	-	-	1	-	1
Coincidental	2	-	-	-	-	2
Spray Drift Exposure	3	-	-	-	1	4
Pesticide Handling between Packaging and End Use	9	-	-	-	-	9
Chamber Fumigation	1	-	-	-	-	1
Manufacturing/ Formulation Plant Workers	1	-	-	-	-	1
Field Worker	2	-	1	-	-	3
Structural Treatment	15	-	-	2	-	17
Miscellaneous Nonoccupational Exposure	11	2	2	-	-	15
Total	51	3	4	3	1	62

[a] Clean/Fix= clean and/or repairing pesticide contaminated equipment; Coincidental= coincidental; Spray drift exposure = exposure to pesticide that has drifted from intended targets; Persons handling pesticide products between packaging and end-use, self explanatory; Chamber fumigation and manufacturing/formulation plant workers are self explanatory; Mixer/loader = mixing and/or loader of pesticide concentrates and dilute pesticides; Miscellaneous = non-occupational miscellaneous exposure; field worker and structural treatment are self explanatory.

[b] Category includes cases where skin, eye, or respiratory effects were also reported

[c] Category includes combined irritative effects to eye, skin, and respiratory system

According to the above activity categories, workers exposed to residue of structural treatment and miscellaneous non-occupational exposure were associated with the majority of the exposures. Most such cases involve indoor workers exposed to residues from a fogger or spray-type application. A number of cases resulted due to faulty equipment. Structural treatment with Dichlorvos was associated with illnesses that included symptoms of shortness of breath, difficulty breathing, chest tightness and pain, loss of concentration, headaches, dizziness, and several other symptoms. The miscellaneous nonoccupational exposure category was associated with illnesses that included symptoms of difficulty breathing, contact dermatitis on the face and nose, chemical conjunctivitis of the eyes, headaches, nausea, and several other symptoms.

National Pesticide Telecommunications Network (NPTN). As stated previously, NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984 to 1991 has been prepared. The total number of calls was tabulated for the categories human incidents, animal incidents, calls for information, and others. On the list of the top 200 chemicals for which NPTN received calls from 1984-1991 inclusively, Dichlorvos was ranked 18th with 188 incidents reported in humans and 32 incidents reported in animals (mostly pets).

ii. Public Comments on Incidence

The Agency received additional information on poisoning incidences associated with Dichlorvos as comments to the PD 2/3. Specific comments on incidences were received from Amvac Chemical Corporation, the Japanese Resin Strip Manufacturer's Association, and two private citizens, Arturo Haran and Philip Levine. Amvac submitted a review of human incident data for Dichlorvos (Feiler 1995), and the Japanese Resin Strip Manufacturer's Association submitted data on poisoning incidences involving Dichlorvos resin strips. Arturo Haran submitted an anecdotal report of health effects and Eric Levine submitted a comment about the potential carcinogenicity of Dichlorvos. The Agency has reviewed this new information (Blondell 1996). The Agency's conclusions are summarized below.

Data reported by the American Association of poison Control Centers (AAPCC) concerning exposure to single products with Dichlorvos often contain other active ingredients. AAPCC reported 21,006 exposures to single products containing Dichlorvos. Most of these exposures involve homeowner use products that contained Dichlorvos in combination with other insecticides such as propoxur, pyrethrins, or piperonyl butoxide. In these cases involving Dichlorvos in combination with other pesticides it is incorrect to attribute any resulting toxicity solely to Dichlorvos.

Dichlorvos resin strips account for a very small proportion of total incidences, about 33 cases per year (1% of total incidences). Incidence reports involving exposure to resin strips usually do not involve any significant acute symptoms that would require medical treatment (Blondell 1996).

Eric Levine commented on epidemiological evidence linking use of Dichlorvos resin strips with childhood cancer. Two epidemiologic studies have reported an association between exposure to Dichlorvos resin strips and childhood cancer. These studies by Liess and Savitz (1995) and Davis et al (1993) have been reviewed by the Agency (Blondell 1996). Reviews of these studies have identified biases and confounders that could explain the observed associations. The Agency concludes that the biases are a more likely explanation for the findings of increased cancer than exposure to resin strips. Additional studies that correct for the control of potential biases and problems of exposure determination are needed before an association between Dichlorvos and childhood cancer can be established.

IV. Exposure and Risk Assessment

A. Dietary Exposure (Food Sources)

I. Background

Dietary (food) exposure to a pesticide depends on two components: the amount of pesticide residue on a commodity and how much of that commodity is consumed. In estimating Dichlorvos residues on food for the PD 2/3, the Agency relied on a variety of data for Dichlorvos, including tolerance levels (the legal maximum residue) and field trial data (measured residues resulting from actual application of Dichlorvos). These estimated residues can be further refined by taking into account the effects of processing and cooking on treated foods, and by estimating the percent of the crop that is treated. The current dietary (food) exposure and risk assessment is based primarily on monitoring data (both regulatory enforcement data and statistically based sampling data) and dietary intake surveys.

The Agency currently uses food consumption data derived from a USDA survey to estimate dietary exposure to pesticides. The USDA conducted a nationwide survey (1977-1978) of the food consumption patterns of 30,770 individuals for 3 days. Based on this survey, The Agency can estimate the dietary exposure and risk for the U.S. population and 22 subgroups of the total population using a computer-based tool called the Dietary Risk Evaluation System (DRES). DRES multiplies the average daily consumption by residue information for each commodity to obtain the total dietary (food) exposure. The Agency initially estimates dietary exposure based on the Theoretical Maximum Residue Contribution (TMRC). The TMRC assumes residues on crops are present at tolerance levels (the maximum residue limit allowed by law) and 100 percent of the crop is treated. When the risk estimated using the TMRC is considered too high, the Agency uses additional data to refine the TMRC, including monitoring data, field trial data, processing data, and estimates of percent of crop treated. The Agency uses this additional information to calculate the Anticipated Residue Contribution (ARC). When available, the ARC is used instead of the TMRC in estimating risk.

ii. Sources of Dichlorvos Residues on Foods

Dietary exposure to Dichlorvos residues may occur as a result of use on or at a variety of sites, including mushroom houses, bulk-stored and packaged or bagged nonperishable processed and raw food, commercial food processing plants, groceries, direct animal treatment, and livestock premise treatment. As a result, Dichlorvos residues may be found in bulk stored and packaged or bagged non perishable processed or raw food. Dichlorvos residues may also be found in mushrooms and in livestock commodities, such as meat, milk, meat byproducts, poultry, and eggs.

Two other pesticides, Naled and Trichlorfon, degrade to Dichlorvos through plant metabolism. The Agency does not expect measurable Dichlorvos residues from Trichlorfon because all Trichlorfon food uses have been canceled and associated tolerances revoked. Therefore, no Dichlorvos residues are expected to occur in food as a result of Trichlorfon use.

Three factors will significantly affect dietary exposure to Dichlorvos from registered uses of Naled; these include, the pre-harvest interval (PHI), the condition and length of storage, and cooking and processing. Plant metabolism studies show that Dichlorvos residues are formed 1 to 3 days after treatment with Naled; however, Dichlorvos residues decline to less than the limit of detection (0.01 to 0.05 ppm) 7 days after treatment. In general, registered uses of Naled have PHIs of less than 7 days. Because of the short PHIs for Naled products, measurable residues of Dichlorvos may be present in the diet from Naled treated food. As a result, the dietary (food) exposure assessment for Dichlorvos includes residues of Dichlorvos resulting from the application of Naled.

Dietary exposure estimates have been refined with residue data from USDA's Pesticide Data Program (PDP), FDA surveillance data, and FDA Total Diet Study (TDS) data.

iii. Residue Chemistry Studies for Dichlorvos

Residue chemistry studies for Dichlorvos provide valuable information on Dichlorvos residues in foods. These studies are submitted to satisfy FIFRA guidelines for pesticide registration as described in the OPPTS Test Guidelines, Series 860. Key studies on the nature and magnitude of Dichlorvos residues in food are summarized below.

Milk and the fat, meat, and meat byproducts of cattle, goats, hogs, horses, and sheep: **Direct Dermal uses:** Cattle, goat, hogs, horses, and sheep may be both dermally, through direct treatment and/or treatment of their premises, and orally exposed to Dichlorvos. Adequate dermal magnitude of the residue studies have been submitted and evaluated for cattle. Residues were nondetectable (<0.01 ppm) in tissues and milk following treatment at 1x the maximum registered rate. **Livestock Premise Treatment:** Applications are made as a mist or fog to livestock premises, while the livestock are present, thus, direct dermal livestock contact is occurring.

Secondary Residues: The maximum theoretical dietary burdens of Dichlorvos to beef and dairy cattle are 7.0 and 6.5 ppm, respectively (see Table 8 below).

Table 8. Calculation of maximum ruminant dietary burden for Dichlorvos.

Feed Commodity	Reassessed Tolerance (ppm)	% Dry Matter	Beef Cattle		Dairy Cattle	
			% of Diet	Burden (ppm)	% of Diet	Burden (ppm)
Wheat, grain	4.0	89	50	2.25	40	1.80
Wheat, aspirated grain fractions	20	85	20	4.71	20	4.71
		TOTAL	70	6.96	60	6.51

An adequate feeding study, reflecting dosing of dairy cattle at 2, 6, and 20 ppm, has been submitted and evaluated. Residues were nondetectable (<0.01 ppm) in tissues and milk at all dosing levels. It was concluded that the cattle feeding study could be translated to swine.

Eggs and the fat, meat, and meat byproducts of poultry: **Direct Dermal Treatment:** Poultry may be both dermally, through direct treatment and/or treatment of their premises, and orally exposed to Dichlorvos. Adequate dermal magnitude of the residue studies have been submitted and evaluated for poultry. Residues were nondetectable (<0.02-<0.05 ppm) to 0.08 ppm in tissues and egg, including poultry skin, following treatment at levels 0.1-6.6x the maximum registered rate; detectable residues were only observed in samples from the 6.6x rate. **Premise Treatment:** Applications are made as a mist or fog to livestock premises, while the livestock are present; thus, direct livestock contact is occurring.

Secondary Residues: The maximum theoretical dietary burden of Dichlorvos to poultry is calculated to be 6.20 ppm based on a diet consisting of 20% soybeans hulls (15-ppm reassessed tolerance) and 80% wheat grain (4-ppm reassessed tolerance). An adequate feeding study, reflecting dosing of laying hens at 2, 6, and 20 ppm, has been submitted and evaluated. Residues were nondetectable (<0.01 ppm) in tissues and eggs at all dosing levels.

The Reregistration requirements for reduction of residue studies are fulfilled. Adequate cooking studies with meat, egg, milk, dried beans, cocoa beans, coffee beans, and tomatoes have been submitted and evaluated. These studies indicate that Dichlorvos residues decrease during cooking, and that the loss is correlated with time and temperature of cooking. The available cooking data can be translated to similar food products cooked under similar conditions.

Adequate degradation studies with bulk stored raw and processed commodities of dried beans, field corn, flour, oats, peanuts, soybeans, sugar, and walnuts also have been submitted. A decline in the level of Dichlorvos residues was observed in all commodities except peanuts. Walnuts had no detectable residues. Adequate degradation studies with similar packaged and bagged raw and processed commodities were additionally submitted. A decline in the level of

Dichlorvos residues was reported for packaged dried beans and sugar. Although no additional data are required concerning this guideline topic for the purposes of Reregistration, the Agency's risk assessment could be better refined if the registrant provides information concerning the typical length of time commodities remain in storage following treatment. This information would include typical total storage times, frequency of applications, and rates of application (g/1000 cu. ft.).

B. Dietary Exposure Estimates

I. Sources of Residue Data for Estimating Chronic Dietary Exposure to Dichlorvos

Sources of data to estimate the levels of residues of pesticides in food include the following: tolerances (legal limits), controlled field trial data, Food and Drug Administration (FDA) surveillance and compliance monitoring data, FDA Total Diet Study data (market basket survey based on a random sampling of residues on food in grocery stores), US Department of Agriculture (USDA) Pesticide Data Program (PDP), and USDA/FSIS (Food Safety Inspection Service) livestock monitoring data (Hummel, 1998a). The estimated levels of residues can then be adjusted for the effects of processing using processing studies, including commercial processing studies, washing studies, cooking studies, and residue degradation studies. Of these sources, the Agency relied on tolerance levels and field trial data (adjusted for the effects of processing and cooking) to estimate dietary exposure to Dichlorvos in the PD 2/3. For a variety of reasons, the other sources did not provide useful data (Hummel 1994a). In this updated assessment, field trial and monitoring data were used. No monitoring data were available for livestock commodities except milk.

