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

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

March 13, 2002

MEMORANDUM

SUBJECT: DIURON: The REVISED HED Chapter of the Reregistration Eligibility Decision Document (RED). PC Code: 035505. Case 0046. DP Barcode D281396.

FROM: Diana Locke Ph D. and
Carol Christensen
Risk Assessors
Reregistration Branch II
Health Effects Division (7509C)

THRU: Alan Nielsen, Branch Senior Scientist
Reregistration Branch II
Health Effects Division (7509C)

TO: Margaret Rice, Chief and
Richard Dumas, Team Leader
Reregistration Branch II
Special Review and Reregistration Division (7508W)

The attached REVISED Human Health Assessment for the 3-(3,4-dichlorophenyl)-1,1-dimethylurea (diuron) RED document was generated as part of Phase 2 of the Interim Public Participation Process. Comments received from the Registrant during the Phase I Error-Only review period have been incorporated in this version of the HED Human Health Assessment for Diuron. The Health Effects Division's (HED) chapter reflects the Agency's current guidelines concerning the retention of the Food Quality Protection Act (FQPA) factor and risk assessment. This chapter includes a summary of the product chemistry from Ken Dockter, residue chemistry and dietary risk assessment from John Punzi, toxicology review from Yung Yang, occupational and residential exposure from Renee Sandvig and Christina Jarvis, incidence review from Ruth Allen, drinking water exposures from Ibrahim Abdel-Saheb [Environmental Fate and Effects Division (EFED)], as well as risk assessment and characterization from Diana Locke. Carol Christensen incorporated the changes to the risk assessment in response to error-only comments.

The Environmental Fate and Effects Division (EFED) revised the drinking water exposure assessment based upon Registrant comments. The new memorandum entitled "Drinking Water Reassessment for Diuron and its Degradates" dated March 11, 2002 has been incorporated into the Revised HED Chapter of the Reregistration Eligibility Decision Document (RED) as appropriate.

TABLE OF CONTENTS

DIURON

1.0 EXECUTIVE SUMMARY

Diuron [3-(3,4-Dichlorophenyl)-1,1-dimethylurea] is a pre- and post-emergent herbicide that controls a wide variety of annual and perennial broad leafed and grassy weeds on both crop and non-crop sites. The mechanism of herbicidal action is the inhibition of photosynthesis. Products containing diuron are intended for both occupational and residential uses. Occupational uses include agricultural food and non-food crops; ornamental trees, flowers, and shrubs; paints and coatings; ornamental fish and catfish production; rights-of-way and industrial sites. Residential uses include ponds, aquariums, and paints. Diuron is formulated as a technical product and formulation intermediate, granular, pellet/tablet, wettable powder, dry flowable, emulsifiable concentrate, flowable concentrate, soluble concentrate, and ready-to-use solution. Diuron is applied using the following equipment: groundboom sprayer, aerial equipment, chemigation, rights-of-way sprayer, high-pressure handwand, low-pressure handwand, tractor-drawn spreader, granular backpack spreader, push-type spreader, airless sprayer, paintbrush, shaker-type applicator, backpack sprayer, belly grinder, and by hand. Products intended for residential use may be applied using a spoon, by hand, by airless sprayer, or by paintbrush/roller. Application rates range from 0.8 lbs active ingredient (ai)/acre for corn to 87.1 lbs ai/acre for non-crop areas.

Diuron has low acute toxicity (Toxicity Category 3-4) by the oral, dermal, or inhalation exposure routes. Diuron is not an eye or skin irritant, and not a skin sensitizer. The primary target organs are the hematopoietic system, the bladder, and renal pelvis. Erythrocyte damage resulted in hemolytic anemia and compensatory hematopoiesis, which were manifested as significantly decreased erythrocyte counts, hemoglobin levels, and hematocrit, and increased mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), abnormal erythrocyte forms, reticulocyte counts, and leukocyte count. Consistent observations of erythrocytic regeneration were seen in chronic toxicity studies in rats, mice and dogs. Gross pathology findings in chronic rat and mouse studies showed increased incidences of urinary bladder edema and wall thickening at high doses. Microscopic evaluation showed dose-related increases in the severity of epithelial focal hyperplasia of the urinary bladder and renal pelvis in both sexes. The available data did not reveal any developmental or reproductive toxicity. The HED Carcinogenicity Peer Review Committee (CPRC) characterized diuron as a "known/likely" human carcinogen based on urinary bladder carcinomas in both sexes of the Wistar rat, kidney carcinomas in the male rat, and mammary gland carcinomas in the female NMRI mouse. The CPRC also recommended a low dose linear extrapolation model with a Q_1^* of 1.91×10^{-2} $(mg/kg/day)^{-1}$ be applied to the animal data for the quantification of human risk, based on the urinary bladder carcinomas in the rat. Diuron was not mutagenic in bacteria or in cultured mammalian cells and no indication of DNA damage in primary rat hepatocytes was observed. There were marginal statistically significant increases in cells with structural aberrations in a Sprague Dawley rat *in vivo* bone marrow chromosomal aberration assay. However, the levels of aberrations were within historical control range and assessed negative.

There are no adverse effects attributed to a single exposure identified in any available studies. In addition, diuron has low acute toxicity and no developmental or neurotoxic concerns. Therefore, no acute dietary endpoint was chosen and no acute dietary risk assessment was conducted. Also, no systemic toxicity was observed following repeated dermal dosing up to 1200 mg/kg/d. Therefore, no short- or intermediate-term dermal endpoints were chosen either. The short-term incidental oral and the inhalation endpoints are based on decreased maternal body weight and food consumption observed in a rabbit developmental toxicity study [No Observable Adverse Effect Level (NOAEL) = 10 mg/kg/d]. The intermediate-term incidental oral and intermediate-term inhalation endpoints are based on hematological effects observed at 10 mg/kg at 6 months in the chronic rat study. The NOAEL is 1 mg/kg/d. The chronic dietary, and long-term dermal and inhalation endpoints are based on hemolytic anemia and compensatory hematopoiesis [Lowest Observable Adverse Effect Level (LOAEL) = 1.0 mg/kg/d]. Since the dose and endpoint for establishing the chronic dietary reference Dose (RfD) is a LOAEL and a NOAEL was not established, a total uncertainty factor (UF) of 300 was applied (UF of 100 to account for both interspecies extrapolation and intra-species variability, an additional UF of 3 to account for the lack of a NOAEL). The FQPA Safety Factor Committee recommended that the FQPA safety factor be reduced to 1x since there is no indication of quantitative or qualitative increased susceptibility of rats or rabbits to *in utero* or postnatal exposure.

Estimated chronic dietary (food) risk estimates associated with the use of diuron do not exceed the Agency's level of concern for any population subgroup including the most highly exposed subgroup, children ages 1-6 years. The chronic dietary risk for children 1-6 years of age is approximately 7% of the chronic Population Adjusted Dose (cPAD = 0.003 mg/kg/d) and approximately 3% for the general U.S. population. The chronic exposure analysis utilized field trial data which include residues of the parent diuron and its metabolites that are hydrolyzable to 3,4-dichloroaniline (3,4-DCA); 3,4-dichlorophenylurea and 3-(3,4-dichlorophenyl)-1-methylurea. The analysis also included processing data, where applicable, and percent crop treated information. Approximately 40% of the exposure to diuron from food is from orange juice and orange juice concentrate. The estimated cancer dietary risk associated with the use of diuron indicates a borderline exceedance above 1×10^{-6} and shows a lifetime risk estimate of 1.68×10^{-6} for the general population but, is not of concern. Though this is the most refined assessment achievable based on the available data/information, it may also be considered conservative since the exposure analysis used data from field trials conducted at the highest application rates and some processing data are still outstanding.

The Agency has determined that there are potential occupational exposures to mixers, loaders, applicators and other handlers during the usual use-patterns associated with diuron. Based on the agricultural and non-crop use patterns, 31 major occupational exposure scenarios were identified and are expected to be of short- (1-30 days) and intermediate- (1-6 months) term duration. For these durations, the Level of Concern (LOC) or target Margin of Exposure (MOE) for occupational workers is 100. MOEs $\geq$ 100 are not considered to be of concern. Calculations of occupational noncancer risk based on inhalation exposures during agricultural and non-crop uses indicate that the inhalation MOEs are more than 100 at the highest possible level of mitigation for all of the short-term occupational exposure scenarios, except applying sprays with a high pressure handwand. Sixteen of the 31occupational scenarios were identified as having intermediate-term durations of exposure. Of these, none have a non-cancer risk of concern for intermediate-term inhalation exposure at the highest level of mitigation Potential occupational cancer risks from diuron use were assessed. Both the potential inhalation and dermal exposures were included in the cancer risk assessment and a 4% dermal absorption factor (upper bound estimate) was applied to dermal exposures. In general, the Agency is concerned when occupational cancer risk estimates exceed 1×10^{-4}. The Agency will seek ways to mitigate the risks, to the extent that it is practical and economically feasible, to lower the risks to 1×10^{-6} or less. Out of a total of 31occupational handler scenarios, five have cancer risks greater than 1×10^{-4} at the highest feasible level of mitigation and are of concern. Twenty-six of the occupational handler scenarios have cancer risks between 1×10^{-4} and 1×10^{-6} at the highest feasible level of mitigation. Both occupational and residential (see below) cancer risk assessments are considered protective based on conservative exposure assumptions and a high-end dermal absorption factor. The Agency has determined that there are potential postapplication exposures to workers during the agricultural and non-crop uses associated with diuron. However, a noncancer postapplication assessment was not conducted, since only dermal exposures are expected and no dermal toxicity is expected from short or intermediate-term exposures. For the postapplication cancer assessment, only the crops whose foliage can be sprayed without damage were assessed for postapplication exposure to foliage. The crops that can be sprayed without foliage damage are oats, wheat, birdsfoot trefoil, clover, grass grown for seed, alfalfa, asparagus, pineapple, and sugarcane. Postapplication cancer risks for private growers (10 days of exposure per year) were calculated at both the typical application rate and the maximum application rates. All potential cancer risks to private growers were estimated to be less than 1×10^{-4} on the day of treatment. Postapplication cancer risks for commercial applicators (30 days per year) were calculated at the typical application rate only. All potential cancer risks to commercial applicators were less than 1×10^{-4} on the day of treatment. Since diuron is applied directly to the soil, there may also be significant postapplication exposure to diuron resulting from contact with treated soil when planting seedlings, moving irrigation lines, or other soil related activities.

Occupational risk assessments were conducted for the use of diuron as a mildewcide in paint. Four occupational handler scenarios were identified for the use of diuron in paint and are expected to be of short- and intermediate-term exposure duration. The calculations of short- and intermediate-term inhalation risk from the use of diuron in paint indicate that MOEs are more than 100 at the assessed level of mitigation for all the exposure scenarios, except applying paints with an airless sprayer (indoors). At the assessed level of mitigation, all four scenarios have potential cancer risks between 1×10^{-4} and 1×10^{-6}. However, it is likely that risks are even lower since the cancer assessment incorporated a number of conservative assumptions, such as maximum application rate and an upper bound dermal absorption factor. Occupational postapplication exposures to paint containing diuron may occur in industrial settings around open vats used in paint processing. Inhalation and dermal exposures may also occur while maintaining industrial equipment. No postapplication exposure data have been submitted to determine the extent of postapplication exposures in the industrial settings. Nonetheless, inhalation exposures are expected to be minimal because of the low vapor pressure of diuron (2×10^{-7} mm Hg at 30 EC) and aerosol formation is not expected. Dermal postapplication exposures are expected to be lower than when handling/loading the formulated product. Therefore, postapplication exposures in the industrial settings are expected to be minimal and not of concern.

Occupational risk assessments were also conducted for the use of diuron as an algaecide in commercial fish ponds. Four short-term occupational handler scenarios were identified for the use of diuron in commercial fish production and the inhalation MOEs from all four of the commercial fish production scenarios were greater than 100 at the baseline level of mitigation and are not of concern. With maximum mitigation measures (engineering control level), all four scenarios have estimated cancer risks of less than 1×10^{-6} and are not of concern. Occupational postapplication exposure to diuron in treated fish production ponds is not likely to result in a risk of concern based on the extremely high dilution rate.

The Agency has determined that there are potential exposures to residential mixers, loaders, and applicators during 1) loading ready-to-use liquids, 2) applying paints/stains with a paintbrush, and 3) applying paints with an airless sprayer (outdoor applications only). Residential exposures to diuron are expected to be short-term. For residential handlers, calculations of noncancer risk indicate that the inhalation MOEs are more than 100 for all of the exposure scenarios and are not of concern. For residential populations, cancer risks less than 1×10^{-6} are not considered to be of concern. All residential handler scenarios have a potential cancer risk greater than 1×10^{-6} and are of concern, except for the loading ready-to-use liquids for ponds and aquariums scenario, which is not of concern. The Agency notes that cancer risk estimates to residential handlers of diuron treated paint are based on two exposures per year, which is considered a high-end assumption.

Postapplication inhalation or dermal exposure resulting from the indoor use of diuron in paints is also expected to be minimal because of the low vapor pressure of diuron, and because diuron-treated paint is only likely to be used in rooms where high humidity is expected (i.e. a bathroom), and would rarely be used in the entire house. Postapplication inhalation and dermal exposure resulting from the use of diuron in residential ponds and aquariums is also expected to be minimal based on the extremely high dilution rate.

When potential food and residential inhalation exposures were combined for short-term aggregate risk estimates, they resulted in aggregate short-term MOEs = 1043 and 1045 for adult males and females, respectively. Based on the lack of systemic toxicity expected by the dermal route, it was not appropriate to combine residential dermal and inhalation exposure estimates for risk assessment purposes. Based on labeled uses, no intermediate- or long-term residential handler, or postapplication exposures of any duration, are expected. Based on supported uses, no incidental oral exposures are expected. Aggregate short-term risk estimates for diuron and its metabolites hydrolyzable to 3,4-DCA would combine exposures from food (average), water, and inhalation. Since measured drinking water data (monitoring data) are limited and cannot be quantitatively included in the risk assessment, estimates of allowable levels of drinking water were calculated instead. The Agency determined that it was unlikely that more than one of the residential handler activities would occur concurrently during a short-term time period. Therefore, the Agency took the protective approach of including the exposures from the activity which could potentially result in the most exposure to the homeowner, applying paint with an airless sprayer, in the aggregate assessment. The Agency can conclude with reasonable certainty that residues of diuron plus its metabolites hydrolyzable to 3,4-DCA, resulting from applications of diuron, in drinking water would not likely result in a short-term aggregate risk to male and female adult homeowners above the Agency's level of concern.

Aggregate chronic (noncancer) risk estimates include the contribution of risk from dietary sources (food + water) and residential sources. However, based on the labeled uses, no long-term or chronic residential exposures are expected. Chronic risk estimates from exposures to food alone, do not exceed the Agency's level of concern. However, the Agency cannot conclude with reasonable certainty that residues of diuron, plus its metabolites hydrolyzable to 3,4-DCA, in drinking water would not likely result in an aggregate chronic risk to infants, children, or adults above the Agency's level of concern. The Agency based this determination on a comparison of estimated concentrations of diuron and its metabolites in surface waters to back-calculated "drinking water levels of comparison" (DWLOCs) for diuron plus its metabolites. The estimated ground water concentrations are not expected to exceed the DWLOCs.

Estimated exposure to food alone results in a cancer risk for the U.S. general population that is not of concern. However, residential exposures to applicators applying paint with a paintbrush or airless sprayer may result in potential cancer risks that are of concern. Since potential cancer risks from exposures during residential activities, alone, are of concern, no aggregate cancer risk and no DWLOCs were calculated. Any potential additional exposure to residues in water are of concern.

The Metabolism Assessment Review Committee (MARC) recommended that a separate dietary cancer assessment be conducted for N'-(3-chlorophenyl)-N,N-dimethyl urea (MCPDMU), a potential residue of concern in drinking water, but not found in food (in plant or animal metabolism studies). The MARC raised concerns for MCPDMU based on an analogous compound, N'-(4-chlorophenyl)-N,N-dimethyl urea (monuron). With the exception of the position of the chlorine, the structures are identical. There are cancer concerns for monuron but the target organs are different than those affected by diuron. In the absence of the data needed for a more comprehensive evaluation of MCPDMU, the carcinogenic risk assessment was conducted using the Q_1^* of monuron [1.52×10^{-2} $(mg/kg/day)^{-1}$] that is based on male rat liver neoplastic nodule and/or carcinoma combined tumor rates. The calculated potential cancer risk to the U.S. general population from exposure to MCPDMU in catfish is 1.02×10^{-7} and is not of concern. However, the estimated concentration of MCPDMU in surface water exceeds the DWLOC and is of concern.

In summary, diuron has low acute toxicity and no systemic toxicity was observed following repeated dermal dosing.

! The potential dietary risks, based on food alone, are not of concern. However, the estimated chronic surface water concentrations exceed the DWLOCs.

! The aggregate short-term risk (food + water + residential) is not of concern.

! Occupational noncancer risks based on inhalation exposures during agricultural and non-crop uses are not of concern at the highest possible level of mitigation for all of the short-term occupational exposure scenarios, except applying sprays with a high pressure handwand. Intermediate-term handler risks from agricultural and non-crop uses are not of concern at the highest possible level of mitigation for all assessed exposure scenarios. Out of a total of 31 agricultural and non-crop occupational handler scenarios, five have potential cancer risks greater than 1×10^{-4} at the highest feasible level of mitigation and are of concern, and 26 have cancer risks between 1×10^{-4} and 1×10^{-6} at the highest feasible level of mitigation. Though there are potential postapplication exposures to workers during the agricultural and non-crop uses associated with diuron, a noncancer postapplication assessment was not conducted, since no dermal toxicity is expected from short or intermediate-term exposures. All potential postapplication cancer risks to private growers and commercial applicators were estimated to be less than 1×10^{-4} on the day of treatment.

! Occupational risk assessments were also conducted for the use of diuron as a mildewcide in paint. With mitigation, there are no concerns for noncancer risks to occupational handlers exposed to paints containing diuron, except for intermediate-term inhalation risks from applying paints with an airless sprayer (indoors). With mitigation, all occupational mildewcide scenarios have potential cancer risks between 1×10^{-4} and 1×10^{-6}. Postapplication exposures are expected to be minimal.

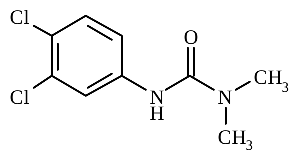
! The occupational handler scenarios identified for the use of diuron in commercial fish production have estimated noncancer risks that are not of concern at the baseline level of mitigation. With maximum mitigation measures, all the fish production scenarios have estimated cancer risks of less than 1×10^{-6} and are not of concern. Postapplication exposures to diuron in treated fish production ponds is minimal and not of concern.

! For residential handlers exposed during paint and, pond and aquarium uses, the noncancer risks are not of concern but, potential cancer risks are greater than 1×10^{-6} and are of concern, except for the loading ready-to-use liquids for ponds and aquariums scenario, which is not of concern. Postapplication inhalation and dermal exposure resulting from the use of diuron in ponds and aquariums, and from the indoor use of diuron in paints, is expected to be minimal.

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

Diuron [3-(3,4-dichlorophenyl)-1,1-dimethylurea]

Empirical formula: $C_9H_{10}Cl_2N_2O$
Molecular weight: 233.1
CAS Registry No.: 330-54-1
PC Code: 035505



The product chemistry data base is not complete; new confidential statement of formula (CSF) data are required which reflect preliminary analyses of current products together with discussions of formation of impurities. Trace amounts of a manufacturing impurity, tetrachloro-azobenzene (TCAB), that are of toxicological concern, may be present (see Section 3.5). The available Generic Series 830 physical and chemical properties of diuron are given below (*Diuron. List A Reregistration Case 0046. PC Code 035505. Product Chemistry Chapter for the Reregistration Eligibility Decision [RED] Document. DP Barcode D274489. Ken Dockter. June 26, 2001*).

Table 1. Generic Series 830 Physical and Chemical Properties

GLN		MRID	Data
6302	Color	[1]	White
6303	Physical state	[1]	Crystal
6304	Odor	[1]	None
7200	MP	[1]	158^{o} C
7840	Water solubility	[1]	42 ppm @ 25^{o} C
7950	vp	[1]	2 x 10^{-7} mm Hg @ 30^{o} C
7550	Log P_{ow}	[2]	2.68
6320	Corrosion characteristics	43842201	Not corrosive

6313	Stability to normal and elevated temperatures, metals, and metal ions	43842201	Stable for 2 yrs. in double polyethylene bag inside a fiber drum under warehouse conditions. Metals and metal ion data not given.
7050	UV/Visible absorption	NG	

NG: Not Given.

[1] Diuron. CASRN: 330-54-1. http://toxnet.nlm.nih.gov/egi-bin/sis/search.

[2] Reddy, K.N. and M.A. Locke. 1996. *Molecular Properties as Descriptors of Octanol-Water Partition Coefficients of Herbicides.* Water, Air and Soil Pollution Vol. 86: pp 389-405.

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

Diuron is a substituted urea herbicide for the control of a wide variety of annual and perennial broad leaved and grassy weeds on both crop and non-crop sites. The mechanism of herbicidal action is the inhibition of photosynthesis. Diuron has a low acute toxicity (Toxicity Category 3 or 4) by the oral, dermal, or inhalation exposure routes. Diuron is not an eye or skin irritant, and not a skin sensitizer. A rat metabolism study indicated that diuron is rapidly absorbed and metabolized within 24 hours post-dose at the low dose and within 48 hours post-dose at the high dose. The urine is the major route of excretion in both sexes. A small amount of diuron is detected in the feces. The highest tissue residue levels were found in the liver and kidneys 4 days post ^{14}C-diuron dose. The metabolism of diuron involved N-oxidation, some ring hydroxylation, demethylation, dechlorination, and conjugation to sulfate and glucuronic acid *(Diuron - Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision. Yung Yang. 0ctober 2, 2001*).

The primary diuron target organs are the hematopoietic system, bladder, and renal pelvis. Erythrocyte damage resulted in hemolytic anemia and compensatory hematopoiesis, which are manifested as significantly decreased erythrocyte counts, hemoglobin levels, and hematocrit, and increased mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), abnormal erythrocyte forms, reticulocyte counts, and leukocyte count. Consistent observations of erythocytic regeneration are seen in chronic toxicity studies in rats, mice and dogs. Gross pathology findings in chronic rat and mouse studies showed increased incidences of urinary bladder edema and wall thickening at high doses. Microscopic evaluation showed dose-related increases in the severity of epithelial focal hyperplasia of the urinary bladder and renal pelvis in both sexes.

Although the developmental toxicity study in rats is classified as unacceptable, the data base as a whole is adequate for pre- and post-natal toxicity evaluation and did not reveal developmental or reproductive toxicity. The NOAELs for maternal/parental toxicity were either less than or equal to the NOAELs for fetal or reproductive toxicity.

The HED Carcinogenicity Peer Review Committee (CPRC) characterized diuron as a "known/likely" human carcinogen, based on urinary bladder carcinomas in both sexes of the Wistar rat, kidney carcinomas in the male rat (a rare tumor), and mammary gland carcinomas in the female NMRI mouse. The CPRC also recommended a low dose linear extrapolation model with a Q_1^* of 1.91×10^{-2} $(mg/kg/day)^{-1}$ be applied to the animal data for the quantification of human risk, based on the urinary bladder carcinomas in the rat. Diuron was not mutagenic in bacteria or in cultured mammalian cells and no indication of DNA damage in primary rat hepatocytes was observed. There were marginal statistically significant increases in cells with structural aberrations in a Sprague Dawley rat *in vivo* bone marrow chromosomal aberration assay. However, the levels of aberrations were within the historical control range and assessed negative.

The Hazard Identification Assessment Review Committee (HIARC) determined that a 28-day inhalation study is required to address the concern for inhalation exposure potential based on the use pattern. The registrant can follow the 90-day inhalation study protocol but cease exposure at 28 days. The HIARC also determined that a repeated chronic dog study is not required; a new study would not provide additional data since the observed effects are similar in the rat and the rat is the more sensitive species for this chemical.

Table 2. Acute Toxicity of Diuron

Guideline No.	Study Type	MRID #	Results	Toxicity Category
870.1100	Acute Oral	00146144	LD_{50} = 4721 mg/kg (M) >5000 mg/kg (F)	III
870.1200	Acute Dermal	00146146	LD_{50} >2000 mg/kg	III
870.1300	Acute Inhalation	40228803	LC_{50} >7.1 mg/L	IV
870.2400	Primary Eye Irritation	00146147	At 48 hrs, all irritation had cleared.	III
870.2500	Primary Skin Irritation	00146148	All irritation had cleared by 72 hrs.	IV
870.2600	Dermal Sensitization	00146149	Nonsensitizer	N/A
870.6200	Acute Neurotoxicity	N/A	Not available	N/A

Table 3. Subchronic, Chronic and Other Toxicity

Guideline #/ Study Type	MRID # (year)/ Classification/Doses	Results
870.3100 90-Day oral toxicity in rats	MRID 40886502 (1988) Acceptable/Nonguideline 0, 4, 10, or 25 ppm (0, 0.3, 0.7, or 1.6 mg/kg/day for males and 0, 0.3, 0.8, 1.8 mg/kg/day for females)	The NOAEL can not be determined based on equivocal findings in the urinary bladder including blood vessel dilation, reduced transparency, and increased firmness.
870.3200 21/28-Day dermal toxicity in rabbits	MRID 42718301 (1992) Acceptable/Guideline 0, 50, 500, or 1200 mg/kg/day	Systemic toxicity NOAEL =1200 mg/kg/day (HDT)
870.3465 90-Day inhalation toxicity	Not available	Not available
870.3700a Prenatal developmental toxicity in rats	MRID 40228801 (1986) Unacceptable/Guideline 0, 16, 80, or 400 mg/kg/day	Maternal toxicity NOAEL = 16 mg/kg/day. Maternal toxicity LOAEL = 80 mg/kg/day, based on decreased body weight gain and food consumption. Developmental toxicity NOAEL= 80 mg/kg/day. Developmental toxicity LOAEL = 400 mg/kg/day, based on whole litter resorption, reduced fetal body weights, and delayed ossification of the vertebrae and sternebrae.
870.3700b Prenatal developmental toxicity in rabbits	MRID 40228802 (1986) Acceptable/Guideline 0, 2, 10, or 50 mg/kg/day	Maternal toxicity NOAEL = 10 mg/kg/day. Maternal toxicity LOAEL = 50 mg/kg/day, based on decreased body weight and food consumption. Developmental toxicity NOAEL = 50 mg/kg/day (HDT).
870.3800 Reproduction and fertility effects in rats	MRID 41957301 (1990) Acceptable/Guideline 0, 10, 250, or 1750 ppm. (0, 0.58, 14.8, or 101 mg/kg/day for males and 0, 0.71, 18.6, or 132 mg/kg/day for females, respectively.	Parental NOAEL = 250 ppm (18.6 mg/kg/day). Parental LOAEL =1750 ppm (132 mg/kg/day) based on decreased body weight, body weight gain, food consumption and food efficiency in both generations. Reproductive NOAEL = 1750 ppm (HDT). Offspring NOAEL = 250 ppm (18.6 mg/kg/day). Offspring LOAEL = 1750 ppm (132 mg/kg/day) based on decreased body weight of the F_1 and F_2 pups during lactation.
870.4200b Chronic toxicity in dogs	MRID 00091192 (1964) Unacceptable/Guideline 0, 25, 125, 250, or 2500/1250 ppm (0, 1.8, 9.4, 18.8, or 93.8 mg/kg/day by conversion factor of 0.075) for 24 months.	NOAEL = 125 ppm (9.4 mg/kg/day) in males and 250 ppm (18.8 mg/kg/day) for females. LOAEL = 250 ppm (18.8 mg/kg/day) for males and 1250 ppm (93.8 mg/kg/day) for females based on anemia and body weight losses.

Guideline #/ Study Type	MRID # (year)/ Classification/Doses	Results
870.4300 Combined Chronic/ Carcinogenicity in rats	MRID 40886501,43871901, 43804501, 44302003 (1986) Acceptable/Guideline 0, 25, 250, 2500 ppm (0, 1.0, 10, or 111 mg/kg/day for males and 0, 1.7, 17, or 203 mg/kg/day for females) for 24 months.	NOAEL = Not established. LOAEL = 25 ppm (1.0 mg/kg/day for males and 1.7 mg/kg/day for females) based on evidence of hemolysis and compensatory hematopoiesis (decreased erythrocyte counts, increased reticulocyte counts, increased spleen weight and bone marrow activation). Dosing was considered adequate.
870.4300 Carcinogenicity in mice	MRID 42159501 (1983) Acceptable/Guideline 0, 25, 250, or 2500 ppm (0, 5.4, 50.8, or 640.13 mg/kg/day for males and 0, 7.5, 77.5, or 867.0 mg/kg/day for females) for 24 months	NOAEL = 250 ppm (50.8 and 77.5 mg/kg/day) for males and females. LOAEL = 2500 ppm (640.1 and 867.0 mg/kg/day) for males and females based on hemolytic anemia and liver toxicity in both sexes and urinary bladder toxicity in females. Dosing was considered adequate.
870.5100 Gene mutation *Salmonella typhimurium* reverse gene mutation	MRID 00146608 (1985), 40228805 (1991) Acceptable/Guideline	Independent trials were **negative** in *S. typhimurium* strains TA1535, TA97, TA98 and TA100 up to the highest doses tested (10 µg/plate -S9; 250 µg/plate +S9); higher concentrations ($50 µg/plate -S9; 500 µg/plate +S9) were cytotoxic.
870.5300 Gene mutation Chinese hamster ovary (CHO)/ HGPRT cell forward gene mutation assay	MRID 00146609 (1985) Acceptable/Guideline	Independent tests were **negative** up to cytotoxic doses without S9 activation (1.250 mM, . 291 µg/mL) and with S9 activation (0.5 mM . 117 µg/mL).
870.5375 Chromosomal aberration in vivo rat bone marrow cytogenetic assay	MRID00146611 (1985) MRID 44350301 (1997) (revised) Acceptable/Guideline	The test was negative in Sprague Dawley rats up to cytotoxic doses. A significant ($p<0.05$) increase in the percentage of abnormal cells and the average number of aberrations per cell was seen but only when the data were combined for the high-and mid-dose males and females at the 48-hour sampling time. A significant positive linear trend was also recorded for the combined (by sex) aberrations per cell and percentage abnormal cells. Nevertheless, the values fell well within the range of historical control ranges.
870.5375 Mouse Bone Marrow Micronucleus	MRID 45494502 (1995) 80% ai, 45494503 (1995) 42.4% ai, 45494504 (1996) 80% ai, 45494505 (1998) 98.1% ai Acceptable/Guideline	Preliminary review indicates <u>no evidence</u> of cytogenetic effect in mice administered either technical grade or formulated diuron.
870.5550 Unscheduled DNA Synthesis	MRID 00146610 (1985) Acceptable/Guideline	The test was **negative** up to cytotoxic doses ($0.33 mM, equivalent to . 76 Fg/mL).

Guideline #/ Study Type	MRID # (year)/ Classification/Doses	Results
870.7485 Metabolism and pharmacokinetics	MRID 42010501 (1996) Acceptable/Guideline	Diuron was rapidly absorbed, metabolized and excreted. Urine was the major route of excretion. Metabolism of diuron involved N-oxidation, ring hydroxylation, demethylation, dechlorination, and conjugation to sulfate and glucuronic acid.
870.7600 Dermal penetration	Not available for diuron.	Not available.

3.2 FQPA Considerations

There is an acceptable developmental toxicity study in rabbits and an acceptable two-generation reproduction study in rats. A developmental toxicity study in rats was classified as unacceptable due to deficiencies in analytical data on the sample analysis; however, the HIARC considered the developmental toxicity study in rats adequate for the FQPA susceptibility assessment based on the observation that the developmental toxicity NOAEL was higher than the maternal NOAEL. The HIARC concluded that a developmental neurotoxicity (DNT) study is not required.