(a). ***Field Trial Data.*** Data from controlled field trials which reflect currently registered uses are available for mushrooms and figs. Data from direct dermal treatments to cattle and poultry are discussed in the Dichlorvos Registration Standard. Field trial data are available for packaged or bagged food, use in food manufacturing and processing facilities, and for secondary residues in livestock commodities. The Agency is including residue estimates for dried figs, even though these tolerances were revoked, because figs may be located in warehouses or areas where similar packaged, bagged, or bulk commodities are treated.

(b). ***FDA Surveillance and Compliance Monitoring Data.*** The FDA Surveillance and Compliance Monitoring Program is designed to ensure that pesticide residues do not exceed established tolerances. Naled and Dichlorvos are included in the FDA surveillance and compliance monitoring programs. However, Dichlorvos is only detected using the Luke method on non-fatty foods, and only when "early eluter" column conditions are used (low column temperature). Thus, the number of samples analyzed for Dichlorvos is low compared to the samples analyzed for other pesticides, although the number of analyses done by FDA that will detect Dichlorvos have increased significantly in the last few years. FDA Surveillance and Compliance monitoring data were obtained from FDA for 1990 through 1996. From 1994

through 1996, FDA analyzed 1471 surveillance monitoring samples for Dichlorvos. The limit of quantitation (LOQ) for Dichlorvos in fruits and vegetables is approximately 0.01 ppm, and the limit of detection (LOD), approximately 0.003 ppm.

All residues reported were non-detectable, with the following exceptions: three samples of strawberries (which had low levels of detectable residues); one tomato sample from Mexico with a trace residue (> LOD, but <LOQ); one sample of garbanzo beans from S. Korea with a trace residue; and 0.03 ppm on one sample of cantaloupe from Honduras. The FDA monitoring data for berries were used in the updated Dichlorvos dietary exposure analysis. Although the FDA monitoring data on other commodities were not used directly in the Dichlorvos dietary exposure assessment, these data are consistent with and support the use of USDA PDP data (see below) for exposure assessment.

(c). *FDA Total Diet Study Data (TDS).* The FDA Total Diet Study Program is designed to measure trends in pesticide residues. Since 1982, approximately four market baskets per year have been collected in a large city in one of four regions of the country. The region of the country in which the market basket samples are collected rotates so that samples are collected in all four regions over one year. FDA summarizes the data expressed as daily intakes for 8 age-sex groups (infants, young children, male and female teenagers, male and female adults, and male and female older persons). Each market basket has consisted of 234-265 individual food items prepared as ready to eat foods (washed and cooked). Individual foods are analyzed separately. Although the TDS includes sampling of meats and poultry, Dichlorvos could not be analyzed in these commodities using the TDS analytical methods. The residue data on which these calculations are based have not yet been published by FDA, but have been made available to The Agency.

Historically, The Agency has not used FDA Total Diet Study data for exposure assessment purposes because the number of samples is limited (approximately four samples per year of each of 234 - 265 individual food items since 1982) and because samples are only collected in large cities, and the treatment history is unknown. The TDS does not include minor crops. However, a total of 43 market basket surveys are now available for 1982 - 1996. Among the commodities collected in the TDS, there were approximately 35 non-fatty commodities analyzed which were similar to crackers and cereals, approximately 11 baked goods which were made from flour, sugar, and dried eggs, 4 coffee and 1 tea commodity, plus raisins, prunes, and cooked eggs. These are commodities that are or are produced from 'bulk stored' and 'packaged and bagged' commodities, and may have been treated with Dichlorvos closer to the point of consumption than the wheat grain samples collected by USDA in their Pesticide Data Program.

By grouping the commodities (generally along crop group classifications), there were more than 100 samples per group of commodities analyzed. The Agency has used extrapolation among members of crop groups in the past when using monitoring data. For example, monitoring data for oranges could be extrapolated to all citrus (tangerines, tangelos, grapefruit, lemons, and limes), provided the use pattern for citrus is the same.

Dichlorvos is not listed specifically as one of the pesticides recovered in the analyses for the FDA Total Diet Study. However, Dichlorvos is known to be detected by the Luke method for non-fatty foods when low column temperatures are used in the analysis ("early eluter" conditions). All of the Total Diet Study samples were analyzed using temperature programming which would allow detection of "early eluters." Therefore, if Dichlorvos were present, it would be detected. The LOD for Dichlorvos in total diet samples is 0.001 ppm (personal communication, B. McMahon, FDA).

(d). ***USDA Pesticide Data Program Data.*** The USDA Pesticide Data Program collects residue data primarily for fresh fruits and vegetables, plus wheat grain and milk. A few canned and frozen commodities have been tested. Samples are collected in terminal markets and large distribution centers. Sampling dates and sites are selected at random following a statistically designed sampling plan. Participating laboratories meet rigorous quality assurance/quality control (QA/QC) criteria including following good laboratory practices (GLP), a check sample program, and confirmation of residue findings. Sampling and analyses are done through a cooperative agreement with nine states and two USDA laboratories. These states represent about 50% of the population of the US and a large percentage of the fresh fruits and vegetables grown in the US. Food commodities collected in the PDP are prepared as normally would be done for consumption, washed and peeled, although not cooked. Canned and frozen commodities are not further cooked before analysis, although they may have been blanched or cooked in the canning or freezing process.

The USDA PDP analyzes for Dichlorvos. The LOD for the analyses varied, depending on the laboratory conducting the analyses, and ranged from 3 ppb to 280 ppb. All samples analyzed for Dichlorvos had non-detectable residues, except for one peach sample analyzed in 1992, which had a residue of 0.059 ppm; one green bean sample analyzed in 1994, which had a residue of 0.012 ppm; one grape sample analyzed in 1996, which had a residue of 0.003 ppm, which was below the LOQ; one milk sample analyzed in 1996, which had a residue of 0.003 ppm, which was below the LOQ; and one pear sample analyzed in 1997, which had a residue of 0.005 ppm, which was below the LOQ. PDP data were used in the Dichlorvos dietary exposure assessment for commodities which could be treated with Naled, and for milk. The PDP data on wheat grain were not used, because packaged and bagged commodities made from wheat grain could have been treated again with Dichlorvos after the PDP samples would have been collected.

(e). ***Processing and Cooking Study Data.*** Residues for raw commodities can be modified by processing factors to account for changes during commercial or other processing and cooking. Processing, cooking and decline (half-life) studies were available for cocoa beans, dry pinto beans, tomato juice, ground roasted coffee beans, raw hamburger meat, raw eggs, and raw whole milk. The resulting cooking factors were used to reduce the Agency's estimate of residues for these commodities and were translated to other commodities based on similarity of cooking time and temperature. Additional cooking studies were available and discussed in the Residue Chemistry Chapter of the Registration Standard. Half-lives of Dichlorvos in various commodities ranged from 0 to over 1,000 hours. The reduction of Dichlorvos upon cooking

appeared to be related to the length of time and temperature used in cooking. Residues were adjusted based on these cooking factors to obtain the ARC.

ii. Anticipated Residues for Dietary (Food) Exposure

Anticipated residues are a realistic estimate of actual pesticide residues in foods based on available data. Reliable data are available for Dichlorvos, including the USDA's PDP data and the FDA Total Diet Study. These data were not available at the time of the PD 2/3, Notice of Intent to Cancel, published in 1995. Anticipated residue values used in the dietary risk assessment are presented in separate memo (Hummel 1998a). The methods for deriving anticipated residues for Dichlorvos are described below.

(a) ***From Use of Dichlorvos.*** For the updated Dichlorvos dietary exposure assessment, FDA Total Diet Study data were used for residues resulting from the use of Dichlorvos per se, where appropriate, by grouping similar commodities made from grain products, sugar, dried eggs, coffee and tea, and dried fruits. These are summarized below.

Raw Agricultural Commodities. The following uses have been canceled: tomatoes, cucumbers, lettuce, and radishes. Therefore, these uses are not included in the exposure assessment.

Meat, Milk, Poultry and Eggs. Residues in livestock tissues, including milk and eggs, may result from consumption of Dichlorvos treated livestock feeds, direct dermal treatments, livestock premise treatments, or from use as a drug in swine. Livestock metabolism studies done at exaggerated rates in ruminants and poultry have demonstrated that oral ingestion of Dichlorvos by cattle and poultry will not result in detectable residues. This conclusion can be extended to the drug use of Dichlorvos in swine. Secondary residues in livestock from consumption of treated feed are expected to be so low that The Agency is estimating these residues as zero. Data reflecting direct livestock treatments are discussed in the Residue Chemistry Chapter of the Dichlorvos Registration Standard. Data from direct dermal studies indicate that detectable residues are not expected, except in skin. Residues are non-detectable (<0.01 ppm) in cattle tissue and milk, and non-detectable (<0.05 ppm) in poultry tissues and eggs. For the PD 2/3 dietary exposure assessment, the Agency used one-half the limit of detection in both cases.

For the updated Dichlorvos dietary exposure assessment, there were no monitoring data available for meat commodities, but PDP data were available for milk. Ratios of residues found in livestock tissues in dermal metabolism studies to residues in milk were calculated. These ratios were then used with the PDP monitoring data in milk to estimate residues of Dichlorvos in livestock tissues. With the exception of eggs, no change was made to the dietary exposure estimates in poultry commodities.

Bulk Stored, Packaged or Bagged Commodities, Food and Feed Handling Uses. The ARCs used in the PD 2/3 exposure assessment for packaged, bagged or bulk stored food were based on field studies submitted by Amvac (Hummel 1994b). Residue data were submitted for many commodities. For those commodities where data were not submitted, the Agency translated residue data from similar commodities. For example, data on dry beans are translated to other legumes; data on wheat flour are translated to all flours and meals, etc. In addition, residue data were provided for corn and oats at various points during processing, and for flour, sugar, dried milk, dried eggs, shortening, and baking mix from a treated manufacturing facility. Bulk stored commodities are assumed to be uncovered when treated. Although pesticide labels state that bulk or unpackaged foods should be covered or removed before spraying, it is not possible to assess the effect of covering food since the type of material used in the cover is not specified and the manner in which food is covered would vary considerably. Therefore, food is assumed to be uncovered, which is likely to overestimate residues. Since the proportion of commodities stored in bulk vs. packaged/bagged is unknown, the ARCs are based on an average of the residues found in bulk and packaged/bagged food for any particular commodity.

FDA TDS data were used for the Dichlorvos dietary exposure assessment on grain products and sugar, eggs, coffee and tea, and raisins and prunes. In the 43 samples of 126 commodities in which Dichlorvos would be detected, only one sample had a detectable residue, one sample of rye bread at 0.01 ppm, which is below the LOQ of 0.03 ppm.

The Food Additive Regulation in 40 *CFR* 185.1900 for packaged or bagged nonperishable processed foods and the tolerance in 40 *CFR* 180.235 for nonperishable packaged, bagged or bulk raw food do not refer to specific commodities. Therefore, the Agency has developed a list of commodities likely to be treated with Dichlorvos that are covered by tolerances and/or Food Additive Regulations. Because these tolerances and Food Additive Regulations were established to cover residues resulting from use at different sites (for example, wheat could be treated in its raw form in a silo, later as flour, during processing into cake mixes, and finally as a stored packaged commodity), cancellation of any one of the site-specific uses does not necessarily eliminate the risk of a commodity from Dichlorvos treatment. The Agency did not combine the residues from different sites in creating the ARCs, although the cumulative residues from treating a commodity at different sites were considered in the estimation of percent of crop treated for the PD 2/3; however, the Agency position has changed. Now we expect that sufficient time will pass between treatments that only the maximum residue from one type of treatment needs to be considered.