There is no indication of increased susceptibility to young exposed to diuron in the available studies. In the developmental toxicity study in rabbits, there were no developmental effects at the highest dose tested. In the developmental toxicity study in rabbits and in the 2-generation rat reproduction study, developmental/offspring effects were observed only at maternally/parentally toxic dose levels.

No acute or subchronic neurotoxicity study is available. However, there are no neurotoxic signs in any of the submitted subchronic or chronic studies and a literature search did not reveal any studies relevant for assessing the potential neurotoxicity of diuron.

The FQPA Safety Factor Committee concluded that the safety factor could be removed (**1x**) for diuron because (*DIURON - Report of the FQPA Safety Factor Committee. Brenda Tarplee. August 7, 2001*):

g) There is no indication of quantitative or qualitative increased susceptibility of rats or rabbits to *in utero* or postnatal exposure;
h) A DNT study with diuron is <u>not</u> required; and
i) The dietary (food and drinking water) and non-dietary (residential) exposure assessments will not underestimate the potential exposures for infants and children.

3.3 Dose Response Assessment

Diuron has low acute toxicity and no developmental or neurotoxic concerns. Since no adverse effects attributable to a single exposure were identified in available studies, no acute dietary endpoint was chosen. Also, no systemic toxicity was observed following repeated dermal dosing up to 1200 mg/kg/d. Therefore, no short- or intermediate-term dermal endpoints were chosen either. The short-term incidental oral and the inhalation endpoints are based on maternal decreased body weight and food consumption observed in a rabbit developmental toxicity study. The chronic dietary, intermediate-term inhalation, and long-term dermal and inhalation endpoints are based on hemolytic anemia and compensatory hematopoiesis (*DIURON: 2nd Report of the Hazard Identification Assessment Review Committee. Yung Yang. August 28, 2001*).

3.3.1 Acute RfD

None selected. No adverse effects attributed to a single exposure (dose) were identified including in the rat or rabbit developmental toxicity studies.

3.3.2 Chronic RfD

The study selected was an acceptable/guideline chronic toxicity/oncogenicity study (MRID 40886501; supplemental MRIDs 43871901, 43804501, and 44302003), in which diuron (98.7% a.i) was administered to groups of 60 male and 60 female Wistar rats at dietary concentrations of 0, 25, 250, or 2500 ppm (0, 1.0, 10, or 111 mg/kg/d, respectively, for males and 0, 1.7, 17, or 203 mg/kg/d for females, respectively) for up to 24 months. At 12 months, 10 animals/sex/group were sacrificed for interim evaluation. Treatment with diuron did not affect the survival of rats. The only reported treatment-related clinical sign was reddish discolored or bloody urine in some high-dose males. A significant decrease in body weight and body weight gain was seen in both sexes of high-dose rats throughout the study.

Diuron affected the hematopoietic system resulting in hemolytic anemia and compensatory hematopoiesis, which were manifested as significantly decreased erythrocyte counts, hemoglobin levels, and hematocrit and increased MCV, MCH, abnormal erythrocyte forms, reticulocyte counts, and leukocyte counts. See *Diuron - Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision. Yung Yang. October 2, 2001*. Gross pathology showed that the incidence of urinary bladder wall thickening was elevated at 24 months for low- and high-dose males and high-dose females ($p<0.05$ or 0.01). Microscopic evaluation showed that epithelial focal hyperplasia of the urinary tract and renal pelvis increased in severity in both sexes at 12 and/or 24 months, and increased in incidence in high-dose males at 12 months and in high-dose females at 12 and/or 24 months with mid-dose females showing an increased incidence at 24 months. Some gross and/or microscopic changes were also seen in the liver (increased weight, swelling, discoloration, vacuolar cell degeneration, round cell infiltration, hyperemia), although these effects were not clearly primary effects of treatment.

The dose and endpoint for establishing the chronic RfD is the LOAEL = 1.0 mg/kg/day based on evidence of hemolytic anemia and compensatory hematopoiesis (decreased erythrocyte count, increased reticulocyte counts, increased spleen weight and bone marrow activation). A NOAEL was not established. A total UF of 300 was applied (UF of 100 to account for both interspecies extrapolation and intra-species variability, an additional UF of 3 to account for the lack of a NOAEL).

$$\textbf{Chronic RfD} = \frac{1.0\ \text{(LOAEL) mg/kg/day}}{300\ \text{(UF)}} = \textbf{0.003 mg/kg/day}$$

3.3.3 Short-term (1-30 days) Incidental Oral Exposure

The study selected was an acceptable/guideline developmental toxicity study in rabbits (MRID# 40228802). In the developmental toxicity study, 24-25 artificially inseminated New Zealand white rabbits per group were administered 0, 2, 10, or 50 mg/kg/day of Diuron (99% a.i.) by gavage on gestation days (GD) 7-19, inclusive. On GD 29, all surviving does were sacrificed and examined grossly. One control animal died on GD 0 due to an anaphylactic shock reaction during insemination and one high-dose doe aborted and was killed on GD 26. These deaths were considered unrelated to treatment. All remaining animals survived to scheduled termination. No treatment-related clinical signs of toxicity were observed in any animal. Maternal liver weights were comparable between the treated and control groups and gross necropsy was unremarkable.

Maternal body weights, body weight gains, and food consumption for the low- and mid-dose groups were similar to the control levels throughout the study. Absolute body weights of the high-dose does were significantly less than the controls on GD 20. Mean body weight gains by the high-dose group were significantly reduced as compared with the controls during the intervals of GD 10-13, 13-16, and 7-20 (weight loss). Weight gain by the high-dose group was significantly greater than the controls during the post-dosing interval. Food consumption by the high-dose group was significantly less than the controls during the GD 13-16, 16-20 and 7-20 intervals. The maternal toxicity LOAEL was established at 50 mg/kg/day based on decreased body weights and food consumption during the dosing interval. The maternal toxicity NOAEL was established at 10 mg/kg/day.

At cesarean section, the pregnancy rates, numbers of corpora lutea, implantation sites, resorptions, and live fetuses, and fetal body weights were similar between the treated and control groups. No dose- or treatment-related external, visceral, or skeletal malformations/variations were observed in any fetus. Therefore, the developmental toxicity NOAEL is $50 mg/kg/day and the developmental toxicity LOAEL is not identified.

The dose and endpoint selected for risk assessment is 10 mg/kg/day (NOAEL) based on maternal toxicity (decreased body weights and food consumption during the dosing interval) at 50 mg/kg/day (LOAEL). An UF of 100 to account for both interspecies extrapolation and intra-species variability was applied and, since the FQPA safety factor was reduced to 1x, the LOC is 100 and the calculated

MOEs must be 100 or above.

NOTE: This study was previously classified as unacceptable/upgradable based on deficiencies in analytical data of sample analysis. However, the HIARC determined that this study is acceptable because the low nominal level of sample concentration was observed at the low dose only and the NOAEL was established at the mid-dose with the LOAEL at the high-dose. Therefore, the deficiencies in the analytical data did not affect the results of the study. The systemic toxicity (expressed as maternal toxicity) is relevant for the populations (infants and children) and duration (1-30 days) of concern.

Short-term incidental oral LOC = 100

3.3.4 Intermediate-term (1-6 months) Incidental Oral Exposure

The study selected was the chronic toxicity/carcinogenicity study in rats (MRID# 40886501, 43871901, 43804501, 44302003). See Chronic RfD, section 3.3.2. The dose and endpoint for risk assessment was a NOAEL of 1.0 mg/kg/day based on hematological effects observed at 10 mg/kg/day (LOAEL) at the 6th month observation. It is noted that this NOAEL/LOAEL is different from the 24th month observation where the NOAEL is not established (LOAEL=1.0 mg/kg/day). The endpoint observed at the 6th month observation period is appropriate for this exposure duration and is relevant for the population of concern.

A UF of 100 and the FQPA safety factor of 1x were applied to the risk assessment; therefore the LOC = 100 and the calculated MOEs must be 100 or above.

Intermediate-term incidental oral LOC = 100

3.3.5 Dermal Absorption

No dermal absorption study is available. An <u>upper-bound estimation</u> of dermal absorption of 4% was extrapolated using the maternal LOAEL of 50 mg/kg/day from the oral developmental toxicity study in the rabbit and the NOAEL of 1200 mg/kg/day (HDT) from the 21-day dermal toxicity study in the rabbit: the ratio is 50/1200 or 4%.

Dermal absorption factor = 4%

3.3.6 Short- (1-30 days) and Intermediate-term (1-6 months) Dermal Exposure

None selected. No systemic toxicity was seen following repeated dermal dosing at 1200 mg/kg/day in the rabbit dermal toxicity study. Also, there is no developmental toxicity concern. No hazard was identified and no quantitative assessment is required.

3.3.7 Long-term (6 months to life-time) Dermal Exposure

The study selected was the chronic toxicity/carcinogenicity study in rats (MRID# 40886501, 43871901, 43804501, 44302003). See Chronic RfD, section 3.3.2. The dose and endpoint selected for risk assessment was 1.0 mg/kg/day (LOAEL) based on evidence of hemolytic anemia and compensatory hematopoiesis (decreased erythrocyte count, increased reticulocyte counts, increased spleen weight and bone marrow activation). A NOAEL was not established. An additional UF of 3 is applied to account for the lack of a NOAEL in this study. Therefore, the LOC = 300. An MOE < 300 with a dermal absorption factor of 4%, is potentially of concern.

3.3.8 Inhalation Exposure (All Durations)

Except for an acute inhalation study, for which diuron was placed in Toxicity Category 4 (LC_{50} >7.1 mg/L), no other studies are available via this route. Therefore, the HIARC selected the NOAELs from oral studies for risk assessment. Since the doses identified for inhalation risk assessment are from oral studies, route-to-route extrapolation should be as follows:

The inhalation exposure component (i.e., Fg a.i./day) using a 100% (default) absorption rate and application rate should be converted to an equivalent oral dose (mg/kg/day). Then, the oral equivalent doses should be compared to the following NOAELs/LOAEL to calculate the MOEs.

Short-term	NOAEL= 10 mg/kg/day (developmental rabbit study)
Intermediate-term	NOAEL= 1.0 mg/kg/day (chronic rat study at 6 month)
Long-term	LOAEL= 1.0 mg/kg/day (chronic rat study)

A UF of 100 for short- and intermediate-term exposures and a UF of 300 (additional 3 is applied to account for the lack of a NOAEL in the study) for long-term exposures, and the FQPA safety factor of 1x, were applied to the risk assessment; therefore the LOCs = 100, 100, and 300, respectively.

Short-term inhalation LOC = 100
Intermediate-term inhalation LOC = 100
Long-term inhalation LOC = 300

3.3.9 Carcinogenic Potential

3.3.9.1 Combined Chronic Toxicity/Carcinogenicity Study in Rats

An acceptable/guideline combined chronic toxicity/carcinogenicity study in rats was submitted (MRID# 40886501, 43871901, 43804501, 44302003). This study showed conclusive evidence for the carcinogenicity of diuron in male and female rats. The incidence of urinary bladder carcinoma was increased at 2500 ppm in both sexes (males: 33/49 vs. 1/50 for controls; females: 11/50 vs. 0/48 for controls; p<0.01). The malignancies were usually characterized as transitional epithelial carcinomas. The slight increase (not statistically significant) in the incidence of urinary bladder papillomas and the 3 neoplasms in the renal pelvis in high-dose males (one papilloma and two carcinomas) were also considered treatment-related. Dosing was adequate based on numerous toxic effects (hematological, microscopic, etc.) observed in the animals at all tested doses.

3.3.9.2 Carcinogenicity Study in Mice

An acceptable/guideline carcinogenicity study in mice was submitted (MRID# 42159501, 43349301). Treatment of up to 102 weeks with 2500 ppm diuron resulted in a significant increase in the incidences of mammary adenocarcinomas (control, 4%; 2500 ppm, 12%, p#0.05) and ovarian luteomas (control, 6%; 2500 ppm, 14%, p#0.01) in female NMRI (SPF HAN) mice under the conditions of this study. However, the incidence of mammary adenocarcinoma in high-dose females was at or near the high range of incidences seen in historic controls. Dosing was adequate based on observations at the highest dose tested, including decreased body weight of both sexes, increased spleen and liver weights in males and increased incidence of urinary bladder edema and epithelial hyperplasia, thickened mucosa and enlarged uterine horn in females.

3.3.9.3 Classification of Carcinogenic Potential

The HED Carcinogenicity Peer Review Committee (CPRC) met on December 18, 1996 and classified diuron as a "known/likely" human carcinogen, based on urinary bladder carcinomas in both sexes of the Wistar rat, kidney carcinomas in the male rat (a rare tumor), and mammary gland carcinomas in the female NMRI mouse (*Carcinogenicity Peer Review of Diuron. Linda Taylor and Esther Rinde. May 8, 1997*). The CPRC also recommended a low dose linear extrapolation model with a Q_1^* of 1.91×10^{-2} $(mg/kg/day)^{-1}$ be applied to the animal data for the quantification of human risk, based on the urinary bladder carcinomas in the rat (*Diuron - Revised Q_1*, (3/4's Interspecies Scaling Factor), 1985 Wistar Rat 2 Year Dietary Study. PC 035505. Bernice Fisher. September 23, 1998*).

3.3.10 Mutagenicity

Acceptable genetic toxicology studies with diuron have been submitted to the Agency. Findings from these studies indicated the following:

Gene Mutations
1) *Salmonella typhimurium* reverse gene mutation assay (MRID# 00146608/40228805): Independent trials were negative.
2) Chinese Hamster Ovary (CHO)/HGPRT) cell forward gene mutation assay (MRID# 00146609): Independent tests were negative up to cytotoxic doses with/without S9 activation.

Chromosome Aberrations

3) *In vivo* bone marrow cytogenetic assay in male Sprague Dawley rats administered 0, 50, 500 or 5000 mg/kg/day by single oral gavage (MRID# 00146611 and 44350301): The test was negative. Signs of overt toxicity (mortality, body weight loss, ocular discharge, depression, labored respiration, diarrhea, and tremors) were noted at 5000 mg/kg. Cytotoxicity to the target organ as indicated by the significantly decreased (p#0.01) mitotic indices at 24 and 48 hours for high-dose males; data combined for both sexes were also significantly decreased at 24 hours. A significant positive linear trend was also recorded for the combined (by sex) aberrations per cell and the percentage of abnormal cells. Nevertheless, the values fell well within the range of historical controls.

4) Mouse bone marrow micronucleus assays (MRIDs 45494502-05): Preliminary review indicates no evidence of cytogenetic effect in mice administered either technical grade or formulated diuron.

Other Mutagenic Mechanisms

5) Unscheduled DNA synthesis (UDS) in primary rat hepatocytes assay (MRID# 00146610): The test was negative up to cytotoxic doses.

Diuron was not mutagenic in bacteria or in cultured mammalian cells and no indication of DNA damage in primary rat hepatocytes was observed. There were marginal statistically significant increases in cells with structural aberrations in a Sprague Dawley rat *in vivo* bone marrow chromosomal aberration assay. However, the levels of aberrations were within the historical control range and assessed negative.

3.3.11 Mechanism of Carcinogenicity

In 1996, the HED CPRC classified diuron as a "known/likely" human carcinogen, based on urinary bladder carcinoma in both sexes of the Wistar rat, kidney carcinomas in the male rat (a rare tumor), and mammary gland carcinomas in the female NMRI mouse [*Diuron (PC 035505): Assessment of Mode of Action on Bladder Carcinogenicity. Yung Yang. September 20, 2001*]. The CPRC also recommended a low dose linear extrapolation model with Q_1^* of 1.91×10^{-2} $(mg/kg/day)^{-1}$ be applied to the animal data for the quantification of human risk, based on the urinary bladder carcinomas in the rat.

The registrant has argued that this assessment needed reconsideration for the following reasons (MRID 45494501): 1) there is no history of human carcinogenesis as a result of diuron exposure, 2) there is a plausible mode of action that discounts the relevance of the rat bladder carcinomas to humans, 3) the mouse historical data were not considered in their entirety and should be considered 'spontaneous," 4) the structure activity relationships actually decrease the weight-of-the-evidence of diuron carcinogenicity rather than increase the weight, and 5) new guidelines are in place that separate the 'known' from 'likely' category.