(b) ***From Use of Naled.*** All Naled tolerances in 40 *CFR* 180.215 were evaluated as a potential source of Dichlorvos residues. Anticipated residues are based on either tolerance levels or field trials. Naled and Dichlorvos residue estimates were reduced when data were available to account for the effects of washing, cooking, and processing. In addition, wide area application of Naled in mosquito and fly control use could result in residues potentially on all crops in the Agency's Dietary Risk Evaluation System. Therefore, the Agency included all these crops in its estimate of anticipated Dichlorvos residues. Although it is possible that Dichlorvos residues

could occur on any raw agricultural commodity from this use of Naled, it is unlikely that residues would be found on all commodities. As a result, this inclusion of residues of Dichlorvos from all raw crops presents a possible source of overestimation of dietary exposure. As discussed earlier, the Agency does not expect measurable residues from the use of Trichlorfon because it has no tolerances or registered food uses (Hummel, 1998b).

C. Dietary Risk Estimates (Food Sources)

A DEEM analysis was performed to determine acute dietary exposure and risk from Dichlorvos. A DRES analysis was performed to determine dietary exposures and risks for chronic systemic toxicity and cancer from Dichlorvos. Because Dichlorvos residues on food may be derived from either Dichlorvos or Naled, the dietary risk analyses were done for both Dichlorvos and Naled-derived Dichlorvos. No analysis was done for Trichlorfon-derived Dichlorvos because all Trichlorfon tolerances have been revoked, and all food uses have been canceled. The DRES analysis was done for all commodities supported for Reregistration. Two analyses were done: one using tolerance level residues and 100% crop treated and one using anticipated residue values and percent crop treated information, where available.

I. Acute Dietary Exposure and Risk Estimates

Two Tier II acute dietary analyses were performed: one estimating the acute exposure from Dichlorvos from its published tolerances, and the second estimating exposure from Naled-derived Dichlorvos (Steinwand 1998c). For assessing risk from Naled-derived Dichlorvos, Naled residues were converted to Dichlorvos equivalents by multiplying tolerance levels by a factor of 0.58 (Schaible 1994) to reflect the ratio of Dichlorvos's molecular weight (221) to that of Naled (380). The analyses evaluated individual food consumption as reported by respondents in the USDA 1989-91 Continuing Survey of Food Intake by Individuals (CSFII). The acute analysis reflects use of anticipated residues (AR) data for acute dietary exposure (Hummel 1998a). The acute dietary analysis was conducted using the new DEEM software. Results are reported as Margin of Exposure (MOE) for the 95th percentile of the population. The MOE is a measure of how closely the calculated exposure comes to the NOEL (the highest dose at which no effects were observed in the laboratory test), and is calculated as the ratio of the NOEL to the exposure (MOE = NOEL/exposure. A NOEL of 0.5 mg/kg/day (based on the human study) was used for acute dietary risk assessment. For Dichlorvos, the target MOE for the acute dietary analysis is 30 because the NOEL of 0.5 mg/kg/day is from a human study, so the uncertainty factor is 10x for intraspecies variability and 3x for FQPA. All MOEs for acute dietary exposure were above the target MOE of 30 and therefore not of risk concern.

Table 9. Summary of Acute Dietary Risk Assessment for Dichlorvos (based on DEEM software)

DRES Population Subgroup	Dichlorvos		Naled-derived Dichlorvos	
	Acute Exposure, mg/kg/day	MOE (95th %tile)[a]	Acute Exposure, mg/kg/day	MOE (95th %tile)[a]
Total US Population	0.000357	1399	0.002435	205
Nursing Infants < 1 year old	0.000317	1577	0.000205	2437
Non-nursing Infants	0.000680	735	0.003059	163
Children 1-6 years old	0.000623	802	0.004132	121
Children 7-12 years old	0.000436	1147	0.002593	193
Females 20+ years old (potentially childbearing)	0.000240	2087	0.002359	212
Males 20+ years old	0.000280	1783	0.002022	247

[a] Margin of Exposure for the 95th percentile of the population.

ii. Chronic Dietary Exposure

A refined DRES chronic exposure analysis was conducted using percent crop treated data and anticipated residues to calculate the Anticipated Residue Contribution (ARC) for the general population and all subgroups (Steinwand 1998b). Anticipated residues were based on monitoring data from the FDA Total Diet Study and from the USDA's Pesticide Data Program. Therefore, the agency has high confidence in the residue data used to estimate chronic dietary exposure.

As mentioned above, OPP has refined its estimates of dietary exposure for various commodities based on percent of crop treated. Where a range of percent crop treated estimates are supplied for this analysis, the upper end of that range is assumed. The Biological and Economic Analysis Division (BEAD) of OPP provided updated percent of crop treated information that were incorporated into the chronic dietary (food) exposure analysis as appropriate (Steinwand, 1998b). OPP has refined its estimates of dietary exposure for various commodities using processing factors to account for changes in residue levels during commercial or other processing and during cooking.

(a) Chronic Dietary Risk Estimates (% RfD)

A chronic DRES run for all commodities with **existing** Dichlorvos tolerances shows an ARC which represents 1.6% of the RfD for the general US population (Steinwand 1998b). The

ARC for the most highly exposed population subgroup (children ages 1-6) occupies 2.6% of the RfD. A chronic DRES run for all commodities with **proposed** tolerances from the Reregistration tolerance reassessment results in an ARC of < 1% of the RfD for the general US population and 2.3% of the RfD for the most highly exposed population subgroup (children ages 1-6). **In both cases, dietary exposure is below the Agency's level of concern for chronic noncancer risk.**

A chronic DRES run for Naled-derived Dichlorvos shows an ARC which represents less than 0.1% RfD for US and all population subgroups (Steinwand 1998b). **Dietary Exposure to Dichlorvos residues from Naled is below the Agency's level of concern for chronic noncancer risk. The Agency has high confidence in these estimates of chronic noncancer risk.**

Table 10. Chronic Dietary Risk Estimates for Dichlorvos residues in food, % RfD (DRES software).

DRES Population Subgroup	From Dichlorvos		From Naled	
	Exposure, mg/kg/day	% RfD	Exposure, mg/kg/day	% RfD
Total US Population	0.00000125	0.73	<0.000001 (0.000000678)	<1
Infants < 1 year old	0.000001	0.7	<0.000001	<1
Children 1-6 years old (most highly exposed group)	0.000003	2.3	<0.000001	<1
Females 13+ years old	<0.000001	0.6	<0.000001	<1
Males 13+ years old	0.000001	0.7	<0.000001	<1

(b) Dietary Cancer Risk Estimates

The Agency estimated dietary cancer risks for Dichlorvos using the low-dose extrapolation model. Cancer risks were calculated using the following equation:

Extra cancer risk = Q_1^* X ARC Dietary Exposure, where $Q_1^* = 0.272$ $(mg/kg/day)^{-1}$

A chronic DRES run for all commodities with existing Dichlorvos tolerances shows an ARC which results in an upper bound cancer risk estimate of 7.5×10^{-7} (Steinwand 1998b). A chronic DRES run incorporating recommendations of the Dichlorvos tolerance reassessment results in an ARC cancer risk estimate of 3.4×10^{-7} (Steinwand 1998b). The refined ARC cancer risk estimate for Naled-derived Dichlorvos is 1.8×10^{-7}. **The total estimated ARC cancer risk from all food sources of Dichlorvos is 5.2×10^{-7}, which is below the Agency's level of concern. The Agency has high confidence in this estimate of dietary cancer risk.**

D. Drinking Water Exposure

I. Sources of Dichlorvos Residues in Water

Dichlorvos residues can be present as a result of use of three pesticides: Dichlorvos (DDVP), Naled, and Trichlorfon. Dichlorvos is a degradate of Naled and Trichlorfon. The environmental fate and Effects Division (EFED) evaluated the potential for Dichlorvos to contaminate water from these sources. The environmental fate properties of Dichlorvos, Naled, and Trichlorfon are an indicator of the potential of these compound to migrate to ground or surface water. These fate properties are described below.

ii. Fate Properties of Dichlorvos, Naled, and Trichlorfon

(a). Dichlorvos

The major mode of dissipation of Dichlorvos is volatilization from soils because Dichlorvos has a vapor pressure of 1.2×10^{-2} mmHg under field conditions. Also, acceptable laboratory studies indicate rapid dissipation through volatilization. Dichlorvos appears to degrade through aerobic soil metabolism and abiotic hydrolysis as well, but these processes are secondary to volatilization. Hydrolysis is pH dependant where the half-lives were 11 days at pH 5, 5 days at pH 7 and 21 hours at pH 9. Aerobic soil metabolism data showed a half-life of 10 hours; 2,2-dichloroacetic acid was the major metabolite. However, an acceptable soil TLC study (MRID #40279200) indicates that Dichlorvos is moderately mobile (Kd's ranging 0.3 to 1.2) based on the Heiling and Turner's mobility classification. The potential of Dichlorvos to leach to ground water is mitigated by its rapid degradation. However, Dichlorvos has the potential to contaminate surface waters because of a low Koc value and high water solubility (10×10^3 ppm). Substantial fractions of run-off will more than likely occur via dissolution in run-off water rather than adsorption to eroding soil. Dichlorvos should not be persistent in any surface waters due to its susceptibility to rapid hydrolysis.

(b). Naled

Chemical hydrolysis and biodegradation are the major processes involved in the transformation of Naled and its degradates in the environment. Dichlorvos forms from Naled by indirect photolysis in water and soil. In the presence of photosensitizer in water, as much as 20% of the applied dose of Naled can be found as Dichlorvos after 1 day, with rapid decline of Dichlorvos residues afterwards. Under anaerobic aquatic conditions, Dichlorvos can be as high as 15% of the applied Naled dose after 1 day. The degradation of Dichlorvos formed from Naled under anaerobic conditions is slower (half-life 0.9 days) than under aerobic conditions.

(c). Trichlorfon

Dichlorvos is formed from Trichlorfon in both soil and water by aerobic soil metabolism and hydrolysis. Environmental fate data indicate that Trichlorfon degrades rapidly in aerobic soil ($t_{1/2}$ ~ 1.8 days) under non-sterile conditions; however, in a sterile soil, Trichlorfon was stable ($t_{1/2}$ > 40 days). Abiotic hydrolysis studies indicate that Trichlorfon degrades rapidly in aqueous media and that the rate of hydrolysis is pH dependent. The estimated hydrolysis half-life of Trichlorfon is 31 minutes at pH 7, and 34 hours at pH 9, and 104 days at pH 5. This indicates the stability of Trichlorfon to hydrolysis under acidic conditions. The maximum amount of Dichlorvos formed from Trichlorfon by aerobic aquatic metabolism is approximately 56 percent of the amount of Trichlorfon originally applied at pH 8.5. This value was chosen because it maximizes the application rate for Dichlorvos and provides a conservative estimate for potential groundwater contamination.

iii. Groundwater

EFED has limited monitoring data on the concentrations of Dichlorvos, Naled or Trichlorfon in groundwater. Validated monitoring data for Dichlorvos, Naled, and Trichlorfon are available for the states of California and Hawaii from the Pesticides in Groundwater Database (USEPA 1992). These data indicated that Naled, Dichlorvos, or Trichlorfon have not been detected in groundwater. These data were not targeted to the pesticide use area. These data are presented in Table 11 below.

Table 11. Groundwater monitoring data for Dichlorvos, Naled, and Trichlorfon showing number of wells sampled (number of wells with residues) (USEPA 1992)

	Naled	Dichlorvos	Trichlorfon
California	83 (0)	20(0)	280 (0)
Hawaii	3 (0)	7 (0)	

Because the groundwater monitoring data for Dichlorvos are limited, EFED used the Tier I **SCI-GROW** screening model to estimate concentrations of Dichlorvos in groundwater. This model shows that Naled, Trichlorfon, or Dichlorvos will not be found in significant concentrations in groundwater. Concentrations of these compounds were calculated based on a maximum annual application rate of 9.375 lb a.i/acre for Naled (the use rate on Cole crops), 8.17 lb a.i./acre for Trichlorfon (turf), and 0.2 lb a.i./acre for Dichlorvos (turf). The amount of Dichlorvos formed as a degradate of Naled was estimated to be 20% of Naled. Therefore, a conservative Dichlorvos use rate was estimated by using Naled's use rate multiplied by 0.20. The amount of Dichlorvos formed as a degradate of Trichlorfon was estimated to be 56% of Trichlorfon, which is the maximum percent of Dichlorvos (56%) formed as a Trichlorfon degradate determined from the Trichlorfon aerobic aquatic metabolism at pH 8.5. The amount of Dichlorvos formed as a Trichlorfon degradate was estimated by multiplying the maximum application rate for Trichlorfon (8.17 lab a.i/acre) by 56%. The groundwater concentrations estimated from the modeling agree with limited existing groundwater monitoring data for these

compounds. Because groundwater concentrations of Dichlorvos were estimated using a Tier I screening model, EFED has moderate confidence in the groundwater assessment.

Table 12. Estimated Dichlorvos Concentrations in Groundwater.

Source of Dichlorvos Residues	Modeled Groundwater Concentration, µg/L
Dichlorvos Applied 1/week	0.004
Dichlorvos Applied Every Other Day	0.015
Dichlorvos (from Naled)	0.0002
Dichlorvos (from Trichlorfon)	0.002

There may be exceptional circumstances under which groundwater concentrations could exceed the SCI-GROW estimates. However, such exceptions should be quite rare since the SCI-GROW model is based exclusively on maximum groundwater concentrations from studies conducted at sites and under conditions which are most likely to result in groundwater contamination. The groundwater concentrations generated by SCI-GROW are based on the largest 90-day average recorded during the sampling period. Since there is relatively little temporal variation in groundwater concentrations compared to surface water, the concentrations can be considered as acute and chronic values.

iv. Surface Water

Dichlorvos may reach surface water as a result of use of three pesticides: Dichlorvos (DDVP), Naled and Trichlorfon. In the event that all of these pesticides are used in the same use area, then the contribution for each chemical should be incorporated in any risk assessment.

OPP does not have any surface water monitoring data on the concentrations of Dichlorvos, Naled, or Trichlorfon at the present time. Therefore, the GENEEC model was used to estimate surface water concentrations for Naled, Trichlorfon and Dichlorvos. GENEEC is a Tier I model used to screen pesticides to determine which ones potentially pose risk to warrant higher level modeling (Parker et al. 1995). The GENEEC model provides upper-bound values on the concentration that might be found in ecologically sensitive environments due to the use of pesticides. GENEEC is a single event model that simulates one runoff event, but it can account for spray drift from multiple applications. GENEEC represents a 10 hectare field immediately adjacent to 1 hectare pond that is 2 meters deep with no outlet. The pond receives a spray drift event from each application plus one runoff event. The runoff event moves a maximum of 10% of the applied pesticide into the pond. This amount can be reduced due to degradation on the field and by soil sorption. Spray drift is estimated at 5% of the application rate.

Turf was used as the site of interest for Trichlorfon. General outdoor uses (including turf) were used as the site of interest for Dichlorvos. Eight crops were simulated for Naled. The modeling results indicate that all these compounds have the potential to contaminate surface waters by runoff, for short periods of time especially in areas with large amounts of annual rainfall. However, based on its environmental fate characteristics, Naled will degrade/dissipate rapidly ($t_{1/2}$ < 1 day), Trichlorfon and Dichlorvos will persist slightly longer ($t_{1/2}$ 1.4 and ~ 5 days, respectively). Mitigation practices that reduce runoff could be effective in reduction of these chemicals transport into surface waters.

Table 13. Estimated Drinking Water Exposure to Dichlorvos based on GENEEC Model		
Source of Dichlorvos Residues	Acute Surface Water Concentration, µg/L (ppb)	Chronic Surface Water Concentration, µg/L (ppb)
Dichlorvos	0.435	0.060
Naled-derived Dichlorvos	16.5	2.2
Trichlorfon-derived Dichlorvos	194	26

E. Drinking Water Risk Estimates

I. Drinking Water Levels of Comparison

HED has calculated drinking water levels of comparison (DWLOCs) associated with acute, chronic, and lifetime exposure to Dichlorvos in drinking water. These DWLOCs will be compared with the estimated environmental concentrations of Dichlorvos in water. The DWLOC is the concentration of a chemical in drinking water that would be acceptable as an upper limit in light of total aggregate exposure to that chemical from food, water, and residential sources. The acute and cancer DWLOCs for Dichlorvos include aggregate exposure from food and water only. The chronic DWLOC includes residential exposure.

The $DWLOC_{acute}$ was calculated to be for the general population and for children age 1-6 years, who are the most highly exposed population subgroup. Acute water exposures and DWLOC calculations are summarized in Table 14 below. The acute oral NOEL of 0.5 mg/kg/day for Dichlorvos was used to calculate the $DWLOC_{acute}$ using the following formula:

$$DWLOC_{acute} = \frac{\text{acute drinking water exposure (mg/kg/day) X body weight (kg)}}{\text{water consumption (L/day) X } 10^{-3} \text{ mg/µg}} = \text{µg/L}$$

where body weight is 70 kg for adults and 10 kg for children, and water consumption is 2 L/day for adults and 1 L/day for children,

and

where acute water exposure (mg/kg/day) = [Acute NOEL (mg/kg/day) ÷ target MOE] - [95th%tile acute dietary exposure, mg/kg/day]

Table 14. Summary of $DWLOC_{acute}$ Calculations for Dichlorvos.					
DEEM Population Subgroup	Acute Dietary Exposure at 95th %tile, mg/kg/day			Allowable Water Exposure, mg/kg/day	$DWLOC_{acute}$, µg/L
	Dichlorvos	Naled-Derived Dichlorvos	Total Dichlorvos		
US Population	0.000357	0.002435	0.002792	0.01387	485
Children age 1-6	0.000623	0.004132	0.004755	0.01191	119

The RfD of 0.00017 mg/kg/day for Dichlorvos was used to calculate a $DWLOC_{chronic}$ for Dichlorvos, using the following formulas:

$$DWLOC_{chronic} = \frac{\text{(chronic water exposure, mg/kg/day)(body weight)}}{\text{(water consumption, L/day)}(10^{-3}\ \text{mg/µg})} = \text{µg/L}$$

where body weight and water consumption values are as given above
and chronic water exposure = RfD - (chronic food + residential exposure).

The same NOEL (0.05 mg/kg/day) and uncertainty factor (300) are used for both chronic inhalation and chronic dietary risk assessment, so it is appropriate to use the chronic RfD in the exposure calculation. Chronic water calculations are summarized in Table 15 below.

Table 15. Summary of $DWLOC_{chronic}$ Calculations for Dichlorvos.						
DRES Population Subgroup	Chronic Dietary Exposure, mg/kg/day			Chronic Inhalation Exposure, mg/kg/day	Allowable Water Exposure, mg/kg/day	$DWLOC_{chronic}$, µg/L
	Dichlorvos	Naled-Derived Dichlorvos	Total Dichlorvos			

US Population	1.25 X10^{-6}	6.78 X 10^{-7}	1.9310^{-6}	0.047	- 0.04683193	zero
Children age 1-6	1 X 10^{-6}	<1 X 10^{-6}	<2 X 10^{-6}	0.125	-0.124832	zero

Note: Chronic inhalation exposure estimates are based on residential exposure to the Dichlorvos resin strip from Table 16.

The **$DWLOC_{cancer}$** for Dichlorvos was calculated using the following formula:

$$DWLOC_{cancer} = \frac{\text{(chronic water exposure, mg/kg/day)(body weight)}}{\text{(water consumption, L/day)}(10^{-3}\ \text{mg}/\mu\text{g})} = \mu g/L$$

where chronic water exposure = $\frac{1X\ 10^{-6}}{Q_1^*\ \text{of}\ 2.72\ X\ 10^{-1}\ (\text{mg/kg/day})^{-1}}$ - total dietary exposure

$$= 3.7\ X\ 10^{-6} - 1.93\ X\ 10^{-6} = 1.772\ X\ 10^{-6}\ \text{mg/kg/day}$$

and water consumption is 2 L/day, and body weight is 70 kg.

$$\text{Therefore, } DWLOC_{cancer} = \frac{[(1.77\ X\ 10^{-6}\ \text{mg/kg/day})(70\ \text{kg})]}{[(2\ L)(10^{-3}\ \text{mg}/\mu g)]} = 0.062\ \mu g/L$$

The $DWLOC_{cancer}$ was only calculated for oral exposures because the Agency does not have a concern for carcinogenicity following inhalation or dermal exposures.

DWLOCs were not calculated for short or intermediate term exposure. Because the short and intermediate term residential exposure scenarios are associated with risks of concern, the DWLOCs would effectively be zero. Further, food and water exposure are negligible compared to the residential exposure.

ii. Drinking Water Risk Estimates

As mentioned above, the acute, chronic, and cancer DWLOCs are compared with the estimated environmental concentrations of Dichlorvos in water to determine if there is a risk concern,

For acute drinking water exposure, both the modeled groundwater concentrations of 0.0002 to 0.015 ug/L and the modeled surface water concentrations of 0.4 to 194 µg/L are less than the $DWLOC_{acute}$ of 485 µg/L for adults but exceed the DWLOC acute of 119 µg/L for children 1-6. Conservative, Tier I, estimates of drinking water concentration provided by the SCI-GROW are not of risk concern. However, the surface water value of 194 µg/L from the GENEEC models indicates a potential risk concern for children 1-6.

For chronic drinking water exposure, the modeled groundwater concentrations of 0.0002 to 0.015 µg/L exceed the $DWLOC_{chronic}$ of 0 µg/L. The modeled surface water concentrations of Naled and Trichlorfon-derived Dichlorvos (2.2 and 26 µg/L, respectively) also exceed the $DWLOC_{chronic}$ of 0 µg/L. The $DWLOC_{chronic}$ value is driven by the chronic residential inhalation exposure to Dichlorvos from resin strips. As mentioned above, food and water exposure to Dichlorvos is negligible compared with residential exposure. Therefore, any water exposure will add to exposures and risks of concern.

For lifetime drinking water exposure, the modeled ground water concentration of 0.015 µg/L is below the $DWLOC_{cancer}$ of 0.062 µg/L, but the modeled surface water concentration of 0.06 to 26 µg/L are equal to or greater than the $DWLOC_{cancer}$ of 0.062 µg/L.

F. Occupational Exposure and Risk Estimates

Workers may be exposed to Dichlorvos during the following scenarios: crack and crevice treatment by certified pest control operators, coarse spray application to mushroom houses and greenhouses, worker re-entry to mushroom houses and greenhouses, application to domestic animals, such as cattle or poultry, application to domestic animal premises, such as dairy barns, re-entry into domestic animal premises, application to feedlots, application to manure piles, application to ornamental lawns, turf, and plants, and post-application gardening work with ornamental lawns, turf, and plants. Occupational exposure and risk estimates are presented in Table 16 below.

I. Crack and Crevice Treatment in Homes

(a). Application

Exposure and risk analysis was conducted for commercial applicators only (Jaquith 1998f). There are no registered concentrate products for homeowner uses. It was assumed that applicators wear coveralls, chemical resistant gloves, and shoes. Information obtained from the National Pest Control Association (NPCA) indicated that Dichlorvos is used only 1 day per week, resulting in a short term dermal exposure scenario. For short term dermal and inhalation exposure, an MOE of 10 is adequate since a NOEL of 0.5 mg/kg/day from a human study was used for risk assessment. Aggregate exposure and risk were calculated by adding inhalation and dermal dose and comparing the resulting total exposure with the oral NOEL.

Exposure estimates for crack and crevice treatment with Dichlorvos were obtained from PHED (V1.1). It was assumed that a commercial applicator will treat 10 homes with Dichlorvos in a day, which is probably a conservative assumption. The dermal dose was estimated to be 0.0094 mg/kg/day (MOE=53) and the inhalation dose was estimated to be 0.0091 mg/kg/day (MOE=55). The dermal, inhalation, and total MOEs are considered to be acceptable. All MOEs for crack and crevice treatment in homes (by certified pest control operators) are >10.

ii. Mushroom House

(a). Application

Application of Dichlorvos to mushroom houses is restricted to coarse spray and paint-on applications only. The Registrant has recently submitted a request for voluntary deletion of the hand-held fogger use under FIFRA Section 6(f). The exposures were derived from PHED (V1.1) and estimates of the surface areas that would be painted or sprayed during Dichlorvos application. These estimates were derived from mushroom culture textbooks and are considered to be conservative (Jaquith 1998d and n). This application scenario is considered to be intermediate term because a single individual may treat different mushroom houses on different days due to the cyclic nature of mushroom culture. The toxicological endpoint for intermediate term dermal and inhalation exposure is a LOEL of 0.1 mg/kg/day from a repeated dose human study. An MOE of 30 is required for both intermediate term dermal and inhalation exposure since a LOEL from a human study was used (10x for intraspecies, ~3x for LOEL rather than NOEL).