The Agency's CPRC and Mechanism of Toxicity Assessment Review Committee (MTARC) have reviewed the submitted information/data [Cancer Classification and Mechanism of Action (MRID

45494501) and mutagenicity studies (MRIDs 45494502-05)], considered the registrant's proposed mechanism of action and determined that diuron will not be re-classified at this time (*DIURON: Cancer Classification and Mechanism of Action. Yung Yang. October 10, 2001*). The Agency based its decision on: 1) the registrant did not submit any data or information to support its claim that there is no evidence of human carcinogenesis, 2) the submitted information is <u>insufficient</u> to support a mode of action on bladder carcinogenicity for diuron, 3) the mouse historical data have been reviewed and included in the updated DER (MRIDs 42159501 and 43349301) and the Agency concluded that a positive oncogenic response was seen in high-dose female mice compared to the control group, 4) there is insufficient evidence to support the notion that the structure activity relationships actually decrease the weight-of-the-evidence of diuron carcinogenicity rather than increase the weight, and 5) preliminary reviews have been conducted on newly submitted *in vivo* cytogenetic mutagenicity studies [Mouse bone marrow micronucleus assays (MRIDs 45494502-05)] and no evidence of cytogenetic effect was seen in mice administered either technical grade or formulated diuron; however, these studies provide little additional information since the CPRC has already concluded that there is little or no concern for the mutagenic activity of diuron.

Table 4. Summary of Toxicology Endpoint Selection

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	No appropriate endpoint attributed to a single dose was identified. Therefore, an acute RfD was not established.		
Chronic Dietary	LOAEL = 1.0 UF = 300 FQPA SF = 1*	Evidence of hemolytic anemia and compensatory hematopoiesis (significantly decreased erythrocyte counts, hemoglobin levels, and hematocrit, and increased MCV, MCH, abnormal erythrocyte forms, reticulocyte counts, and leukocyte count)	Combined chronic toxicity/carcinogenicity study in rats MRID 40886501, 43871901, 43804501, 44302003
		Chronic RfD = 0.003 mg/kg/day **cPAD = 0.003 mg/kg/day**	
Incidental Oral, short-term (1-30 days)	NOAEL= 10 UF = 100 FQPA SF = 1*	Decreased body weight and food consumption at maternal LOAEL of 50 mg/kg/day.	Developmental toxicity study in rabbits MRID 40228802
	LOC for residential MOE = 100		
Incidental Oral, Intermediate-Term (1-6 months)	NOAEL = 1.0 UF = 100 FQPA SF = 1*	Altered hematological parameters at LOAEL of 10 mg/kg/day, observed at 6 months.	Chronic toxicity/carcinogenicity study in rats MRID 40886501, 43871901, 43804501, 44302003
	LOC for residential MOE = 100		
Dermal, Short-Intermediate-Term	No systemic toxicity was seen following repeated dermal dosing at 1200 mg/kg/day in the rabbit dermal toxicity study. Also, there is no developmental concern. No hazard was identified and no quantitative assessment is required.		
Dermal, Long-Term (6 months to life-time) Absorption factor of 4% used for conversion from oral to dermal route	LOAEL = 1.0 UF = 300 FQPA SF = 1*	Evidence of hemolytic anemia and compensatory hematopoiesis (significantly decreased erythrocyte counts, hemoglobin levels, and hematocrit, and increased MCV, MCH, abnormal erythrocyte forms, reticulocyte counts, and leukocyte count).	Chronic toxicity/carcinogenicity study in rats MRID 40886501, 43871901, 43804501, 44302003
	LOC for occupational/residential MOE = 300		
Inhalation, Short-Term (1-30 days)**	NOAEL = 10 UF = 100 FQPA SF = 1*	Decreased body weight and food consumption at maternal LOAEL of 50 mg/kg/day.	Developmental toxicity study in rabbits MRID 40228802
	LOC for occupational/residential MOE = 100		

Inhalation, Intermediate-Term (1-6 months)**	NOAEL = 1.0 UF = 100 FQPA SF = 1*	Altered hematological parameters at LOAEL of 10 mg/kg/day, observed at 6 months.	Chronic toxicity/carcinogenicity study in rats MRID 40886501, 43871901, 43804501, 44302003
	LOC for occupational/residential MOE = 100		
Inhalation, Long-Term (6 months to life-time)**	LOAEL = 1.0 UF = 300 FQPA SF = 1*	Evidence of hemolytic anemia and compensatory hematopoiesis (significantly decreased erythrocyte counts, hemoglobin levels, and hematocrit, and increased MCV, MCH, abnormal erythrocyte forms, reticulocyte counts, and leukocyte count).	Chronic toxicity/carcinogenicity study in rats MRID 40886501, 43871901, 43804501, 44302003
	LOC for occupational/residential MOE = 300		
Cancer	Known/likely human carcinogen	Urinary bladder carcinoma in both sexes of the Wistar rat, kidney carcinomas in the male rat (a rare tumor), and mammary gland carcinomas in the female NMRI mouse	Carcinogenicity study in rats and mice MRID 40886501, 43871901, 43804501, 44302003 and 42159501, 43349301
	$Q_1^* = 1.91 \times 10^{-2}$ (mg/kg/day)$^{-1}$		

* FQPA SF only applied to residential and other non-occupational exposures
** An oral endpoint was used for inhalation exposure: inhalation exposure assumed equivalent to oral exposure.

3.4 Endocrine Disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, diuron may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

At this time, neither the available submitted studies on diuron nor the literature show any indication of endocrine disruption effects.

3.5 Potential Tetrachloroazobenzene Contamination

Diuron has been reported to contain trace amounts of a manufacturing impurity, 3,3',4,4'-tetrachloroazobenzene, a.k.a. TCAB, which has been shown to be a cytochrome P450 enzyme inducer. A summary of short-term bioassays compiled by the National Toxicology Program states that (*TOX-65, 1998*),

> “3,3',4,4'-tetrachloroazobenzene caused typical dioxin-like effects, such as thymic atrophy, an increase in liver weights, induction of hepatic cytochrome P4501A, and decreased mean body weight gains. Furthermore, in the 13-week studies, a sharp decrease in circulating thyroxine concentrations was observed even at the lowest dose (0.1 mg/kg) tested in rats. Other effects included a decrease in epididymal spermatozoal concentration in mice, major effects on the hematopoietic system, and increased incidences of hyperplasia of the forestomach in 3 and 30 mg/kg males and 30 mg/kg females. A no-observable-adverse-effect-level (NOAEL) was not reached in rats. The NOAEL in mice was 0.1 mg/kg. Comparison of various dioxin-like effects in these studies with those reported in the literature indicate that 3,3',4,4'-tetrachloroazobenzene is six to two orders of magnitude less potent than 2,3,7,8-tetrachlorodibenzo-p-dioxin.”

Chronic toxicity/carcinogenicity studies are not available for TCAB. The specific endpoint(s) and related dose levels that may be observed in chronic toxicity studies, or the specific carcinogenic potential of this compound is not known. However, since it is assumed that TCAB may have been present in all diuron toxicological test materials, including the test material for the chronic toxicity/carcinogenicity studies, the Agency believes that the risks from exposure to diuron (including carcinogenic potential) have not been underestimated.

4.0 EXPOSURE ASSESSMENT AND CHARACTERIZATION

4.1 Summary of Registered Uses

Diuron is an herbicide currently registered for use on a variety of fruit, vegetable, nut, and field crops. At this time, products containing diuron are intended for both occupational and non-occupational (residential) uses. Occupational uses include agricultural food and non-food crops; fruit and nut crops; ornamental trees, flowers, and shrubs; paints and coatings; ornamental fish and catfish production; and non-crop areas such as rights-of-way and industrial sites. Non-occupational uses include residential ponds, aquariums, and paints.

Diuron is a pre- and post-emergent herbicide that controls a wide variety of annual and perennial broad leafed and grassy weeds on both crop and non-crop sites. Examples of the types of weeds that diuron is used to control include (but are not limited to) the following: button weed, pigweed, carpetweed, poison ivy, milkweed, vines, chickweed, ragweed, aster, thistle, dandelion, morning glory, mustard, wild turnip, pepper weed, wild oat, Bermuda grass, orchard grass, crabgrass, love grass, fescue, velvet grass, rye grass, witch grass, and blue grass. Diuron is also used as a mildewcide in paints and an algaecide in ponds.

Diuron is formulated as a technical product and formulation intermediate (98.8 to 80 % ai), granular (0.2 % to 20 % ai), pellet/tablet (0.51 % to 19 % ai), wettable powder (25 % to 80 % ai), dry flowable (water dispersible granules; 40 % to 80 % ai), emulsifiable concentrate (2 % to 80 % ai), flowable concentrate (19 % to 47.5 % ai), soluble concentrate (5.1 % to 40 % ai), and ready-to-use solution (0.67 % to 19 % ai). Application rates range from 0.8 to 87.1 lbs ai/acre.

Equipment for commercial use includes groundboom sprayer, aerial equipment, chemigation, rights-of-way sprayer, high-pressure handwand, low-pressure handwand, tractor-drawn spreader, push-type spreader, airless sprayer, paintbrush, shaker-type applicator, backpack sprayer, backpack granular spreader, belly grinder, and by hand. Products intended for residential use may be applied using a spoon, by hand, by airless sprayer, or by paintbrush/roller.

Diuron is generally applied to the soil prior to germination of weed seeds or when weeds are in an active growth stage. Diuron may also be applied as a post-emergent herbicide, either as a directed spray or over the top of resistant foliage. It may be applied one to two times per season, with the exception of sugarcane (three times per season) to control a wide range of broad leafed and grassy weeds.

Occupational-Use Sites

The occupational crop use sites in this assessment have been grouped as follows:

Vegetables and Field Crops: alfalfa (forage), artichokes, asparagus, barley, blackberries, boysenberries, blueberries, cane berries, corn (field corn only), cotton, currants, dewberries, elderberries, gooseberries, grapes, huckleberries, loganberries, mint, oats, olives, peas (field or southern), pineapples, raspberries, sorghum, sugarcane, and wheat.

Fruit and Nut Trees (orchard crops), including apples, bananas, citrus, filberts (hazelnuts), macadamia nuts, pecans, peaches, pears, papayas, plantains, and walnuts.

Ornamental Trees, Flowers, and Shrubs, including shade trees, citrus trees (non-bearing and nursery stock), tree plantings (including ash, cedar, elm, oak, pine, poplar, and fir), Easter lilies, gladiolus, iris, lilies, narcissus, and ornamental grasses.

Cotton Defoliant (state labels only)

Non-crop Areas, including rights-of-way; industrial sites; drainage systems; irrigation systems; lakes, ponds, holding basins, and other similar sites that have been drained; airports and landing fields; fire plugs; cable closures; and warehouses.

Paints, Solvents, Adhesives, and Coatings

Ornamental Fish and Catfish Ponds

Residential Use Sites

Residential Ponds and Aquariums

Paints, Solvents, Adhesives, and Coatings

4.2 Dietary Exposure/Risk Pathway

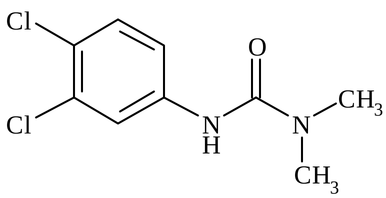
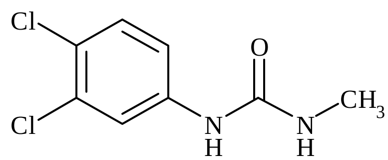
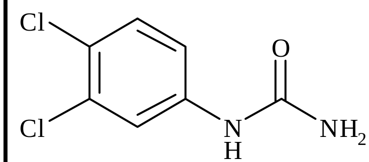
Tolerances range from 0.05 ppm (meats, milk) to 7 ppm in/on asparagus *(Residue Chemistry Chapter for the Diuron Reregistration Eligibility Decision Document. John Punzi. July 29, 2001*). Diuron is applied 1 or 2 times per season using single application rates of approximately 1 pound per acre. Usage data concerning domestic percent crop treated data from the Biological and Economic Assessment Division (BEAD) indicate that ~50% of citrus, 25% of berries, 15% of nuts, 10% of cotton, grapes, peaches, or pome fruit, and 1% of field crops are treated with diuron. Nearly 10 million pounds of diuron are used annually in the United States.

Tolerances for residues of diuron in/on plant and animal commodities are established under 40 CFR §180.106. Diuron tolerances are currently expressed as diuron *per se*. The Agency is recommending that the tolerance expression for diuron be revised to include metabolites hydrolyzable to 3,4-dichloroaniline (3,4-DCA). This determination is based on the results of the reviewed plant and animal metabolism studies. Adequate analytical methods exist for data collection and tolerance enforcement in plants. Independent laboratory validation of the enforcement method is required for livestock methods prior to Agency validation. Label revisions are required for many crops in order to reflect the parameters of use patterns for which residue data are available. Many of the revisions concern retreatment intervals, preharvest intervals (PHI's) and rotational crop restrictions.

The Metabolism Assessment Review Committee (MARC) met on July 3, 2001 to discuss the metabolism of diuron in plants and animals from the results of wheat, corn, orange, ruminant, and poultry studies together with the environmental fate studies conducted in soil and water (*Diuron Metabolism Committee Briefing Memo. John Punzi. August, 27, 2001*).

The ^{14}C-containing residues that were identified in plants (Table 5): diuron, 3,4-dichlorophenylurea (DCPU), and 3-(3,4-dichlorophenyl)-1-methylurea (DCPMU). No other dichloroaniline-containing metabolites were identified. The majority of radioactivity in the aqueous/organic fractions was characterized as polar unknowns. Radiovalidation of a GC/ECD data collection method which is similar to the enforcement method suggested that a good portion of these polar metabolites can be converted to 3,4-DCA.

Table 5. Parent and Major Metabolites

		
Diuron: 3-(3,4-dichlorophenyl)-1,1-dimethylurea	**DCPMU; IN-15654**: 3-(3,4-dichlorophenyl)-1-methylurea	**DCPU; IN-R915**: 3,4-dichlorophenylurea

In animals, the principal residue identified was DCPU. The parent and other dichloroaniline-containing metabolites (i.e., 3,4-DCA and DCPMU) that can be determined by the current enforcement methods were detected in much smaller quantities. Four minor hydroxylated metabolites (2-OH-DCA; 2-OH-DCPU; 2-OH-DCPMU; and N-acetyl-2-OH-DCA) were also detected; these metabolites were not observed in plants and would not be determined by the current enforcement method.

The major portion of radioactive residues in milk (in lactating goats) was comprised of several conjugated polar components which collectively accounted for 56% of total radioactive residue (TRR). These polar components also accounted for substantial portions of the total radioactivity in liver (collectively 25% of TRR) and kidney (collectively 23% of TRR). Attempts to further elucidate the nature of these polar materials using various techniques (e.g., enzyme digestions, heat treatment) were not successful. Although these polar components were not wholly identified, the registrant noted that the results from a radiovalidation study suggest that a large portion of these polar components are hydrolyzable to 3,4-DCA and would be quantified using the residue enforcement method.

The environmental data base indicates that diuron has potential for leaching to ground and surface water. The environmental metabolism studies, conducted under a variety of conditions, demonstrate that monochlorinated methylphenyl urea (MCMPU) and monochlorinated dimethylphenyl urea (MCDMPU) can be formed under some conditions and that MCDMPU is a major degradate in aquatic aerobic and anaerobic studies. DCPMU was also identified as a major environmental degradate in several studies and 3,4- DCA, DCMU, PDMU were identified as minor metabolites.

The MARC concluded that for tolerance expression and risk assessment purposes, the residues of concern in/on plants and animals are diuron and its metabolites that are hydrolyzable to 3,4-DCA [*Diuron. Results of the Health Effects Division (HED) Metabolism Assessment Review Committee(MARC) Meeting Held on 03-JULY-2001. John Punzi. August 10, 2001*]. This decision was based on: 1) the assumption that the metabolites would not be any more toxic than the parent and 2) the consideration that the analytical methods used to collect the field trial data are not capable of measuring each metabolite individually. To account for the poor recovery of hydroxylated metabolites from milk, it was determined that the levels of diuron residues in milk identified in the ruminant feeding study would be multiplied by 10 (*The Metabolism Committee Meetings for Diuron Held on October 21 and November 5, 1993. Randy Perfetti. November 17, 1993*) to account for all of the exposure to diuron-related residues in the risk assessment.