The inhalation exposures ranged from 0.0015 to 0.0045 mg/kg/day (MOEs of 11 to 33) and dermal exposures ranged from 0.0014 to 0.022 mg/kg/day (MOEs of 71 to 4.5), depending on application equipment (Jaquith 1998n). Dermal, inhalation, and total MOEs < 30 are considered to be of concern; specifically, the Agency has a risk concern for scenarios involving use of a backpack sprayer and a portable sprayer on a cart.

(b). Post-application

The post-application exposures for mushroom houses were derived from information from a textbook on mushroom culture and a study conducted by CDFA (Now CALEPA) in which air and surface residues were measured in mushroom houses where Dichlorvos had been applied (Maddy 1981, Jaquith 1998d). Because of the aeration pattern of mushroom houses, the volatility of Dichlorvos, and dissipation of Dichlorvos in mushroom houses, this is considered to be a short-term exposure scenario. As stated above, a NOEL of 0.5 mg/kg/day is used for both dermal and inhalation risk assessment. An MOE of 10 is required for both dermal and inhalation exposure. The doses following a 24 hour reentry period were 0.0015 mg/kg/day (MOE=333) and 0.0049 mg/kg/day (MOE=102) for the dermal and inhalation routes, respectively. Respirators are not worn during reentry. The dermal, inhalation, and total MOEs are considered to be acceptable.

iii. Greenhouse

(a). Application

Application of Dichlorvos to greenhouse plants was previously allowed by hand-held foggers and by smoke generators. The Registrant has recently submitted a request for voluntary deletion of the hand-held fogger use under FIFRA Section 6(f). Total release foggers and smoke generators are considered to result in negligible exposure since the applicator vacates the premises immediately upon activation of the foggers.

(b). Post-application

The reentry interval for greenhouses following the use of Dichlorvos was obtained using data from a greenhouse culture textbook and a transfer coefficient from a study found in the scientific literature (Van Hemmen 1992). Because of the volatile nature of Dichlorvos, this is considered to be a short-term exposure scenario. The oral NOEL of 0.5 mg/kg/day from an acute human study and 11% dermal absorption were used for the dermal risk assessment. The same oral NOEL of 0.5 mg/kg/day is used for inhalation risk assessment. An MOE of 10 is required since the NOEL is from a human study.

The exposures after 10 hours were estimated to be 0.0023 mg/kg/day (MOE=210) via the dermal route and 0.000097 mg/kg/day (MOE=5100) by inhalation. Both inhalation and dermal MOEs are considered to be acceptable when re-entry occurs 10 hours after application of Dichlorvos.
The MOE for total exposure (with re-entry at 10 hours) is 208, which is considered to be acceptable.

iv. Domestic Animal Premises (food and nonfood) and Direct Animal Sprays, Feedlots, Manure Treatment, Garbage Dumps, and Baits

(a). Application

Dairy barn application and direct application to cattle were used as the reference facility for these exposure assessments (Jaquith 1998l). There are no data addressing the use of Dichlorvos in other types of animal facilities. Worker exposure from direct application to animals is based on dairy cattle treatment. A one percent solution of Dichlorvos is applied with a handheld sprayer to an average herd of dairy cattle consisting of 65 head, each requiring 24 seconds to spray, two times per day during treatment. Applicators were assumed to wear long sleeve shirts, long pants, and gloves. Fly control is required from May to October with application occurring weekly during this time (26 times per year). Although permitted on product labels, the Agency does not believe that direct application with a handheld sprayer is used. Rather, some type of automated equipment is used to apply Dichlorvos directly to animals.

Space and premise treatments also help control insects on animals. Since several registered products provide guidance on use with a handheld sprayer, the exposure and risk are estimated here for that application method, which is expected to result in a much higher exposure than automated methods. While some labels indicate that daily application (probably for direct application to cattle) is allowable, the use assessment indicates that the material is applied at 2 week intervals. This is considered to be an intermediate term scenario, and a LOEL of 0.1 mg/kg/day from a repeat dose human study is used for both dermal and inhalation risk assessment. A dermal absorption factor of 11% is also used for dermal risk assessment. An MOE of 30 is considered acceptable for both inhalation and dermal exposure (10x for intraspecies variation and ~3x for use of a LOEL).

Exposure assessments for direct application to dairy cattle using hand-held sprayers were conducted using PHED V1.1. Dermal doses were estimated to range from 0.000024 to 0.0037 mg/kg/day (MOE= 27 to 4200) and respiratory doses from 0.000037 to 0.00010 mg/kg/day (MOE= 1000 to 2700), depending on application equipment. Inhalation, dermal, and total MOEs are considered to be acceptable. Risks from Dichlorvos application to domestic animal premises are also acceptable (Table 16). There are no data addressing potential reentry into animal facilities.

v. Ornamental Lawns, Turf, and Plants

(a). Applicator

There are no chemical specific usage data addressing the potential exposures of commercial lawn care operators to Dichlorvos. There are no registered homeowner uses. The material is applied only in tank mixtures with Chlorpyrifos. The types of equipment used and clothing worn by lawn care operators is likely to be similar to that used/worn by workers applying the material to dairy barns. Because of the enclosed nature of a barn versus an open lawn area, this would probably be conservative. The exposures and risks are considered to be similar to those for dairy barn treatments.

vi. Warehouse Treatment

(a). Application

Dichlorvos can be applied to warehouses with wall-mounted automatic foggers. Exposure to mixer/loaders through automatic application is expected to be negligible; however, there would still be reentry exposure.

(b). Post-application

In estimating reentry exposure, EPA assumed 6 hours elapsed before reentry is allowed, as required on labels; and that workers spend 8 hours per day in the treated area for the next 3

days. Dichlorvos is applied at the rate of 2.0 grams active ingredient per 1,000 ft^3 over a period of 125 minutes per application. Exposure estimates are for the day following treatment. Dermal exposure was measured for the hands only and represents an average of the total exposure measured for three work stations. This exposure scenario was considered to be short term due to rapid dissipation of Dichlorvos. Therefore, a NOEL of 0.5 mg/kg/day from the acute human study was used for the short term inhalation and dermal risk assessments and an 11% dermal absorption were used for dermal risk assessment. An MOE of 10 is required.

The dermal exposure estimate was 0.000029 mg/kg/day (MOE = 17000) and inhalation exposure was 0.18 mg/kg/day (MOE =2.8). The dermal MOE is considered to be acceptable, but the inhalation MOE is of concern. The total MOE of 2.8 is also of concern.

vii. Insect Traps

Exposure is believed to be negligible since the pesticide is in the form of an impregnated strip and the traps are placed in outdoor areas (such as forests) where there is no human exposure.

G. Residential Exposure and Risk Estimates

Dichlorvos is registered for several residential uses. Resident handlers may be exposed to Dichlorvos during application of Dichlorvos in pressurized aerosol spray cans. Residential post application exposure may occur after use of the following products containing Dichlorvos: pressurized aerosol spray can, total release fogger, crack and crevice treatment, resin pest strips, and pet flea collars. Residential Exposure and Risk Estimates are summarized in Table 16 below. Exposure estimates are based on several sources of information. Information sources and major assumptions for each residential scenario are described below. Additional information is available in the referenced documents (Jaquith 1998a through n).

I. Residential Handler

(a). Pressurized Aerosol Spray Can

The exposure assessment for pressurized spray cans was derived from data in the Pesticide Handlers Exposure Database (PHED V1.1). Resident use of pressurized aerosol product is based on application of an entire 16 ounce pressurized aerosol can of one percent Dichlorvos (Jaquith 1998f). This is considered to be a short term exposure scenario. A NOEL of 0.5 mg/kg/day from an acute human study is used for inhalation and dermal risk assessment. Also, 11% dermal absorption is assumed for the dermal risk assessment. A dermal MOE of 30 is required (10x for intraspecies variability and 3x FQPA safety factor).

The Agency estimated the risk to residents for different clothing scenarios. Pressurized aerosol products containing Dichlorvos do not list any clothing requirements, therefore the

Agency is assuming that Dichlorvos is applied during hot weather when an individual will be wearing the least amount of clothing (ie, shorts and shoes) with a dermal exposure of 0.0038 mg/kg/day (MOE = 132). Respiratory exposure was estimated to be approximately 79 ng/kg/day (MOE = 633). Inhalation, dermal, and total MOEs are considered to be acceptable.

ii. Residential Post-application

Indoor post application exposures for all scenarios were obtained from a single study measuring the exposures of individuals performing defined activity patterns following the activation of a total release fogger. This study was intended to be used as a conservative estimate for all types of indoor applications (Jaquith 1993b). The multi-phase study measured deposition on whole body dosimeters and (in a separate phase) the urinary concentrations of the metabolite DMP. In order to estimate the potential oral exposure from hand to mouth activity of children, the amount of Dichlorvos measured on the hands in the passive dosimetry phase was considered to be available for ingestion. The total exposure, including the estimated contribution of hand to mouth ingestion, was 0.015 mg/kg/day (Jaquith 1998e). This is considered to be a short-term exposure scenario, so an oral NOEL of 0.5 mg/kg/day from an acute oral human study is used for risk assessment. An MOE of 30 is required (10x for intraspecies extrapolation, 3x FQPA safety factor). The total exposure from the biomonitoring phase, plus amount of Dichlorvos measured on the hands in the dosimetry phase, was compared to the oral NOEL. The resulting MOE for short term exposure was 33, which is considered to be acceptable. It is recognized that this may be a conservative estimate for other Dichlorvos uses such as directed applications (crack and crevice treatments).

(a). Resin Pest Strips

Respiratory exposures resulting from the use of resin pest strips were estimated using a study found in the scientific literature (Collins and DeVries 1973). Fifteen homes were monitored for a period of 91 days. A decay curve measuring the decline of airborne residues was derived for each of these homes. The resulting equations were integrated over a 120 day period and an average daily concentration was calculated (Jaquith 1998a and b). It was assumed that an individual was present in the home for 16 hours per day, as recommended by the July 30, 1998 FIFRA Science Advisory Panel (Lewis 1998). The inhalation NOEL of 0.05 mg/kg/day from a chronic rat study was used to calculate the risks for this exposure scenario because exposure is expected to occur primarily via inhalation. An MOE of 300 is required (10x intraspecies variation, 10x interspecies variation, 3x FQPA safety factor).

Exposure estimates and MOEs were calculated for 4 population groups; adult males, adult females, children, age 1-4 years; and children, age 5-11 years. The average exposures were 0.0022 mg/kg/day (MOE=29), 0.0019 mg/kg/day (MOE=34), 0.0058 mg/kg/day (MOE=11), and 0.0039 mg/kg/day (MOE=16), respectively. These MOEs are all of concern.

(b). Pet Flea Collars

The assessment for flea collar exposure was derived from a study submitted by a previous registrant. There were a number of technical problems with that study and it is considered a weak data set (Jaquith 1987) . The inhalation NOEL of 0.05 mg/kg/day from a chronic rat study was used for inhalation risk assessment. An MOE of 300 is required. It was assumed that an individual spends 1 hour per day in close proximity to an animal wearing a flea collar and 8 hours per day in the general area (Jaquith 1998c). There are no data with which to estimate dermal exposure from contact with pets. Respiratory exposures were estimated for 7 population groups; adult males; adult females; children, age 1-2; children, age 3-5; children, age 6-8; males, age 9-11; and females, age 9-11. The corresponding exposures were 0.0015 mg/kg/day (MOE=33), 0.0013 mg/kg/day (MOE=38), 0.0037 mg/kg/day (MOE=14), 0.0033 mg/kg/day (MOE=15), 0.0027 mg/kg/day (MOE=19), 0.0026 mg/kg/day (MOE=19), and 0.0023 mg/kg/day (MOE=22). These MOEs are all of concern.

(c). Ornamental Lawns, Turf and Plants - Post-Application

The assessment was obtained by using dislodgeable foliar residue information from a study found in the scientific literature and a registrant submitted study measuring the exposures of individuals performing defined activities on carpets following the activation of a total release fogger (Jaquith 1998h). The dislodgeable foliar residue study indicated that residues declined rapidly, resulting in a short term exposure scenario; therefore, the NOEL of 0.5 mg/kg/day from an acute human study was used for risk assessment. An MOE of 30 is required. Inhalation exposure was considered to be negligible due to rapid dissipation of Dichlorvos under these conditions. Since lawn care products are intended to be used in a residential/park setting, an exposure interval of 3 hours was used for this assessment. This approximates the amount of time required for drying of the spray, which is a label requirement before reentry in some cases.

To account for the possibility of oral exposure resulting from accidental exposure due to hand to mouth activity it was assumed that the material detected on the hands of individuals during the passive dosimetry phase of the indoor study would be available for oral exposure (Jaquith 1998h). These were added to the exposure estimates from biological monitoring during activity to yield a total exposure. The estimated exposures for a scenario where activity occurs for 20 minutes was 0.002 mg/kg/day (MOE=250). If the activity pattern is extrapolated to 1 hour of activity, which is conservative, the exposure becomes 0.006 mg/kg/day (MOE=83). These MOEs are not of concern.

Table 16. Summary of Occupational/Residential Exposure and Risk Estimates for Dichlorvos							
USES	NOTES	EXPOSURE PATTERN[1]	Current Exposure (mg/kg/day)		Current MOE/ Acceptable MOE[1]		
			Dermal	Inhalation	Dermal	Inhalation	Total
RESIDENTIAL HANDLER	2						
Pressurized aerosol spray can	3	Short-term	0.0038	7.90e-05	132/30	6330/30	128/30
RESIDENTIAL POST-APPLICATION							
Total release fogger	4	Short-term	0.015	Included in the dermal dose from a biomonitoring study	33/30	Included in the dermal dose from a biomonitoring study	33/30
Pressurized aerosol	5	Short-term					
Crack and crevice treatment	6	Short term					
Resin pest strips	7	Long-term, Inhalation Only	N/A	Adult Male 0.047	N/A	1.1/300	1.1/300
			N/A	Adult Female 0.040	N/A	1.2/300	1.2/300
				Child, 1-4 0.125	N/A	0.4/300	0.4/300
			N/A	Child, 5-11 0.085	N/A	0.6/300	0.6/300

Table 16. Summary of Occupational/Residential Exposure and Risk Estimates for Dichlorvos							
USES	NOTES	EXPOSURE PATTERN[1]	Current Exposure (mg/kg/day)		Current MOE/ Acceptable MOE[1]		
			Dermal	Inhalation	Dermal	Inhalation	Total
Pet flea collars	8	Long-term, Inhalation Only	No Data	Adult Male;0.0015	N/A	33/300	33/300
				Adult Female;0.0013	N/A	38/300	38/300
				Child, 1-2;0.0037	N/A	14/300	14/300
				Child 3-5;0.0033	N/A	15/300	15/300
				Child 6-8; 0.0027	N/A	19/300	19/300
				Male 9-11; 0.0026	N/A	19/300	19/300
				Female, 9-11; 0.0023		22/300	22/300
Ornamental lawns, turf and plants Post-application	19	Short-term	0.002	Negligible	250/10	N/A	250/10
			0.006	Negligible	83/10	N/A	83/10
OCCUPATIONAL EXPOSURE	9						
Crack & crevice treatment in homes	10	Short-term	0.0094	0.0091	53/10	55/10	27/10
Mushroom house	11						
Applicator, Coarse Spray		Intermediate					
Hand Held Sprayer			0.0014	0.0015	71/30	67/30	34/30
Backpack Sprayer (471)			0.022	0.0015	4.5/30	67/30	4.2/30
Backpack Sprayer (416)			0.0023	0.0036	43/30	28/30	17/30
Portable Sprayer on Cart			0.0058	0.0045	17/30	22/30	10/30
Reentry (24-hour REI)		Short-term	0.0015	0.0049	333/10	102/10	78/10

Table 16. Summary of Occupational/Residential Exposure and Risk Estimates for Dichlorvos							
USES	NOTES	EXPOSURE PATTERN[1]	Current Exposure (mg/kg/day)		Current MOE/ Acceptable MOE[1]		
			Dermal	Inhalation	Dermal	Inhalation	Total
Greenhouse	12						
Applicator		Short-term	N/A: Hand Held Application voluntarily canceled; total release foggers negligible				
Reentry (10-hour REI)		Short-term	0.0023	0.000097	210/10	5100/10	210/10
Domestic food/nonfood animals (non-poultry)	13	Intermediate					
Hand Held Sprayer			0.000024	0.000037	4200/30	2700/30	1600/30
Backpack Sprayer (471)			0.0037	0.000037	27/30	2700/30	27/30
Backpack Sprayer (416)			0.000039	0.000083	2600/30	1200/30	820/30
Portable Sprayer on Cart			0.00010	0.00010	1000/30	1000/30	500/30
Domestic food/nonfood animals (poultry)	14	Intermediate	No data; not expected to exceed dairy barn				
Domestic animal premises (food and non-food) (Dairy barns)	15	Short-term					
Applicator							
Hand Held Sprayer			0.000009	0.000013	56000/10	38,000/10	23,000/10
Backpack Sprayer (471)			0.0013	0.000013	380/10	38,000/10	380/10
Backpack Sprayer (416)			0.000014	0.00003	36000/10	17,000/10	11,000/10
Portable Sprayer on Cart			0.000036	0.000036	14000/10	14,000/10	6,900/10
Reentry			No data	No Data	N/A	N/A	N/A
Granular and liquid baits		Short-term	No data for liquids, not expected to exceed dairy barns. Granular baits, negligible exposure.				

Table 16. Summary of Occupational/Residential Exposure and Risk Estimates for Dichlorvos							
USES	NOTES	EXPOSURE PATTERN[1]	Current Exposure (mg/kg/day)		Current MOE/ Acceptable MOE[1]		
			Dermal	Inhalation	Dermal	Inhalation	Total
Feedlots	16	Short-term	No data; not expected to exceed dairy barns				
Manure	17	Short-term	No data; not expected to exceed dairy barns				
Ornamental lawns, turf and plants Applicator	18	Short-Term	No data; not expected to exceed dairy barns				
Ornamental lawns, turf and plants Post-application	19	Short-term	0.002	Negligible	250/10	N/A	250/10
			0.006	Negligible	83/10	N/A	83/10
Warehouse treatment	20						
Applicator		Short-term	Handheld foggers deleted; exposure and risk from automatic foggers is negligible				
Reentry		Short-term	0.000029	0.18	17000/10	2.8/10	2.8/10
Insect traps	21	Short-term	Negligible				
Garbage dumps	22	Short-term	No data; not expected to exceed dairy barns				

NOTES: The following notes define the assumptions used in calculating the margins of exposure.

1. Doses and toxicological endpoints for short term dermal and inhalation occupational and residential risk assessments are based on an oral NOEL of 0.5 mg/kg/day from an acute human study; intermediate term dermal and inhalation occupational and residential risk assessments are based on a LOEL of 0.1 mg/kg/day from a repeated dose human study. Based on the use pattern, long-term dermal risk assessment is not required. The long-term inhalation risk assessment is based on a NOEL of 0.05 mg/kg/day from a chronic inhalation study in rats.

   For occupational dermal and inhalation exposures, the target MOEs are 10 and 30 for short and intermediate term risk assessments, respectively, and 100 for long-term inhalation exposure. For residential dermal and inhalation exposures, the target MOEs are 30 and 100 for short and intermediate terms, respectively and 300 for long-term inhalation exposures; the residential exposure MOEs include the 3x FQPA Safety Factor.

2. An average resident applicator weighs 70 kg and has a respiratory volume of 1.5 m^3 /hour (PHED default value). No protection from clothing is assumed.

3. Resident use of pressurized aerosol product is based on application of an entire 16 ounce can of 0.5 percent Dichlorvos pressurized aerosol (0.005 lb ai). EPA estimated the risk to residents for different clothing scenarios. The dermal MOE of 132 assumes the resident is wearing only shorts and shoes. Pressurized aerosol products containing Dichlorvos do not have any clothing requirements, therefore EPA is assuming that Dichlorvos is applied during hot weather when an individual will be wearing the least amount of clothing. Surrogate data from PHED V1.1 and a dermal absorption factor were used to estimate dermal exposure. The risk assessment is based on application by a 70 kg male.

4. Based on biomonitoring data (blood samples) and represents the dose to the individual rather than exposure. Estimate of oral exposure obtained by assuming that all material on hands (from passive dosimetry data) is available for ingestion. The values reflect total absorbed dose and are based on biomonitoring data (urinary excretion of DMP). Children, performing the same activities as adults were considered to have the same exposure on a mg per kg basis.

5. Same as for fogger.

6. Same as for fogger.

7. Assumes 365 days of exposure per year, 16 hours per day. A time weighted average concentration, derived from integration of decay equations for Dichlorvos in homes, was used to estimate daily exposure (Jaquith 1998g).

8. Assumes 365 days of exposure per year, 1 hour in close contact to animal, 8 hours casual exposure per day (Jaquith 1998i).

9. An average worker weighs 70 kg and has a respiratory volume of 1.5 m^3 /hour. Therefore, a variety of scenarios are presented for these three uses. At a minimum, the following protective clothing was used in the exposure scenarios: gloves, long-sleeve shirt, long pants.

10. A 0.5% solution of Dichlorvos is applied using a hand-held low-pressure sprayer. It is assumed that Dichlorvos is applied by PCO 10 times per day, 1 day a week for 44 weeks. An average commercial applicator wears coveralls, chemical resistant gloves, and shoes. A respirator is not worn. Frequency of use is considered to be short-term (1 application/week) based on use frequency information from the National Pest Control Association. Dermal and inhalation exposures were obtained from PHED V1.1. A respiratory volume of 1.5 m^3 /hour has been used. The dermal and inhalation MOEs were both calculated using a NOEL of 0.5 mg/kg/day from the acute human study and an 11% dermal absorption factor.

11. An average mushroom house has a volume of 30,000 ft^3. Dichlorvos is applied at a rate of 3.0 grams of active ingredient per 1000 ft^3 or 90 grams per treatment; 16 days per year, 10 houses per day; 4 minutes per house or 40 minutes per day. Protective clothing was slightly different for each application method. For reentry exposure, assumed that a worker reenters a ventilated mushroom house 24 hours after treatment and is exposed for 8 hours.

For the coarse spray, Dichlorvos is applied at 5.3 lb ai/day. Protective clothing represents long pants, long sleeve shirt and gloves. The exposure values are corrected for a dermal absorption of 11%. Dermal reentry exposure represents the maximum expected at any REI. The inhalation reentry exposure is 0.0085 mg/kg/day and 0.0049 mg/kg/day at 12- and 24-hour reentry intervals, respectively. The MOE for 24-hours is reported in the table.

12. A typical greenhouse operation consists of seven greenhouses, each with a volume of 85,000 ft^3. All seven greenhouses are treated in 1 day. There are a maximum of three applications per crop and three crops are produced per year. Dichlorvos is applied at the rate of 1.4 grams of active ingredient per 1,000 ft^3.
1998: For reentry, a 1981 CDFA (now Cal/EPA) Dichlorvos study was used rather than translating data from the warehouse assessment as was done for the PD2/3.

13. Worker exposure from direct application to animals is based on dairy cattle treatment. A one percent solution of Dichlorvos is applied with a handheld sprayer. An average herd of dairy cattle consists of 65 head, each requiring 24 seconds to spray, two times per day during treatment. Fly control is required from May to October with application occurring weekly during this time (26 times per year). Although permitted on product labels, EPA does not believe that direct application with a handheld sprayer is used. Rather, some type of automated equipment is used to apply Dichlorvos directly to animals. Space and premise treatments also help control insects on animals. Since several registered products provide guidance on use with a handheld sprayer, the exposure and risk are estimated here for that application method, which is expected to result in a much higher exposure than automated methods. Exposure assessment for direct application to dairy cattle using a handheld sprayer were conducted using PHED V1.1. Applicators were assumed to wear long sleeve shirts, long pants, and gloves.