The MARC also concluded that for risk assessment purposes, the residues of concern in drinking water are parent, and metabolites that are hydrolyzable to 3,4-DCA, and MCPDMU. The MARC raised concerns for MCPDMU based on an analogous compound, monuron. With the exception of the position of the chlorine, the structures are identical. There are cancer concerns for monuron but the target organs are different than those affected by diuron. The MARC recommended that a separate cancer assessment be conducted for MCPDMU.

4.2.1 Residue Profile

Diuron is used on a wide variety of food and feed crops. Residue levels from United States Department of Agriculture (USDA) and Food and Drug Administration (FDA) monitoring programs do not include all the residues of concern needed for the Agency's diuron risk assessment (diuron and metabolites convertible to 3,4-DCA) and would be inappropriate for this analysis. Anticipated residues (ARs) from field trial data were utilized to estimate the dietary exposure to diuron from the diets of the U.S. population as well as certain population subgroups. These ARs were developed previously (D250038, Rick Loranger. October 8, 1998 and D169227, Christina Swartz. April 27, 2001). The field trials were conducted at the highest application rates for the crop tested and therefore, the residues from these trials are considered high end. Available processing data for apple, citrus and grapes were available and indicated that there was no concentration, nor reduction, in residue values for these processed commodities (i.e. juice, dried fruit). The sugarcane processing study showed a reduction of residues in refined sugar but a concentration of residues in molasses. With the exception of residue data from the processing of sugarcane into refined sugar and molasses, the only additional refinements to the residue data are the use of averaged percent crop treated (%CT) information (*Quantitative Usage Analysis for Diuron. Alan Halvorson. March 20, 2001* and *Updated QUA. Alan Halvorson. April 27, 2001*).

The registrants have committed to label changes which would restrict the application of diuron to asparagus plantings <u>prior to the appearance of spears</u>. Residues of diuron in/on asparagus are reduced by approximately one order of magnitude (from 2.8 to 0.26 ppm) by this proposed use. To examine the effect of the differing residue values for asparagus on the dietary risk, calculations were performed using residue levels reflecting treatment of asparagus crops before and after spears appear. There were minimal changes in the chronic exposure estimates using data from pre-emergence or post-emergence applications of diuron to asparagus.

4.2.2 Acute Dietary

Diuron is not acutely toxic. No adverse effects attributed to a single exposure were identified in any available study. Therefore, no acute dietary risk assessment was conducted.

4.2.3 Chronic Dietary

A chronic exposure analysis for diuron and its metabolites that are hydrolyzable to 3,4-DCA was performed utilizing the Dietary Exposure Evaluation Model (DEEM™) software Version 7.73, which incorporates USDA's Continuing Surveys of Food Intake by Individuals (CSFII), 1989-1992. The 1989-1992 data are based on the reported consumption patterns of more than 10,000 individuals over three consecutive days, and therefore represent more than 30,000 unique "person days" of data. Foods "as consumed" (e.g. apple pie) are linked to raw agricultural commodities and their food forms (e.g. apples cooked/canned or wheat flour) by proprietary recipe translation files within DEEM. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment. For chronic exposure and risk assessment, an estimate of the residue level in each food or food form (e.g. orange or orange juice) on the commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food form is summed with the residue consumption estimates for all other food/food forms on the commodity residue list to arrive at the total estimated exposure. The calculated chronic exposure (residue x consumption) was compared to a cPAD of 0.003 mg/kg/day, which reflects an FQPA factor of 1x. Noncancer dietary exposure estimates are expressed in mg/kg bw/d and as a percent of the cPAD (*Diuron - Chronic Dietary Exposure Assessment (PC Code 035505); DP Barcode D276683; Case 0046. John Punzi. September 10, 2001*).

Estimated chronic dietary (food) risk estimates associated with the use of diuron <u>do not exceed</u> the Agency's level of concern (> 100% cPAD) for any population subgroup including the most highly exposed population subgroup, children ages 1-6 years. The chronic dietary risk for children ages 1-6 years is 7% of the chronic PAD and 3% for the general U.S. population (Table 6). Approximately 40% of the exposure to diuron from food is from orange juice and orange juice concentrate.

Table 6: Chronic Dietary Risk Estimates

Population	Exposure mg/kg/day	% Chronic PAD
U.S. Population	0.000088	3
All Infants (<1 year)	0.000077	3

Population	Exposure mg/kg/day	% Chronic PAD
Children 1-6 years	0.00020	7
Children 7-12 years	0.000118	4
Females 13-50 years	0.000069	2
Males 13-19 years	0.000098	3
Males 20+ years	0.000066	2
Seniors 55+ years	0.000083	3

4.2.4 Cancer Dietary

The estimated cancer dietary risk associated with the use of diuron indicates a borderline exceedance above 1×10^{-6} and shows a lifetime risk estimate of 1.68×10^{-6} for the general population but, is not of concern (Table 7). As discussed earlier, the residues used in the calculations are from field trials conducted at the highest application rates and some processing data are still outstanding. Therefore, the exposure calculation is a conservative estimate. Again, the Agency assumed that exposure was to diuron and its metabolites that are hydrolyzable to 3,4-DCA. For the cancer risk assessment, the calculated chronic exposure (residue x consumption) was calculated with a Q_1^* of 1.91×10^{-2} $(mg/kg/day)^{-1}$ in human equivalents.

Table 7. Summary of Dietary Exposure and Risk for Diuron

Population	Acute Dietary	Chronic Dietary		Cancer Dietary	
	NA	**Exposure (mg/kg/day)**	**Risk (% cPAD)**	**Exposure (mg/kg/day)**	**Lifetime Risk (Q_1^*= 0.0191)**
U.S. Population		0.000088	3	0.000088	1.68×10^{-6}
All Infants < 1 year		0.000077	3	Not Applicable	
Children 1-6 years		0.000200	7		
Children 7-12 years		0.000118	4		
Females 13-50 years		0.000069	2		

4.3 Water Exposure/Risk Pathway

The diuron drinking water exposure assessment was based primarily on 1) submitted environmental fate studies, 2) limited but targeted monitoring data for diuron and its degradates, and 3) monitoring data for the parent only. Although monitoring data for the parent and its degradates were not extensive, the available measured data were revealing. For example, monitoring of 32 lakes in Texas showed that diuron was the predominant contaminate detected. Surface and ground water conclusions from these sources were compared with simulation model predictions. Monitoring sources included United States Geological Survey (USGS) and published literature (*Drinking Water Assessment for diuron and its degradates. Ibrahim Abdel-Saheb. March 11, 2001*). There is no Maximum Contaminant Level Goal (MCLG) or Maximum Contaminant Level (MCL) established by the Agency's Office of Water for diuron.

Diuron has the potential to leach to ground water and to contaminate surface waters through run-off. Environmental fate data analyzed by EFED show that diuron is persistent. Diuron is stable to hydrolysis at pH's 5, 7, and 9. The calculated half-lives in aqueous and soil photolysis studies were 43 and 173 days, respectively. The half-lives in aerobic and anaerobic soil metabolism studies were 372 and 1000 days, respectively. However, in viable laboratory aquatic systems, degradation appeared to be accelerated with half-lives of 33 and 5 days in aerobic and anaerobic systems, respectively. The predominant degradate formed in both the soil photolysis and aerobic soil metabolism studies was DCPMU. The only significant (>10 % of applied) degradate in the aerobic and anaerobic aquatic metabolism studies was MCDMPU. Diuron dissipated from bare ground plots with half-lives ranging from 73 to 133 days, and the major degradate (MCDMPU) dissipated from the same plots with half-lives ranging from 217 to 1733 days. Diuron and MCDMPU residues were detected mainly at the upper 15-30 cm depths at all sites and sporadically detected below this depth. An upgradable adsorption/ desorption/leaching study (MRID# 44490501) showed that diuron has a low-medium K_{oc} (468-1666). In addition, diuron has low water solubility (42 ppm).

The degradate 3,4-DCA is an environmental degradate common to diuron, linuron, and propanil. EFED does not have sufficient fate and transport data on 3,4-DCA. In an aerobic soil metabolism study with the compound <u>propanil</u>, 3,4-DCA had a half-life of 30 days (MRID# 41537801), and in a water paddy the half-life ranged from 2-3 days (MRID# 42200401, 42200501). Even though these studies suggest that 3,4-DCA will not persist in soil or water, 3,4-DCA has been detected often in surface water. Thus, more data are needed to understand the fate of this degradate in soil and water. TCAB, also a compound of concern for human health (see Section 3.5), was identified as having a minor presence in a diuron soil photolysis study (MRID# 41719302) with a maximum concentration of 0.038 ppm.

<u>Surface Water Exposure:</u> EFED has targeted, but, limited monitoring data on the concentrations of diuron and its degradates in surface water.

A study on the occurrence of cotton herbicides and insecticides in the Playa lakes of the high plains of western Texas concluded that diuron was the major pesticide detected in water samples collected from 32 lakes with a mean concentration of 2.7 ppb. Diuron metabolites (DCPMU, DCPU, and 3,4-DCA) were found in 71% of the samples analyzed. The mean concentrations of these metabolites were 0.45 ppb for DCPMU, 0.31 ppb for 3,4-DCA, and 0.2 ppb for DCPU. In this study, water samples were taken within two days after diuron application to cotton in the region. Diuron usage on cotton in this part of the state reached an average of $1.379 lb ai/mile/yr. Even though, the monitoring of diuron concentrations from use on cotton in this part of the state is an example of a targeted study, the frequency of surface water sampling and the length of the sampling period were insufficient to satisfy the temporal and spatial requirements for regulatory purposes. This study has limited use in a national assessment because EFED does not expect western Texas to be one of the most vulnerable use areas for runoff. However, because the samples were taken within two days after application, the results may represent a lower bound of possible peak concentrations that could occur in drinking water in that area.

The USGS National Water Quality Assessment Program (NAWQA) collected 1420 surface water samples from 62 agricultural stream sites during the period from 1992-1998. Sampling was for the parent only. One to two samples were collected each month throughout the year during periods when pesticide transport in the streams was expected to be low. At most sites, the sampling frequency was increased to 1 to 3 samples per week during periods when elevated levels of pesticides were expected in the streams. Diuron was detected in 7.32% of the samples (detection limit = 0.05 ppb) with an average concentration of 0.13 ppb in 95% of samples. The maximum concentration of diuron was 13 ppb (estimated concentration).

The monitoring data, though useful in a limited capacity, are either not nationally representative or did not monitor for any of the degradates and would underestimate potential drinking water exposures. Therefore, EFED calculated estimated exposure concentrations (EEC) in surface waters employing Tier II surface water modeling using the Index Reservoir (IR) and Percent Crop Area (PCA) modifications to PRZM and EXAMS. The IR represents a potential vulnerable drinking water source from a specific area (Illinois) with specific cropping patterns, weather, soils, and other factors. The PCA is a generic watershed-based adjustment factor which represents the portion of a watershed planted to a crop or crops and will be applied to pesticide concentrations estimated for the surface water component of the drinking water exposure assessment. The IR-PCA PRZM/EXAMS model was used to determine estimated surface water concentrations of diuron and its degradates DCPMU, DCPU, 3,4-DCA, and N'-(3-chlorophenyl)-N-N-dimethylurea (MCPDMU). Modeling results are shown in Table 9. The modeled concentrations are higher (9-100 times) than the levels found in existing surface water monitoring data targeted to pesticide use areas.

<u>Ground Water Exposure:</u> EFED has limited targeted monitoring data on the concentrations of diuron and its degradates in groundwater. Table 8 shows validated monitoring data for diuron that were collected for the states of California (CA), Florida (FL), Georgia (GA), and Texas (TX) from 1971-1991.

Table 8. Groundwater monitoring data for diuron (USEPA 1992). Number of wells sampled (number of wells with residues).

State	number of well (detections)	range of conc. (ppb)

CA	2010 (82)	0.05 - 3.95
FL	15385 (9)	1.18 - 5.37
GA	70 (67)	1.00 - 5.00
TX	31 (2)	0.01 - 0.02

According to the Ground Water Protection Section of the Florida Department of Environmental Protection, ground water samples collected from wells between May/1990 and November/1997, showed diuron detections ranging from 0.94 - 12 ppb (detection limit = 0.48 ppb). The arithmetic mean concentration was 2.44 ppb. Well water samples were collected from the following counties: Highlands, Jackson, Lake, Orange, and Polk. With the exception of the 12 ppb sample in Orange County, the majority of the detections were in Highlands County where citrus is grown. Diuron concentrations in Highlands County decreased with time to about 1 ppb but were detected every year. In Polk County, diuron concentrations showed a seasonal pattern, with the highest concentrations in the spring and lowest concentrations in the fall, but it was not detected in all years.

The USGS NAWQA analyzed pesticide occurrence and concentrations for major aquifers and shallow ground water in agricultural areas (detection limit = 0.05 ppb). Analysis of 2608 samples (major aquifers study) showed diuron in 71% of the samples analyzed with a maximum concentration of 0.34 ppb. The maximum diuron concentration in 897 samples from shallow groundwater sites was 2.0 ppb, with diuron detected in only 1.23% of samples analyzed (USGS, 1998). A major component of the sampling design in the NAWQA study was to target specific watersheds and shallow ground water areas that are influenced primarily by a single dominant land use(agricultural or urban) that is important in the particular area. The ground water data were primarily collected from a combination of production and monitoring wells.

Even though the ground water monitoring data collected by NAWQA are from sites considered typical for use areas, the frequency of sampling and the length of sampling period were not sufficient to represent the temporal and spatial requirements for regulatory purposes. In addition, USGS studies only monitored for the parent. Therefore, the Screening Concentration in Groundwater (SCI-GROW) model was used to estimate potential ground water concentrations for diuron and its degradates. Modeling results are shown in Table 9.

Table 9. Estimated environmental concentrations in surface and ground water for diuron and its degradates from diuron use on citrus.							
	model EECs (Fg/L)					use(s) modeled	PCA
	Diuron	DCPMU	DCPU	3,4-DCA	MCPDMU	one application of diuron on citrus @ 9.6 lb ai/acre, ground application	Default (0.87)
Surface water/ peak	613	130	5.80	0.08	136		
Surface water/ 1-10-year average	128	27.0	1.20	0.02	36.4		
Surface water/ mean of annual values	85.0	18.0	0.80	0.01	25.5		
Groundwater/ (peak and long-term average)	6.5	2.50	0.1	$2X10^{-4}$	1.38		

The IR-PCA modeling results indicate that diuron and its degradates have the potential to contaminate surface waters by runoff in areas with large amounts of annual rainfall. Modeling results (EECs) were several orders of magnitude (ranging from 9-100 times) higher than diuron surface water monitoring data from known pesticide use areas. Though environmental metabolism studies indicate that MCPDMU is an environmental degradate of diuron, it either was not detected in any of the monitoring studies or the researchers did not look for it. Since EFED lacks complete environmental fate data (such as the aerobic aquatic and anaerobic aquatic studies) on any of the degradates, the EECs for surface and ground water were based on half-lives that were calculated on cumulative residues (*Drinking Water Assessment for diuron and its degradates. Ibrahim Abdel-Saheb. March 11, 2001*).

4.4 Residential Exposure/Risk Pathway

4.4.1 Home Uses

There are potential residential exposures from activities associated with: 1) pond and aquarium use and 2) paint use. Though there are existing labels for applications of granular formulations of diuron to turf, most are limited to industrial and non-crop uses. Others (reg. #33560-46 and #802-352) are either pending cancellation by the registrant or the registrant has agreed to place language specifically restricting residential uses on the label. Therefore, with these actions by the registrants of the labels mentioned above, no residential turf uses exist for diuron and a residential assessment for turf was not conducted (*Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document for Diuron. Renee Sandvig and Christina Jarvis. October 16, 2001*).

Pond and Aquarium Use

Three diuron products are designed for residential use as algaecide in ponds and aquariums and are being supported for reregistration. They are Pond Block (0.51% ai, reg. #33034-1) and No More

Algae (0.67% ai, reg. #33034-2), which are both in tablet/block form, and No More Algae (0.67% ai, reg. #33034-3), which is in ready to use liquid form. No exposure data exist for the use of the algaecide tablets/blocks. Since the products are formulated as tablets/blocks and dissolve in less than 5 minutes, minimal exposure is expected and was not quantified. Furthermore, exposure from the block/tablet forms of diuron are expected to be less than exposure from the liquid formulation, since spillage may occur from measuring and pouring liquid diuron.

The No More Algae liquid is used at a rate of one teaspoon (5 ml) for every 10 gallons of aquarium or pond water. Treatment should be repeated once a month or when algae growth reappears. Residential exposure may result from measuring the liquid and pouring the liquid into the aquarium or pond. Unit exposure data from the Pesticide Handlers Exposure Database (PHED) for the mixing/loading of liquids will be used to assess this exposure. Dermal exposure for noncancer risk estimates was not calculated, since no toxicity by the dermal route is expected for this duration. Exposure is expected to be short-term (1 to 30 days).

Paint Use

Antimicrobial exposures to handlers are defined by the Antimicrobial Division (OPP/EPA) as *"primary"* and *"secondary"* handlers. The primary handlers are defined as those individuals exposed to the formulated product (adding the diuron product into vats of paint during its manufacturing), while the secondary handlers are those individuals exposed to the active ingredient as a direct result of its incorporation into an end use product (individuals using the caulk or paint that in itself is not a registered pesticidal product). HED has identified and assessed the primary handlers as those individuals who mix and load diuron formulation at the manufacturing facility for use as a mildewcide in adhesives, caulks, sealants, and paints. The secondary handlers are commercial and residential applicators who apply adhesives, caulks, sealants, and paints. Since diuron is only added during the manufacturing process, only the secondary handler use (application of the products containing diuron) was assessed in the residential assessment.

No handler exposure data have been submitted to determine the extent of these exposures. Secondary residential handlers were assessed using an airless sprayer and a paint brush. Unit exposure data used to assess the exposure resulting from applying paint containing diuron with an airless sprayer and a paintbrush were taken from a previous chlorothalonil assessment (*Revised Occupational and Residential Exposure Assessment for the Chlorothalonil Reregistration Eligibility Decision (RED). Jeff Evans. January 22, 1997*). This assessment used data from a proprietary worker exposure study conducted on the use of chlorothalonil in paint. These data were merged with data contained in PHED to increase the number of replicates and the quality of the unit exposure data. The surrogate chlorothalonil study data are assumed to be representative of the exposure from the use of diuron using the same equipment, since the two chemicals are formulated together in three out of the four currently registered diuron paint products. The clothing and personal protective equipment (PPE) scenarios for each type of exposure reflect the clothing and PPE worn in the study from which the unit exposure values were derived. The clothing worn in the chlorothalonil assessment were long pants and long sleeved shirt, which are different from the short sleeved and short pants clothing normally considered possible for residential exposures. Therefore, for comparison, data representing both clothing scenarios (long sleeves and long pants, as well as short sleeves and short pants) were also included in the assessment for the application of paint with an airless sprayer and a paint brush/roller.

Although there is potential exposure during the application of the other treated materials (e.g., caulks and sealants), they were not included in this assessment because no data are available to assess these uses. There is also a potential for exposure from applying paint with a roller. It is HED's professional judgement that the airless sprayer and paintbrush scenarios represent the high end exposures for diuron antimicrobial secondary uses and therefore, would likely be protective of the exposures from caulk and sealant uses and painting with a roller.

No data are available to determine whether or not diuron contained in paint products would be more or less readily absorbed through the skin.

4.4.1.1 Handler

The Agency has determined that there are potential exposures to residential mixers, loaders, and applicators during the usual use-patterns associated with diuron. Based on the use patterns, five major residential exposure scenarios were identified for diuron: (1) Loading ready-to-use liquids; (2) Applying paints/stains with a paintbrush; (3) Applying paints/stains with a paintbrush (study data); (4) Applying paints with an airless sprayer; and (5) Applying paints with an airless sprayer (study data).

In addition to diuron's mildewcide use in paints and stains, it is also used in plaster, stuccos, sealants, caulking, and fillers. Unit exposure data only exists for the use of paints/stains with airless sprayer and paintbrush. These exposure scenarios are assumed to have a higher exposure than the use of diuron in plaster, stucco, sealants, caulking and fillers, since less material would be applied in a day. Therefore, the paint/stain assessment is considered protective for exposure resulting from the use of diuron in plaster, stucco, sealants, caulking, and fillers.

The exposures to residential secondary handlers are expected to be of a short-term duration (less than 30 days). For homeowners, the airless sprayer is assumed to be used for outdoor applications only. Homeowner use of diuron treated paint indoors is restricted to small rooms such as bathrooms, laundry rooms, etc. where the use of an airless sprayer is unlikely to occur. For the cancer risk assessment, homeowners applying diuron treated paint are assumed to be exposed two days per year, which is considered a high-end assumption.

Short-term Exposure/Risk

Table 10 presents the short term (1-30 days) dermal and inhalation exposures at baseline as well as the risk assessments for the inhalation exposures. No systemic toxicity was seen following repeated dermal dosing in the dermal toxicity study therefore, no quantitative assessment of risk by the dermal route is required. No PPE or engineering controls are assumed for residential exposures. Residential handlers are assumed to be wearing short-sleeved shirts and short pants.

The short-term risk assessment incorporated a NOAEL of 10 mg/kg/day for noncancer inhalation exposures and had an LOC or target MOE of 100, including the 1x FQPA factor. The calculations of short-term inhalation risk indicate that the inhalation MOEs are more than 100 at the baseline level for the all the assessed exposure scenarios and are not considered risks of concern.

Cancer Exposure/Risk

To assess cancer risk, an average daily dose, a lifetime daily dose and a total cancer risk are calculated. For the cancer assessment, potential dermal exposure was included with a high-end dermal absorption factor (measured from a submitted study) of 4%. Assumptions included in the calculations were an average adult lifetime of 70 years and an exposure duration of 50 years. The number of exposures per year for the pond and aquarium uses are based on the label recommendations. The "No More Algae" liquid label states that "For regular maintenance, use once a month or as algae starts to reappear." Therefore, 12 exposures per year were assumed. Homeowners applying diuron treated paint are exposed two days per year. Since it would be unusual for a homeowner to paint their house every year with diuron treated paint, this is considered a high-end estimate.

Cancer risks equal to or less than 1×10^{-6} are not considered to be of concern. Risks greater than 1×10^{-6} for the general population are considered to be of concern. The residential cancer risk assessment was conducted using the diuron Q1* of 1.91×10^{-2} and is summarized in Table 11.

The following scenarios have <u>cancer risks greater than 1×10^{-6}</u> at the baseline level of exposure (bracketed numbers can be matched to the exposure scenarios in the tables):

(2) Applying paints/stains with a paint brush;

(3) Applying paints/stains with a paint brush (study data) for stains;

(4) Applying paint with an airless sprayer; and

(5) Applying paint with an airless sprayer (study data).

The following scenarios have <u>cancer risks less than 1×10^{-6}</u> at the baseline level of exposure:

(1) Loading ready to use liquids for ponds and aquariums

All scenarios were assessed at the maximum rate of application. Average application rate for the paint use is unknown and is requested to refine this risk. The residential cancer risk is considered conservative since an upper bound dermal absorption rate was used (no dermal penetration study was submitted), coupled with maximum application rates.

4.4.1.2 Postapplication

Postapplication inhalation and dermal exposure resulting from the use of diuron in ponds and aquariums is expected to be minimal. Diuron is applied to ponds/aquariums in the form of a liquid and an effervescent tablet. Due to the high dilution rate of the liquid in pond and aquarium water (0.0000074 lb ai per gallon of water), and the effervescent nature of the tablet (expected to dissolve in less than five minutes), postapplication exposure to diuron in pond and aquarium water is expected to be minimal. Furthermore, postapplication activities in and around ponds/aquariums treated with diuron are assumed to be infrequent.

Postapplication inhalation and dermal exposure resulting from the indoor use of diuron in paints is also expected to be minimal. The Agency has conducted a screening-level inhalation assessment using the Multi-Chamber Concentration and Exposure Model (MCCEM). MCCEM uses air infiltration and interzonal air flow rates, together with user inputs for emission rates, decay rates, and outdoor concentrations to calculate time-varying indoor concentrations and associated indoor inhalation exposure due to product or material emissions in several zones or chambers within a residence. The results of this model, coupled with diuron's low vapor pressure (2×10^{-7} mm Hg at 30 EC), show minimal postapplication inhalation exposure. Furthermore, diuron-treated paint is only likely to be used in rooms where high humidity is expected (i.e. a bathroom), and would rarely be used in the entire house. It is unlikely that a homeowner would receive a significant amount of postapplication inhalation exposure from diuron-treated paint, as the very nature of its use is as a mildewcide, and any substantial loss of the active ingredient from the paint would render the product ineffective.

4.4.2 Recreational

There are no recreational use sites for diuron.

4.4.3 Other (Spray Drift; Farm Worker Children, etc.)

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from groundboom application methods. The Agency has been working with the Spray Drift Task Force, EPA regional offices and state lead agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, of which U.S. pesticide registrants are members, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types, where appropriate.

Table 10: Residential Short-Term Baseline Table

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)[a]	Inhalation Unit Exposure (µg/lb ai)[b]	Data Source	Site/Use	Application Rate[c]	Amount Treated[d]	Dermal Dose[e]	Inhalation Dose (mg/kg/day)[f]	Inhalation MOE[g]
Mixer/Loader									
Loading Ready to Use Liquids (1)	2.9	1.2	PHED V1.1	Pond	0.0000074 lb ai per gallon	3000 Gallons per day	0.00092	0.00000038	26,000,000
			PHED V1.1	Pond	0.0000074 lb ai per gallon	1000 Gallons per day	0.00031	0.00000013	79,000,000
			PHED V1.1	Aquarium	0.0000074 lb ai per gallon	50 Gallons per day	0.000015	0.0000000063	1,600,000,000
Applicator									
Applying Paint/Stains with Paintbrush (2)	230	280	PHED V1.1	Paint	0.0532 lb ai per gallon	2 Gallons per day	0.35	0.00043	23,000
			PHED V1.1	Stain	0.0532 lb ai per gallon	5 Gallons per day	0.87	0.0011	9,400
Applying Paint/Stains with Paintbrush (study data) (3)	290	507	Chlorothalonil Study/ PHED	Paint	0.0532 lb ai per gallon	2 Gallons per day	0.44	0.00077	13,000
			Chlorothalonil Study/ PHED	Stain	0.0532 lb ai per gallon	5 Gallons per day	1.1	0.0019	5,200
Applying Paint with Airless Sprayer (4)	79	830	PHED V1.1	Paint	0.0532 lb ai per gallon	15 Gallons per day	0.90	0.0095	1,100
Applying Paint with Airless Sprayer (study data) (5)	33.33	433	Chlorothalonil Study/ PHED	Paint	0.0532 lb ai per gallon	15 Gallons per day	0.38	0.0049	2,000

Footnotes:

a Baseline dermal exposure represents short pants, short sleeves and no gloves, except for the chlorothalonil study, MRID 43600102, which represent long pants, long sleeved shirts and no gloves.

b Baseline inhalation unit exposure represents no respirator.

c Application rates are based on the maximum application rates listed on the "No More Algae" liquid label and paint labels.

d Amount treated per day are from EPA estimates of average aquarium and pond size and the maximum pond size listed on the label. Paint/stain assumptions are from Expo SAC policy #12.[15]

e Daily Dermal Dose (mg/kg/day) = (Dermal Unit Exposure (mg/lb ai) x Application Rates (lb ai/A and lb ai/sq. ft.) x Area Treated per day (acres and square feet))/ body weight (70 kg).

f Daily Inhalation dose (mg/kg/day) = (Inhalation Unit Exposure (Fg/lb ai) x (1mg/1000 Fg) Conversion Factor x Application Rate (lb ai/gallon) x Amount Treated per day (gallons/day))/ body weight (70 kg).

g Short-term Inhalation MOE = Inhalation NOAEL (10 mg/kg/day) / Daily Inhalation Dose (mg/kg/day).

Table 11: Residential Cancer (Q*) Risk Table

Exposure Scenario (Scenario #)	Use site	Application Rate	Amount Treated	Total Daily Dose[a]	Baseline Daily LADD[b,c]	Baseline Risk[d]
Mixer/Loader (12 days/year)						
Loading Ready to Use Liquids (1)	pond	0.0000074 lb ai per gallon	3000 Gallons per day	0.000037	8.7 E-7	1.7 E-8
	pond	0.0000074 lb ai per gallon	1000 Gallons per day	0.000012	2.9 E-7	5.5 E-9
	aquarium	0.0000074 lb ai per gallon	50 Gallons per day	0.00000062	1.5 E-8	3.0 E-10
Applicator (2 days/year)						
Applying Paint/Stains with Paintbrush (2)	Paint	0.0532 lb ai per gallon	2 Gallons per day	0.014	5.5 E-5	1.1 E-6
	Stains	0.0532 lb ai per gallon	5 Gallons per day	0.036	1.4 E-4	2.7 E-6
Applying Paint/Stains with Paintbrush (study data) (3)	Paint	0.0532 lb ai per gallon	2 Gallons per day	0.018	5.0 E-5	9.5 E-7
	Stains	0.0532 lb ai per gallon	5 Gallons per day	0.046	1.3 E-4	2.4 E-6
Applying Paint with Airless Sprayer (4)	Paint	0.0532 lb ai per gallon	15 Gallons per day	0.045	1.8 E-4	3.4 E-6
Applying Paint with Airless Sprayer (study data) (5)	Paint	0.0532 lb ai per gallon	15 Gallons per day	0.020	5.5 E-5	1.1 E-6

Footnotes:

a Total Daily Dose (mg/kg/day) = Daily Dermal Dose (mg/kg/day) * Dermal Absorption (4%) + Daily Inhalation Dose (mg/kg/day). See Table 10 for daily dermal and inhalation doses.

b The number of exposures per year are based on the label recommendations. The No More Algae Liquid label states that " For regular maintenance, use once a month or as algae starts to reappear." Therefore, 12 exposures per year were assumed. Two exposures per year assumed for residential person painting their home.[15]

c Lifetime average daily dose (LADD) (mg/kg/day) = Total Daily Dose (mg/kg/day) * (number of days of exposure per year / 365 days/year) * (50 years exposed / 70 years in a lifetime).

d Cancer risk = LADD (mg/kg/day) * Q1 (1.91E-2 $mg/kg/day^{1}$).

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATIONS

Risk is a function of exposure multiplied by hazard (Risk = Exposure x Hazard). Exposure may be measured or modeled, depending on the available data. Ideally the exposure data would be chemical specific occupational or residential monitoring data, at-the-tap drinking water data, and close-to-the-plate food residue data on all crops. In the absence of an ideal data set, surrogate data, and other factors are incorporated into the exposure assessments (dietary and non-dietary) to present a reasonable exposure picture based on the best available data. The hazard portion of the risk equation has several layers of safety built into it to provide a cushion between exposure and the dose at which adverse effects were seen in an animal study. Generally, endpoints are based on the dose at which <u>no</u> observable adverse effect is seen in an animal study. This is the No Observable Adverse Effect Level (NOAEL). The Lowest Observable Adverse Effect Level (LOAEL) is the next highest dose in an animal study, up from the NOAEL, at which the adverse effect of concern is seen. Since the toxicity studies used for endpoint selection are conducted in animals, and there are differences between individual humans, additional uncertainty factors for inter- and intra-species variability are integrated into the hazard portion of the risk equation. Since the passage of the FQPA, an additional layer of protection is factored in (when appropriate) to provide an even greater safety cushion between exposure and toxic effects for particularly sensitive populations. It is in this light that expressions of risk (risk numbers) should be viewed with an understanding that they are not portrayals of imminent toxic effects to humans but as a measure of the distance between potential exposure and possible toxic effects.