14. Data for cattle cannot be extrapolated to poultry, because of the different application method and less frequent applications. Individual animals are less likely to be treated directly and the equipment is more likely to be automated. As a result, exposure from applying Dichlorvos to poultry is expected to be much lower than for cattle.

15. An average dairy barn has the dimensions 30 ft x 100 ft x 9 ft (total area covered is 5,340 ft^2). Dichlorvos is applied at two week intervals for 22 weeks, one barn per day. A 1.0 percent solution of Dichlorvos is applied using a low pressure hand sprayer at a rate of 0.0115 lb a.i. per 1000 ft^2. A worker wears long sleeve shirt, long trousers, shoes and impervious gloves at a minimum.

16. Feedlots include stockyards, corrals, holding pens and other areas where large groups of animals are contained. EPA assumes that some type of power sprayer capable of treating a large number of animals in a short time is probably used. A short application time period in an outdoor or partially enclosed area would minimize exposure to less than that of dairy applications.

17. MOE is expected to be greater than 100 for manure use. Application equipment may be similar to those used in a dairy barn; however, the application time would probably be less and the treated area would be well ventilated - either outdoors or in a partially enclosed area.

18. Use on ornamental lawns, turf and plants is expected to have an exposure pattern similar to use of a dairy barn sprayer.

19. Includes estimate of oral exposure due to hand to mouth activity. Reentry exposure to commercial turf farms is considered to be negligible because of cultural practices is such facilities. The primary reentry activities in a commercial turf farm are mowing and the cutting of sod. The characteristics of Dichlorvos make it unlikely that such a product would be used immediately preceding such activities.

20. Dichlorvos can be applied to warehouses with wall-mounted automatic foggers. Exposure to mixer/loaders through automatic application is expected to be negligible; however, there would still be reentry exposure. In estimating reentry exposure, EPA assumed 6 hours elapsed before reentry is allowed, as required on labels; and that workers spend 8 hours per day in the treated area for the next 3 days. Dichlorvos is applied at the rate of 2.0 grams active ingredient per 1,000 ft^3 over a period of 125 minutes per application. Exposure estimates are for the day following treatment. Dermal exposure was measured for the hands only and represents an average of the total exposure measured for three work stations.

21. Exposure is believed to be negligible since the pesticide is in the form of an impregnated strip and the traps are placed in outdoor areas (such as forests) where there is no human exposure.

22. Exposure at a garbage dump is believed to be less than dairy exposure.

V. Food Quality Protection Act Considerations

a. Cumulative Effects

I. Need for Assessment

Section 408(b)(2)(D)(V) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

Dichlorvos is related to Naled and Trichlorfon, which are members of the organophosphate class of pesticides. Naled and Trichlorfon can metabolize or degrade to Dichlorvos in food or water. Therefore, FQPA requires OPP to estimate cumulative risk from consumption of food and water containing Dichlorvos derived from Naled and Trichlorfon.

b. Aggregate Exposure and Risk Estimates

(I). Multiple routes of Exposure (Same Scenario)

The aggregate risk index was not calculated for many occupational and residential scenarios because (1) the exposure estimates for these scenarios were based on biomonitoring data, which measures total exposure measured as excretion of urinary DMP, and does not allow for separation of exposure by route (2) many exposures are limited to a single route; e.g., residential exposure from the Dichlorvos resin strip is limited to the inhalation route.

(ii). Multiple Pathway (Residential plus food and water)

The Agency considered aggregate exposure and risk estimates for residents who might be exposed to Dichlorvos from multiple sources, such as residential use, food, and water. This was taken into consideration in calculating DWLOCs. As noted below, the exposures from food and water are negligible compared to the exposure from residential use. Nonetheless, the aggregate exposure and risk estimates suggest the need to further refine the drinking water exposure estimates.

Aggregate Acute Dietary (Food and Water) Exposure and Risk. Acute dietary risk estimates for food do not exceed the Agency's level of concern. The aggregate acute dietary risk estimate for food and water does not exceed the Agency's level of concern for adults. However, the aggregate acute risk estimate for food and water slightly exceeds the Agency's level of concern for children. This indicates a need to refine the Agency's Tier I drinking water exposure estimates.

The $DWLOC_{acute}$ value is 485 µg/L for the total US Population and 119 µg/L for children age 1-6. These $DWLOC_{acute}$ values reflect the allowable drinking water exposure after food is subtracted. Both the modeled Tier I acute groundwater concentrations of 0.0002 to 0.015 µg/L and the modeled Tier I acute surface water concentrations of 0.4 to 194 µg/L are less than the $DWLOC_{acute}$ of 485 µg/L for adults. However, the modeled Tier I acute surface water concentration of 194 µg/L exceeds the $DWLOC_{acute}$ of 119 µg/L for children age 1-6, indicating a potential concern and a need to refine the surface water estimate.

Aggregate Short and Intermediate Term Dietary and Residential Exposure and Risk. DWLOCs were not calculated for short or intermediate term exposure. Because the short and intermediate term residential exposure scenarios are associated with risks of concern, the DWLOCs would effectively be zero. Further, food and water exposure are negligible compared to the residential exposure.

Aggregate Chronic Dietary (Food and Water) and Residential Exposure and Risk. Chronic dietary exposure and risk estimates from food do not exceed the Agency's level of concern. However, the chronic residential inhalation exposure estimates from resin strips exceed the Agency's level of concern. Therefore, the $DWLOC_{chronic}$ value is effectively 0 µg/L. Food and water exposure to Dichlorvos is negligible compared with residential exposure. Therefore, any water exposure will only add to exposures and risks already of concern.

The Agency did not aggregate exposure from multiple uses in the residential environment because it is unlikely that a resident would be using multiple Dichlorvos products at the same time. Further, no data addressing this issue are available.

Lifetime Exposure (Cancer) Food and Water. The cancer endpoint for Dichlorvos is considered relevant to oral exposures only. Therefore, the $DWLOC_{cancer}$ value for Dichlorvos reflects the allowable drinking water exposure after food is subtracted. For lifetime drinking water exposure, the modeled Tier I ground water concentration of 0.015 µg/L is below the $DWLOC_{cancer}$ of 0.062 µg/L, but the modeled Tier I surface water concentrations of 0.06 to 26 µg/L are equal to or

greater than the $DWLOC_{cancer}$ of 0.062 µg/L. This suggests the need for a more refined Tier II drinking water exposure assessment.

c. Endocrine Disruption

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

VI. Risk Characterization

The Dichlorvos risk assessment contains strengths, weaknesses, and uncertainties based on the existing toxicological and exposure data, modeling methodologies, data gaps, and gaps in scientific knowledge. This assessment uses standard assumptions regarding human body weight, work life, and other exposure parameters; interspecies extrapolation; and exposure prorated over a lifetime to estimate cancer risks. Additional assumptions were made regarding route to route extrapolation. Strengths and uncertainties of the assessment are described below.

The carcinogenicity of Dichlorvos has been evaluated by internal and external peer review committees: the OPP Carcinogenicity Peer Review Committee, the Agency CRAVE Workgroup, and the FIFRA Science Advisory Panel. In addition, the Dichlorvos Registrant, AMVAC, has conducted an independent peer review of the carcinogenicity and mutagenicity of Dichlorvos by a Blue Ribbon Panel. The Agency has classified Dichlorvos as a Group C, possible human, carcinogen, based on the incidence of mononuclear cell leukemias and recommended use of a linearized low dose model for dose-response quantitation. A Q_1^* of 0.272 $(mg/kg/day)^{-1}$ in human equivalents has been calculated for human health risk assessment.

The Agency has concluded that there is no evidence that Dichlorvos is carcinogenic via inhalation or dermal routes of exposure. The issue of route specificity for carcinogenicity has been peer reviewed by the Agency CRAVE Workgroup and the Office of Pesticide Programs' Carcinogenicity and RfD Peer Review Committees.

The cholinesterase effect was noted in several species following acute, subchronic, or chronic oral exposure. In the animal studies, the NOEL for cholinesterase inhibition was within the range of 0.1 to 3 mg/kg/day for all species. In the acute oral human volunteer study, the NOEL was 0.5 mg/kg in for red blood cell cholinesterase inhibition. Plasma cholinesterase was not measured in the human study. Dichlorvos is also associated with cholinesterase inhibition in a chronic rat

inhalation study, with a NOEL of 0.05 mg/kg/day. The chronic dog feeding study and the chronic rat inhalation study have similar NOELs, which supports the use of the rat inhalation study for chronic exposure.

The rat chronic inhalation study has been reviewed OPP's toxicologists and internal peer review committees and by the Agency RfC Committee. This study is the basis for the NOEL of 0.05 mg/kg/day for this assessment and the basis for the Agency RfC for Dichlorvos cited in the on-line IRIS database.

The Dichlorvos Registrant has conducted an independent peer review of the cholinesterase endpoint for Dichlorvos by a Blue Ribbon Panel of Experts. The conclusions of the Blue Ribbon Panel were presented orally at the July 1998 SAP. The Agency has not yet had an opportunity to review the Blue Ribbon Panel Report.

As noted above, most of the toxicology data used to support the cholinesterase endpoint were from oral studies. Occupational and residential exposure to Dichlorvos occurs by dermal and inhalation routes. For the purposes of this risk assessment, the Agency uses 11% dermal absorption (based on animal data) and 100% inhalation absorption (default assumption). Data from a rat dermal absorption study show that Dichlorvos applied to the shaved skin was absorbed at a rate of 11%. Therefore, the Agency has high confidence in the use of 11% dermal absorption.

The Agency has high confidence in the residue data used for dietary exposure estimate. For most commodities, the Agency used residue monitoring data from USDA's Pesticide Data Program and FDA's Total Diet Study, which are the best available residue data. These data showed very few detects of Dichlorvos. Therefore, the anticipated residues used in the dietary exposure assessment are primarily based on one-half the level of detection for Dichlorvos. This is a conservative assumption which is not likely to underestimate dietary exposure and risk.

Dichlorvos residues may be present in water as a result of use of three pesticides: Dichlorvos (DDVP), Naled, and Trichlorfon. Dichlorvos is a degradate of Naled and Trichlorfon. The environmental fate and Effects Division (EFED) evaluated the potential for Dichlorvos to contaminate water from these sources. The environmental fate properties of Dichlorvos, Naled, and Trichlorfon are an indicator of the potential of these compounds to migrate to ground or surface water. EFED has limited monitoring data on the concentrations of Dichlorvos, Naled, or Trichlorfon in groundwater. Validated monitoring data for Dichlorvos, Naled, and Trichlorfon are available for the states of California and Hawaii from the Pesticides in Groundwater Database. These data indicated that Naled, Dichlorvos, or Trichlorfon have not been detected in groundwater; however, these data were not targeted to the pesticide use area. OPP does not have any surface water monitoring data on the concentrations of Dichlorvos, Naled, or Trichlorfon at the present time. Therefore, the Tier I screening model GENEEC was used to estimate surface water concentrations for Naled, Trichlorfon and Dichlorvos.

Exposure estimates for a number of occupational and residential scenarios were derived from limited data from the scientific literature, textbooks, and knowledge of cultural practices. Other

estimates, particularly in the residential environment, were derived from chemical specific monitoring data, including biomonitoring, in combination with models and literature studies. Any residential exposure assessment conducted by the Agency contains appreciable uncertainty because of limits in scientific knowledge of human behavior patterns. Nonetheless, the Agency considers the occupational and residential exposure estimates to be the best available with current methodologies.

VII. Data Needs

Most of the Reregistration data requirements for Dichlorvos have been fulfilled. The few remaining data requirements are described below.

A. Toxicology

Although the guideline toxicology data requirements for Dichlorvos have been fulfilled, the Agency has requested a modified developmental toxicity study in guinea pigs to address the issues of special susceptibility raised by the study by Mehl et al. The Mehl study is a non-guideline study from the literature which raises numerous questions about the potential special susceptibility of Dichlorvos, which could not be dismissed by the Agency. The Food Quality Protection Act of 1996 mandates careful consideration of the issue of special susceptibility.