In accordance with current HED policy (effective 03/11/99) the acute and chronic dietary endpoints are expressed as acute Population Adjusted Dose (aPAD) and chronic PAD (cPAD), and no longer as an adjusted Reference Dose (RfD).

$$\text{RfD} = \frac{\text{acute or chronic NOAEL}}{\text{Uncertainty Factor (UF)}}$$

Generally, an UF of 100 is applied for intra- and inter-species differences.

$$\text{PAD} = \frac{\text{acute or chronic RfD}}{\text{FQPA factor}}$$

The use of the PAD will apply whether the FQPA factor is retained (10x or 3x) or not (1x). When a PAD is used, such as in the dietary assessment, the risk is expressed as a percentage of the PAD which is equal to the measured exposure divided by the PAD and then multiplied by 100 or:

$$\text{Risk (\% PAD)} = \frac{\text{Exposure}}{\text{PAD}} \times 100$$

Occupational, residential (when applicable), and the aggregate risk (when appropriate) will still be expressed as the Margin of Exposure (MOE).

$$MOE = \frac{\text{NOAEL (mg/kg/d}}{\text{Exposure (mg/kg/d)}}$$

Current HED policy requires that FQPA safety factors be retained for dietary and non-occupational exposures, when appropriate, not occupational exposures (Memorandum, Special Report of the FQPA Safety Factor Committee, B. Tarplee and J. Rowland, April 15, 1998). Therefore, an MOE of $\geq$ 100 is generally needed in the occupational exposure risk assessment. For diuron, if there were long-term occupational exposures (none are expected) an MOE of $\geq$ 300 would be needed since a 3x was factored in because a LOAEL was selected for the endpoint. Since the FQPA factor is 1x, for residential uses, MOEs $\geq$ 100/300 are also needed for short- and intermediate-term, and long-term exposures, respectively.

Generally, the Agency calculates Drinking Water Levels of Comparison (DWLOC) for comparison to measured or modeled drinking water concentrations for the risk analysis. The DWLOC is the concentration in drinking water, as part of the aggregate exposure, that occupies no more than 100% of the PAD. The dietary exposure from food and DWLOC together, cannot be greater than 100% of the PAD. Any measured or modeled drinking water estimates that are less than the DWLOC are not of concern.

The Agency has calculated DWLOCs for chronic (noncancer) and short-term exposure to diuron and its degradates (metabolites hydrolyzable to 3,4-DCA) in surface and ground water for the population subgroups; children 1-6 years (most highly exposed population), infants < 1 year, females 13-50 years, and the general U.S. population. No adverse effects attributed to a single exposure to diuron were identified in any available studies. Therefore, no acute dietary risk assessment was conducted and hence, no acute DWLOC ($DWLOC_{acute}$) was calculated. The $DWLOC_{cancer}$ is the concentration in drinking water as a part of the aggregate chronic exposure that results in a negligible cancer risk (10^{-6}). Residential exposures to adult handlers would be factored into the $DWLOC_{cancer}$; however, the estimated residential risks alone are above the Agency's level of concern, therefore, $DWLOC_{cancer} = 0$.

Since no systemic toxicity was seen in the dermal toxicity study, no short- or intermediate-term occupational or residential risk assessment by the dermal route was needed. The exception was for the cancer assessment, for which the oral study and a dermal absorption factor (measured from a submitted study) were used. Based on the labeled uses, no incidental oral exposures are expected. Due to the lack of availability/submission of acceptable/guideline inhalation studies using diuron, occupational and residential risk assessments were conducted using endpoints selected from oral studies. To fully characterize the hazard and subsequent potential risk from exposures to diuron and its metabolites a 28-day inhalation study in rats is needed.

5.1 Acute Risk

No adverse effects attributed to a single exposure to diuron were identified in any available studies. Therefore, no acute dietary risk assessment was conducted, no $DWLOC_{acute}$ was calculated, and hence, no acute aggregate risk was conducted.

5.2 Short-term Risk

5.2.1 Aggregate Short-term Risk Assessment

When potential food and residential inhalation exposures are combined they result in aggregate short-term MOEs = 1043 and 1045 for adult males and females, respectively, which are <u>not of concern</u>. Based on labeled uses, no intermediate- or long-term residential handler, or postapplication exposures of any duration, are expected.

Aggregate short-term risk estimates for diuron and its metabolites hydrolyzable to 3,4-DCA would combine exposures from food (average), water, and inhalation. Since measured drinking water data (monitoring data) are limited and cannot be quantitatively included in the risk assessment, estimates of allowable levels of drinking water were calculated (see DWLOCs below) instead. The Agency determined that it was unlikely that more than one of the residential handler activities would occur concurrently during a short-term time period. Therefore, the Agency took the protective approach of including the exposures from the activity which could potentially result in the most exposure to the homeowner, applying paint with an airless sprayer, in the aggregate assessment. It should be noted that residential exposures are calculated at baseline (no personal protective equipment, no engineering controls).

The "MOE approach" was used to calculate the short-term aggregate risk, combining food and inhalation exposures, and using a NOAEL of 10 mg/kg/day. A UF of 100 (10x for interspecies extrapolation, 10x for intraspecies variability) and the 1x FQPA safety factor for diuron were applied to the assessment; therefore, an MOE of greater than 100 is not of concern.

5.2.2 Short-term DWLOC Calculations

Though some limited chemical-specific water monitoring data are available, they are not nationally representative and not at-the-tap data. Though they may be indicative of surface water and ground water levels of diuron and its metabolites, under very limited conditions, the Agency believes that they are unsuitable to be quantitatively included in aggregate risk assessment. Therefore, estimated environmental concentrations (EECs) were calculated by EFED to estimate the potential contribution to the averaged (chronic) exposure from drinking water, and the EECs were compared to the short-term DWLOCs.

The current Agency default body weight and consumption values are 10 kg and 1 liter/day, respectively, for all infants and children, 70 kg and 2 liters/day for adult males, and 60 kg and 2 liters/day for adult females. These default values and others are presently under review in the Agency (Office of Research and Development). If at a future time, the Agency decides to change the default assumptions used, the impact of the changes on the diuron risk assessment will be considered.

The $DWLOC_{short\text{-}term}$ is the concentration in drinking water, as part of the aggregate exposure, that combined with average food exposures and residential exposures and divided into the short-term NOAEL, results in an MOE that is greater than the LOC or target MOE. Any measured or modeled drinking water estimates that are less than the DWLOC are not of concern. As part of the aggregate risk assessment for diuron, the short-term assessment was handled using the reciprocal MOE equation ("1/MOE approach") for calculating the aggregate MOE and solving for the term MOE_{water}. The reciprocal MOE equation is only used when the toxic effects on which the endpoints are selected are the same and when the LOCs are identical for all MOEs in the calculation.

Based on the supported uses of diuron, no incidental oral (hand-to-mouth) exposures are expected and therefore, were not factored into the aggregate and DWLOC calculations, i.e. no exposures to children are expected. Also, no systemic toxicity following repeated dermal dosing was observed in submitted studies therefore, dermal exposures were not factored into the equation either.

Taking into account the uses proposed in this action, the Agency can conclude with reasonable certainty that residues of diuron plus its metabolites hydrolyzable to 3,4-DCA, resulting from applications of diuron, in drinking water would <u>not likely result in an aggregate short-term risk</u> to male and female adult homeowners above the Agency's level of concern. The Agency based this determination on a comparison of estimated concentrations of diuron and its metabolites (DCPMU, DCPU, 3,4-DCA) in surface and ground waters to back-calculated "levels of comparison" for diuron plus its metabolites in drinking water. The EECs in surface and ground waters were derived from water quality models that used conservative assumptions (health-protective) regarding the pesticide transport from the point of application to surface or ground water, and were supplemented with limited monitoring data.

Modeled Tier 2 (PRZM/EXAMS) estimates of concentrations of diuron plus its metabolites in surface water were below the short-term DWLOCs for male and female adults and are <u>not of concern</u>. The EECs calculated by EFED were based on the highest labeled rate of application for citrus. Modeled Tier 1 SCI-GROW estimates of ground water concentrations of diuron plus its metabolites were below the short-term DWLOCs and are <u>not of concern</u>.

Table 12. Aggregate Short-Term Risk and DWLOC Calculations (Inhalation/Oral Endpoints and NOAELs the Same)										
Population	Short -Term Scenario									
	NOAEL mg/kg/d	LOC[1]	Max Exposure[2] mg/kg/d	Average Food Exposure mg/kg/d	Residential Exposure[3] mg/kg/d	Aggregate MOE (food and residential)[4]	Max Water Exposure[5] mg/kg/d	Surface Water EEC[6] (Fg/L)	Ground Water EEC[6] (Fg/L)	Short-Term DWLOC[7] (Fg/L)
Adult Male	10	100	0.1	0.000088	0.0095	1043	0.09	104	9.1	3153
Adult Female	10	100	0.1	0.000069	0.0095	1045	0.09	104	9.1	2700

[1] LOC (Target MOE) includes safety factors totaling 100 for inter-species extrapolation (10x) and intra-species variability (10x).
[2] Maximum Exposure (mg/kg/day) = NOAEL/LOC
[3] Residential Exposure = Inhalation Exposure
[4] Aggregate MOE = [NOAEL ÷ (Avg Food Exposure + Residential Exposure)]
[5] Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure)
[6] The crop producing the highest level was used to assess exposure to diuron, DCPMU, DCPU, 3,4-DCA, total.
[7] DWLOC(Fg/L) = <u>[maximum water exposure (mg/kg/day) x body weight (kg)]</u>
[water consumption (L) x 10^{-3} mg/Fg]

5.4 Chronic Risk

5.4.1 Chronic Aggregate Risk Assessment

Aggregate chronic (noncancer) risk estimates include the contribution of risk from dietary sources (food + water) and residential sources. However, based on the labeled uses, no long-term or chronic residential exposures are expected. Chronic risk estimates from exposures to food, associated with the use of diuron <u>do not exceed</u> the Agency's level of concern for the most highly exposed population subgroup, children ages 1-6 years of age. The chronic dietary (food only) risk estimate for children ages 1-6 years of age was < 7% of the chronic PAD.

As mentioned above, though some limited chemical-specific water monitoring data are available, they are not nationally representative and not at-the-tap data. Therefore, EECs were calculated by EFED to estimate the potential contribution to the chronic exposure from drinking water, and the EECs were compared to the chronic DWLOCs.

5.4.2 Chronic DWLOC Calculations

To calculate the DWLOC for chronic (noncancer) exposure relative to a chronic toxicity endpoint, the dietary food exposure (from DEEM™) was subtracted from the PAD to obtain the exposure to diuron and its 3,4-DCA-containing metabolites in drinking water that would not be of concern.

A chronic DWLOC ($DWLOC_{chronic}$) was calculated using the following formulae:

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

chronic water exposure (mg/kg/d) = [cPAD - (chronic food + residential(ADD)(mg/kg/d))]

Where ADD = average daily dose

Residential exposures were not factored into the $DWLOC_{chronic}$ since no long-term residential exposures (handler or postapplication) are expected.

Taking into account the uses proposed in this action, the Agency cannot conclude with reasonable certainty that residues of diuron plus its metabolites hydrolyzable to 3,4-DCA, resulting from applications of diuron, in drinking water would not likely result in a chronic dietary risk to infants, children, and adults above the Agency's level of concern. The Agency based this determination on a comparison of estimated concentrations of diuron and its metabolites in surface waters to back-calculated "levels of comparison" for diuron plus its metabolites in drinking water.

Modeled Tier 2 (PRZM/EXAMS) estimates of concentrations of diuron plus its metabolites (DCPMU, DCPU, 3,4-DCA) in surface water were above the chronic DWLOCs for all population subgroups and are of concern (Table 13). The EECs calculated by EFED were based on the highest labeled rate of application for citrus. Modeled Tier 1 SCI-GROW estimates of ground water concentrations of diuron plus its metabolites (DCPMU, DCPU, 3,4-DCA) were below the chronic DWLOCs and are not of concern.

Table 13 Summary of Chronic DWLOC Calculations

Population Subgroups	cPAD mg/kg/d	Food Exposure mg/kg/d	Maximum Water Exposure mg/kg/d	PRZM/EXAMS (ppb) surface water (total EECs)	SCI-GROW (ppb) ground water (total EECs)	$DWLOC_{chronic}$ (ppb)
U.S. Population	0.003	0.000088	0.0029	104	9.1	102
Females 13-50 yrs	0.003	0.000069	0.0029	104	9.1	88
Infants <1 yr	0.003	0.000077	0.0029	104	9.1	29

Children 1-6 yrs	0.003	0.00020	0.0028	104	9.1	28

5.5 Cancer Risk

5.5.1 Aggregate Cancer Risk Assessment

Though estimated exposure to food alone results in a cancer risk (1.68×10^{-6}) for the U.S. general population, it is not of concern. The estimates of exposures from food are based on a refined analysis (%CT and some processing data), but used data from field trails conducted at the maximum application rates and cannot be further refined without additional data (processing data, monitoring data that includes the parent and its metabolites that are hydrolyzable to 3,4-DCA). Residential exposures to applicators (adults) applying paint with a paintbrush or airless sprayer result in potential cancer risks that are of concern (range 1.9×10^{-6} to 6.8×10^{-6}). This is a conservative assessment based on Residential SOPs and includes an estimate of dermal exposure and an upper bound dermal absorption factor. Residential exposures to homeowners loading ready-to-use liquids do not result in potential cancer risks that are of concern.

5.5.2 Cancer DWLOC Calculations

For the cancer (Q_1*) exposure calculations, the Agency uses a multi-year mean water concentration values. The $DWLOC_{cancer}$ is the concentration in drinking water as a part of the aggregate chronic exposure that results in a negligible cancer risk (10^{-6}). Residential exposures to adult handlers would be factored into the $DWLOC_{cancer}$ however, since the potential cancer risks from exposures during residential activities, alone, are of concern, no DWLOCs were calculated and <u>allowable exposures to water are essentially "0."</u>

5.5.3 Additional Cancer Risks

The MARC recommended that a separate dietary cancer assessment be conducted for <u>MCPDMU, a potential residue of concern in water, but not found in plant or animal residue studies</u>. The MARC raised concerns for N'-(3-chlorophenyl)-N,N-dimethyl urea (MCPDMU) based on an analogous compound, N'-(4-chlorophenyl)-N,N-dimethyl urea (monuron). With the exception of the position of the chlorine, the structures are identical. There are cancer concerns for monuron but the target organs are different than those affected by diuron. Monuron produces kidney and liver tumors in male rats (*NTP technical Report 266, 1988*). The most potent unit risk, Q_1^* of those calculated for monuron is that for male rat liver neoplastic nodule and/or carcinoma combined tumor rates at 1.52×10^{-2} $(mg/kg/day)^{-1}$, in human equivalents (*MONURON: Quantitative Risk Assessment (Q_1^*) Based On F344/N Rat Dietary Study With $^3/_4$'s Interspecies Scaling Factor. PC Code 035501. Lori L. Brunsman. July 5, 2001*).

Since there is potential for MCPDMU to occur in water, the Agency considered possible exposures to MCPDMU from ingestion of catfish, as well as from drinking water. The AR of MCPDMU in catfish was calculated using the following inputs:

2 ppm tolerance for catfish x 0.25^1 x 0.35^2 = anticipated residue

Where:
[1] The fraction of applied radioactive diuron converted to MCPDMU in an aerobic aquatic metabolism study (see EFED chapter). The data were obtained from a sample taken 30 days after initiation of the study and was the highest residue value found. The study indicated an approximately linear correlation of MCPDMU vs time and the 30 day sample was the longest interval provided.
[2] %CT for catfish.

Using the Q_1* for monuron, the calculated cancer risk to the U.S. general population from potential exposure to MCPDMU in catfish alone is 1.02×10^{-7} and is <u>not of concern</u>.

A $DWLOC_{cancer}$ for MCPDMU was calculated to determine whether potential exposures to MCPDMU only (*Drinking Water Assessment for diuron and its degradates. Ibrahim Abdel-Saheb. March 11, 2001*) in drinking water from surface or ground water sources is of concern. As illustrated below, the EEC of MCPDMU from surface water (PRZM/EXAMS) exceeds the $DWLOC_{cancer}$ and <u>is of concern</u>.