B. Product and Residue Chemistry Data Requirements

GLN 860.1380: Storage Stability Data

The Reregistration requirements for storage stability data are not fulfilled. Information pertaining to the storage intervals and conditions of samples of the following commodities, from studies that were reviewed in the Residue Chemistry Chapter of the Guidance Document, must be submitted: packaged and bagged raw agricultural commodities and processed food; bulk stored raw agricultural commodities; milk; eggs; and meat, fat, and meat byproducts of dairy cows and poultry. Alternatively, the registrant may demonstrate that there are sufficient residue data which are supported by storage stability data to support all registered uses of Dichlorvos.

The available storage stability data indicate that residues of Dichlorvos are stable under frozen storage conditions for up to 90 days in/on plant commodities, up to 4.5 months in/on peanuts, and up to 8 weeks in animal commodities.

GLN 860.1480: Meat, Milk, Poultry, Eggs

The Reregistration requirements for data pertaining to this guideline topic are not completely fulfilled. A dermal magnitude of the residue study must be submitted for swine. No additional data are required for milk and edible tissues of ruminants, and for eggs and edible tissues of poultry.

C. Occupational and Residential Exposure Data Requirements

Outstanding exposure data requirements exist for turf and greenhouse uses. For turf, both application and postapplication data are required. For the greenhouse use, postapplication data are required. The Dichlorvos Registrant is a member of both the Agricultural Re-entry Task Force (ARTF) and the Outdoor Residential Exposure Task Force (ORETF). These data have been called in under the generic Data Call Ins (DCIs) for Turf and Agriculture. The following guideline studies are required:

GDLN 875.2100 Foliar Residue Dissipation Study (replaces GDLN 132-1(a))

GDLN 875.1100 Dermal Exposure - Outdoor Use (replaces GDLN 133-3)

GDLN 875.1200 Dermal Exposure - Indoor Use (replaces GDLN 133-3)

GDLN 875.1300 Inhalation Exposure - Outdoor (replaces GDLNs 133-4)

GDLN 875.1400 Inhalation Exposure - Indoor (replaces GDLN 133-4)

GDLN 875.2400 Dermal Exposure (replaces GDLN 133-3, Dermal Passive Dosimetry)

GDLN 875.2500 Inhalation Exposure (replaces GDLN 133-4, Inhalation Passive Dosimetry)

The Agency has recently received two foliar dissipation studies from the Registrant. These two studies are under review, and will be incorporated into the risk assessment upon completion of the Agency's review.

It is the Agency's understanding that the exposure monitoring studies for use of Dichlorvos in greenhouses is being conducted in conjunction with the Agricultural Re-entry Task Force (ARTF). However, the Registrant has not provided an anticipated date for submission of the greenhouse exposure monitoring data.

VIII. REFERENCES

Beringer MJ. 1993. Occupational and Residential Risk Assessment for Dichlorvos. Memo to Dennis Utterback, Review Manager, Special Review Branch, Special Review and Reregistration Division. September 8, 1993.

Beringer MJ. 1993.Updated Dichlorvos Occupational/Residential Risk Assessment. Memo to Dennis Utterback, Review Manager, Special Review Branch, Special Review and Reregistration Division. February 23, 1994.

Blondell J. 1994. Memorandum: Review of Poison Control Center Data Call In. To Joshua First, December 5, 1994. US EPA.

Blondell J. 1996. Review of Comments on Dichlorvos Incidences. Memo to D. Utterback. May 17, 1996.

Blondell J and Spann M. 1998. Review of Dichlorvos Incidence Reports. DP Barcode D242971, Chemical # 084001, Reregistration Case # 0310. March 31, 1998.

Collins RD and DeVries DM. 1973. Air Concentrations and Food Residues from Use of Shell's No-Pest Insecticide Strip. Bull. Environ. Contam. Toxicol. 9(4):227-233, 1973.

Dannan G. 1998. Toxicology Review for Reregistration Eligibility Document on Dichlorvos (DDVP). February 20, 1998.

Dawson JL. 1998. Dichlorvos Indoor Air Calculations using MCCEM. June 29, 1998.

Ghali G. 1993. Dichlorvos (DDVP): Reconsideration of Quantification of Human Risk. Memorandum to G. LaRocca and D. Utterback. July 7, 1993.

Ghali G. 1997. Dichlorvos (DDVP): Hazard Identification Committee Report. December 19, 1997.

Hummel S. 1998a. Dichlorvos (0804001) Special Review: Response to PD 2/3 and Anticipated Residues for Dichlorvos resulting from the use of Dichlorvos, Naled, and Trichlorfon. April 9, 1998.

Hummel S. 1998b. Dichlorvos (084001). Anticipated Residues for Dichlorvos resulting form use of Dichlorvos and Naled. June 15, 1998.

Jaeger R. 1989. Transmittal of the Final FIFRA Science Advisory Panel Report on the September 28-29 Meeting. Memo to D. Campt. October 16, 1989.

Jaquith D. 1987a. Exposure Assessment for Dichlorvos. August 4, 1987.

Jaquith D. 1987b. Refinement of Exposure Assessment for Dichlorvos. August 7, 1987.

Jaquith D. 1987c. Further Refinement of Exposure Assessments for Dichlorvos. August 14, 1987.

Jaquith D. 1993a. Revisions to Exposure Assessment for Dichlorvos. April 15, 1993.

Jaquith D. 1993b. Assessment of Exposures of Residents to Dichlorvos Applied as a Total Release Fogger. May 10, 1993.

Jaquith D. 1996 Response to Public Comments on Dichlorvos PD 2/3. June 4, 1996.

Jaquith D. 1998a. Exposures from Dichlorvos (DDVP) Resin Strips. March 5, 1998.

Jaquith D. 1998b. Re-entry Exposures to Dichlorvos Resulting from Application to Residential and Recreational Areas. March 16, 1998.

Jaquith D. 1998c. Exposures to Dichlorvos (DDVP) from flea Collars. March 18, 1998.

Jaquith D. 1998d. Exposure Assessment for Dichlorvos (DDVP) Applied to Greenhouse and Mushroom Houses. April 22, 1998.

Jaquith D. 1998e. Exposure to Dichlorvos resulting from the Use of Bait Products. April 28, 1998.

Jaquith D. 1998f. Inhalation Exposures from Dichlorvos (DDVP) Resin Strips. June 12, 1998.

Jaquith D. 1998g. Revised Applicator Exposures to Dichlorvos resulting from Crack and Crevice Use and the Use of Aerosol Products. June 24, 1998.

Jaquith 1998h. Revisions of Exposures from Dichlorvos (DDVP) Resin Strips. September 30, 1998.

Jaquith D. 1998i. Exposures to Dichlorvos Resulting from the Use of Bait Products. Under Internal Review, November 1998.

Jaquith D. 1998j. Response to Comments from EXPOSAC on Exposure Assessment for Dichlorvos (DDVP) from Flea Collars. November 6, 1998.

Jaquith D. 1998k. Response to EXPOSAC Comments on Exposure Assessment for Total Release Foggers Containing Dichlorvos (DDVP). Under Internal Review, November 1998.

Jaquith D. 1998l. Revised Applicator Exposures to Dichlorvos (DDVP) Resulting from Dairy Barn and Animal Spray Uses. Under Internal Review, November 1998.

Jaquith D. 1998m. Response to Comments from the EXPOSAC and Others on Assessment of Re-entry Exposures to Dichlorvos Resulting from Application to Residential Turf and Recreation Areas. Under Internal Review, November 1998.

Jaquith D. 1998n. Revised Exposure Assessment for Greenhouses and Mushroom Houses. Under Internal Review, November 1998.

Kent R. 1998. Personal communication (e-mail) to C. Scheltema. Dichlorvos- Application of Inhalation Endpoint. November 20, 1998.

Lewis. P. 1998. Transmittal of the Final Report of the FIFRA Scientific Advisory Panel Meeting Held July 29-30, 1998. Memorandum to M. Mulkey, Director, Office of Pesticide Programs.
Mehl et al. 1994. The Effect of Trichlorfon and other Organophosphates on Prenatal Brain Development in the Guinea Pig. Neurochemical Research 19 (5):569-574.

Maddy KT, Schneider F, Lowe J, Ochi E, Frederickson S, and Margotich S. 1981. Vapona (DDVP) Exposure Potential to Workers in Mushroom houses in Ventura County, California in 1981. HS-861. As cited in Jaquith 1998d.

Parker RD, Nelson, HP, and Jones D. 1995. GENEEC: a Screening Model for Pesticide Environmental Exposure Assessment. The International Symposium on Water Quality Monitoring. American Society of Agricultural Engineers. P. 485.

Rowland J. 1998. Dichlorvos (DDVP) - RE-EVALUATION - Report of the Hazard Identification Assessment Review Committee. June 3, 1998.

Sahib I. 1998. Drinking Water Assessment for Dichlorvos. March 25, 1998.

Sahib I. 1998. Drinking Water Assessment for Dichlorvos (Revised). May 21, 1998.

Schaible 1994. Acute and Chronic Dietary Exposure Analysis for Dichlorvos. December 2, 1994.

Sette, W.F. 1998. Dichlorvos(084001): Pathology Working Group Peer Review of 28 day Neurotoxicity Study. April 9, 1998.

Sette, W.F. Dichlorvos (084001), Trichlorfon (057901). D237270: Summary Review of Published studies on Metrifonate, a drug metabolized to Dichlorvos, and their relevance to Dichlorvos risk assessment (MRID 44308001). April 10, 1998.

Steinwand B. 1998a. Dietary Exposure Analysis for Dichlorvos in support of the Reregistration Eligibility Decision. May 26, 1998.

Steinwand B. 1998b. Dietary Exposure Analysis for Dichlorvos in Support of the Reregistration Eligibility Decision. June 23, 1998

Steinwand 1998a.. Review of "Amvac's Dietary Cancer and Non-Cancer Risk Assessments of Dichlorvos (084001)" in response to EPA's PD 2/3. May 26, 1998.

Steinwand B. 1998b. Dietary Exposure Analysis for Dichlorvos in Support of the Reregistration Eligibility Decision. June 23, 1998

Steinwand B. 1998c. Acute Dietary Exposure Analysis for Dichlorvos in Support of the Reregistration Eligibility Decision. PC Code 084001; D250328. October 27, 1998.

Stewart J. 1998. Review of Toxicity Studies on Dichlorvos Using Human Volunteers. March 24, 1998. MRIDs 44317901, 4416201, 44248801, 44248802.

Stewart 1996a. Dichlorvos Special Studies. MRID 42880101, 42881101. May 30, 1996.

Stewart J. 1996b. Review of Supplementary Pathology Data: Staging of Severity of Mononuclear Cell Leukemia observed in Male fisher 344 Rats in the Two Year Carcinogenicity Study. MRID 43565601. June 20, 1996

Stewart J. 1996. Dichlorvos. Transmittal of the Quantitative Risk Assessment and Response to Registrant's questions concerning Neurotoxicity Study and Cancer Peer Review. October 4, 1996.

Stewart and Burnam 1996. Fifth Carcinogenicity Peer Review of Dichlorvos. Tox Chem # 328, PC Code 084001. August 28, 1996.

Stewart J. 1997. Toxicology Branch Response to Public Comments on the PD 2/3 for Dichlorvos. April 16, 1997.

Stewart J. 1998. Review of Toxicity Studies on Dichlorvos Using Human Volunteers. March 24, 1998. MRIDs 44317901, 4416201, 44248801, 44248802.

Tarplee B. and Rowland J. 1998. Dichlorvos (DDVP) - Report of the FQPA Safety Factor Committee. June 2, 1998.

USEPA 1992. Pesticides in Groundwater Database - A Compilation of Monitoring Studies fromm 1971 to 1991. US Environmental Protection Agency, Office Of Pesticides, Prevention, and Toxic substances. EPA Document Number 734-12-92-0001.

USEPA 1997. Reregistration Eligibility Decision (RED): Trichlorfon. US Environmental Protection Agency, Office Of Pesticides, Prevention, and Toxic substances. EPA Document Number 738-R-96-017.

Van Hemmen JJ, Brouwer R, and Brower DH. 1992. Worker Exposure to Pesticides in Greenhouses: Health Risks During the Harvesting of Flowers. Med. Fac. Landbouww. Univ. Garn. 57/3b.