Summary of Cancer DWLOC Calculations for MCPDMU

Population Subgroup	**Negligible Risk**	**Q_1* $(mg/kg/d)^{-1}$**	**Chronic Food Exposure**	**PRZM/EXAMS (ppb)**	**SCI-GROW (ppb)**	**$DWLOC_{cancer}$ (ppb)**
U.S. Population	0.000001	0.0152	0.000007	26	1.4	2.0

There are several issues to consider when characterizing the magnitude of the potential cancer risk from exposure to MCPDMU, and the appropriateness of the analogy to monuron (Personal communication. Alberto Protzel. October 4, 2001):

• There is no proven mechanism for the carcinogenic effect of monuron in rats, to allow for the satisfactory evaluation of the effect on carcinogenicity of going from the 4-chloro isomer in monuron to the 3-chloro isomer in the water metabolite.

• There are no toxicity data on the 3-chloro isomer to comfortably rule it out as a carcinogen.

In the absence of the data needed for a more comprehensive evaluation, the carcinogenic risk assessment was conducted using the Q_1^* of monuron. It is possible to speculate that the actual risk for the 3-chlorophenyl isomer might be lower (how much lower cannot be established) than the calculations indicate based on the following observations:

• Both monuron and its metabolic product p-chloroaniline (a.k.a. 4-chloroaniline) have been shown to be carcinogens. Monuron produced tumors of the kidney and liver in male rats (*NTP technical Report 266, 1988*). PCA produced tumors of the liver and spleen in male mice (*NTP Technical Report 351, 1989*). In contrast, the pesticide chlorpropham (isopropyl-m-chlorcarbanilate), which releases 3-chloroaniline (excreted in urine as 1-2% of the dose and is a moiety associated with the 3-chloro water metabolite of diuron), is currently classified by the Agency as an E-carcinogen. Although 3-chloroaniline produced a statistically significant increase in testicular interstitial cell adenomas in rats, well above historical controls, the significant increase occurred at 1000 mg/kg/day, a dose considered by the Agency to be excessive.

• Sabbioni and Neuman (*Carcinogenesis 11:111-115,1990*) studied the in-vivo binding of arylamines to a cellular macromolecule (hemoglobin). 3-Chloroaniline (administered to rats pure or as chlorpropham) produced 1/10 or less the amount of hemoglobin adducts that was produced by 4-chloroaniline (administered to rats pure or as monuron). This observation might suggest less avidity of 3-chloroaniline than 4-chloroaniline for cellular macromolecules.

6.0 CUMULATIVE

The Agency does not currently have data available to determine with certainty whether diuron has a common mechanism of toxicity with any other substances. For purposes of this human health risk assessment, the Agency has assumed that diuron does not have a common mechanism of toxicity with any other pesticides. Additional weight-of-the-evidence supports this approach as is discussed below.

In May 1999, the Agency performed a Section 18 risk assessment for diuron use in catfish ponds (*ID# 99MS0001. SECTION 18 EXEMPTION FOR THE USE OF DIURON 80W IN CATFISH PONDS IN MISSISSIPPI. DP Barcode: D255462. Pamela Hurley, Richard Loranger, Steven Weiss. May 13, 1999*). At that time, the estimated residues of propanil and linuron were added to those of diuron and the risk assessment was performed using the noncancer endpoints selected for diuron. All three chemicals contain within their structures, 3,4-DCA. However, linuron and diuron are ureas, while propanil is not. Though propanil readily metabolizes to 3,4-DCA, neither diuron nor linuron metabolize to 3,4–DCA in plant or animal metabolism studies.

Since 1999, the Agency has received and evaluated new information, performed a more comprehensive assessment of propanil and linuron, and re-evaluated its approach to the assessment of diuron. The MARC does not recommend aggregating residues of 3,4-DCA for the propanil and diuron risk assessments [Personal communication. Christine Olinger (MARC Chair) to Sherrie Kinard. September 19, 2001]. 3,4-DCA is a significant residue of concern for propanil, but is not a residue of concern *per se* for diuron. The analytical method for quantifying residues of concern from applications of diuron converts all residues to 3,4-DCA as a technical convenience. However, 3,4-DCA is not a significant residue in diuron plant and animal metabolism or hydrolysis studies. Therefore, the MARC recommended that all residues hydrolyzable to 3,4-DCA would be included in the tolerance expression for diuron, because no validated enforcement method is available for quantification for the actual residues of concern for diuron [*Diuron. Results of the Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Meeting Held on 03-JULY-2001. John Punzi. August 10, 2001*]. Additionally, propanil and its metabolite 3,4-DCA were found to induce methemoglobinemia, the endpoint of concern for propanil. Diuron has not been shown to cause this effect. Diuron induces hemolytic anemia and compensatory hematopoiesis, which are mechanistically different from methemoglobinemia.

Linuron and diuron metabolism studies show that both chemicals metabolize to DCPU and DCPMU. However, for reasons that are yet unknown, these chemicals do not induce the same toxic effects in mammals. Submitted data indicate that diuron is primarily (though not exclusively) metabolized by the hydroxylation of the urea group in either the methyl or the amino position and conjugated. Linuron, on the other hand, appears to be primarily ring-hydroxylated and conjugated. The methoxy group is removed, followed by the methyl group, with ring hydroxylation. Unlike linuron, hydroxylation of the phenyl ring is not a major metabolite pathway of diuron and, both methyl groups are lost. Methemoglobinemia is the dominant toxic effect of concern for linuron. As mentioned above, diuron does not induce methemoglobinemia. Mechanistic and reproductive studies show that linuron, and to some extent propanil, is an androgen receptor antagonist and that linuron induces testicular abnormalities in rodents. Studies with diuron showed no indications of any endocrine effects and no developmental or reproductive effects. Though the mechanisms of action for the differing effects induced by the two ureas, diuron and linuron, are not entirely known, there is sufficient cause to believe that exposures from the two compounds should not be cumulated.

In addition, in 1999 the estimated dietary cancer risk for diuron did not include residues from linuron and propanil since it was recognized that the target organs for tumor induction for diuron are different from those for linuron and propanil, and data were available which indicated that the mechanism of action may be different for diuron. Currently available data support that decision.

In conclusion, the Agency has assumed that diuron does not have a common mechanism of toxicity with any other pesticides. For purposes of this human health risk assessment, a cumulative risk assessment is not warranted.

7.0 OCCUPATIONAL EXPOSURE

The Agency has determined that there are potential exposures to mixers, loaders, applicators and other handlers during the usual use-patterns associated with diuron. Based on the use patterns, 31 major occupational exposure scenarios were identified for diuron. Calculations of noncancer risk based on inhalation exposure indicate that the inhalation margins of exposure (MOEs) are more than 100 at the highest possible level of mitigation for all of the short-term occupational exposure scenarios except applying sprays with a high pressure handwand. Sixteen of the 31 occupational scenarios were identified as having intermediate-term durations of exposure. Of these, none have a non-cancer risk of concern for intermediate-term inhalation exposure at the highest possible level of mitigation. A noncancer postapplication risk assessment was not conducted, since no systemic toxicity by the dermal route is expected for the short- or intermediate-term durations. Postapplication cancer risks for private growers were calculated at both the typical application rate and the maximum application rate for each crop grouping. All cancer risks to private growers were less than 1×10^{-4} on the day of treatment. Postapplication cancer risks for commercial applicators were calculated at the typical application rate for each crop grouping. All potential cancer risks to commercial applicators were less than 1×10^{-4} on the day of treatment.

Occupational risk assessments were conducted for the use of diuron as a mildewcide in paint. Four occupational handler scenarios were identified for the use of diuron in paint and are expected to be of short- and intermediate-term exposure duration. The calculations of short- and intermediate-term inhalation risk from the use of diuron in paint indicate that MOEs are more than 100 at the assessed level of mitigation for all the exposure scenarios, except applying paints with an airless sprayer (indoors). At the assessed level of mitigation, all four scenarios have potential cancer risks between 1×10^{-4} and 1×10^{-6}. Occupational postapplication exposures to paint containing diuron may occur in industrial settings around open vats used in paint processing. Inhalation and dermal exposures may also occur while maintaining industrial equipment. No postapplication exposure data have been submitted to determine the extent of postapplication exposures in the industrial settings. Nonetheless, inhalation exposures are expected to be minimal because of the low vapor pressure of diuron (2×10^{-7} mm Hg at 30 EC) and aerosol formation is not expected. Dermal postapplication exposures are expected to be lower than when handling/loading the formulated product. Therefore, postapplication exposures in the industrial settings are expected to be minimal and not of concern.

Occupational risk assessments were also conducted for the use of diuron as an algaecide in commercial fish ponds. Four short-term occupational handler scenarios were identified for the use of diuron in commercial fish production and the inhalation MOEs from all four of the commercial fish production scenarios were greater than 100 at the baseline level of mitigation and are not of concern. With maximum mitigation measures (engineering control level), all four scenarios have estimated cancer risks of less than 1×10^{-6} and are not of concern. Occupational postapplication exposure to diuron in treated fish production ponds is not likely to result in a risk of concern based on the extremely high dilution rate.

7.1 Agricultural and Non-crop/Utility Uses

7.1.1 Handler

The EPA has determined that there are potential exposures to mixers, loaders, applicators, and other handlers during usual use-patterns associated with diuron. Based on the use patterns, 31 major occupational exposure scenarios were identified for diuron: (1a) mixing/loading liquid formulations for aerial application; (1b) mixing/loading liquid formulations for chemigation; (1c) mixing/loading liquid formulations for groundboom application; (1d) mixing/loading liquid formulations for rights-of-way sprayers; (1e) mixing/loading liquid formulations for high-pressure hand wand; (2a) mixing/loading dry flowables for aerial application; (2b) mixing/loading dry flowables for chemigation; (2c) mixing/loading dry flowables for groundboom application; (2d) mixing/loading dry flowables for rights-of-way spray application; (2e) mixing/loading dry flowables for high-pressure hand wand; (3a) mixing/loading wettable powders for aerial application; (3b) mixing/loading wettable powders for chemigation; (3c) mixing/loading wettable powders for groundboom application; (3d) mixing/loading wettable powders for rights-of-way spray application; (3e) mixing/loading wettable powders for high-pressure hand wand; (4) loading granulars for tractor-drawn spreaders; (5) applying sprays for aerial application; (6) applying sprays for groundboom application; (7) applying sprays with a rights-of-way sprayer; (8) applying sprays with a high-pressure hand wand; (9) applying granulars for a tractor-drawn spreader; (10) applying granulars with a spoon; (11) applying granulars for hand application; (12) flagging aerial spray applications; (13) mixing/loading/applying liquids with a low-pressure hand wand; (14) mixing/loading/applying liquids with a backpack sprayer; (15) mixing/loading/applying wettable powders with a low-pressure hand wand; (16) loading/applying granulars with a pump feed backpack spreader; (17) loading/applying gravity feed backpack spreader; (18) loading/applying granulars for a belly grinder application; and (19) loading/applying granulars with a push-type spreader. Since granulars are only used on non-crop/utility areas, aerial application of granulars and flaggers supporting aerial operations were not assessed.

Current diuron labels have PPE requirements ranging from no PPE listed to long-sleeved shirt and long pants, waterproof gloves, shoes, socks, protective eye wear, chemical resistant headgear, and a dust/mist filtering respirator. Mixer and loaders must also wear a chemical resistant apron.

Table 3 in the attached document, *Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document for Diuron. Renee Sandvig and Christina Jarvis. October 16, 2001,* summarizes the caveats and parameters specific to the surrogate data used for each handler scenario and the corresponding exposure/risk assessment. These caveats include the source of the data and an assessment of the overall quality of the data. The assessment of data quality is based solely on the number of observations and the available quality control data. The quality control data are based on a grading criteria established by the PHED Task Force. The PHED Task Force is comprised of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide regulation, and member companies of the American Crop Protection Association. The sources of the surrogate include:

! Pesticide Handlers Exposure Database (PHED).

- Outdoor Residential Exposure Task Force (ORETF). The task force recently submitted proprietary data to the Agency on hose-end sprayers, push-type granular spreaders, and handgun sprayers (MRID # 44972201). The ORETF data were used in this assessment in place of PHED data for the “loading/applying granulars using a push-type spreader” scenario.

- Worker Exposure Study During Application In Banana Plantation With Temik 10G (MRID #451672-01). The Agency has used data from the aldicarb (Temik) study to assess exposures and risks to handlers applying granulars with a pump feed backpack sprayer.

- Worker Exposure Study During Application of Regent 20GR In Banana Plantation (MRID #452507-02). The Agency has used data from the fipronil (Regent 20 GR) study to assess exposures and risks to handlers loading and applying granulars with a gravity feed backpack sprayer. In addition, the Agency has also used data from the fipronil study to assess exposures and risks to occupational handlers loading and applying granulars using a scoop and bucket.

Calculations for the handler risk assessment were completed for a range of maximum application rates for specific crops recommended by the available diuron labels and the LUIS report. These rates were assessed in order to bracket risk levels associated with the various use patterns.

7.1.1.1 Noncancer Exposure and Risk Estimates

Noncancer handler exposure assessments were completed using a baseline exposure scenario and, if required, increasing levels of risk mitigation (PPE and engineering controls) in an attempt to achieve an appropriate margin of exposure. The baseline scenario generally represents a handler wearing long pants, a long-sleeved shirt, no respirator, and no chemical-resistant gloves (there are exceptions pertaining to the use of gloves, and these are noted). Noncancer dermal risks from the use of diuron were not calculated. No systemic toxicity following repeated dermal dosing at 1200 mg/kg/day was seen in the rabbit dermal toxicity study; therefore, a quantitative noncancer dermal risk assessment (short- and intermediate-term) is not required. However, calculations of daily dermal exposure and daily dermal dose were included for purposes of the cancer risk assessment.

Handler exposures to diuron are expected to be mainly of short-term duration (one day to one month). Intermediate-term exposure (one month to several months) for handlers is possible for large field crops, including corn, wheat, oats and cotton, because of their long planting seasons. Rights-of-way sprayer scenarios for utility and industrial areas are assumed to be of intermediate-term duration, because utility workers could possibly treat rights-of-way areas (roadsides, railroads, etc) all summer long. The short-term inhalation MOEs were calculated using the NOAEL of 10 mg/kg/day, from the developmental toxicity study in rabbits. The intermediate-term MOEs were calculated using the NOAEL of 1.0 mg/kg/day, from the chronic toxicity study in rats. An LOC or target MOE of 100 has been identified as the target risk level for short- and intermediate-term occupational exposure scenarios. Tables14 and 15 show a summary of the short- and intermediate-term exposures and MOEs.

Of the 31 identified occupational handler exposure scenarios, all short- and intermediate-term exposure scenarios resulted in MOEs greater than 100 with PPE and Engineering Control mitigation for all scenarios for which engineering controls are feasible. The only scenario for which the estimated risks (MOEs) were calculated to be less than 100, and therefore of concern to the Agency, is Applying Sprays for High-Pressure Handwand Application at the maximum application rate of 0.96 lb ai per gallon, at both minimum and maximum levels of PPE protection (MOEs range from 46 to 92). Engineering Controls are not feasible for this scenario.

7.1.1.2 Cancer Exposure and Risk Estimates

The cancer handler exposure scenarios are identical to those assessed in the noncancer handler assessment. To assess cancer risk, a total daily dose, a lifetime daily dose and a total cancer risk are calculated. The total daily dose is calculated to include both dermal and inhalation exposure (dermal dose includes dermal absorption since an oral cancer endpoint was used) and used a $Q_1^* = 1.91 \times 10^{-2}$ $(mg/kg/day)^{-1}$ in human equivalents.

The assessment assumed that the average lifetime is 70 years, exposure duration is 35 years, and that the exposures per year are: 10 days per year for the private grower and 30 days per year for a commercial applicator. Maximum application rates were used in the private grower assessment. Typical application rates were used in both the private grower and commercial applicator assessments. It was assumed that as the frequency of exposure increased, the probability of being exposed to a maximum application rate would decrease. Therefore, maximum application rates were not assessed for the commercial applicator. Table 16 summarizes the cancer risks associated with the handling of diuron for the baseline, maximum PPE and engineering control level of mitigation. In general, the Agency is concerned when occupational cancer risk estimates exceed 1×10^{-4}. The Agency will seek ways to mitigate the risks, to the extent that it is practical and economically feasible, to lower the risks to 1×10^{-6} or less.

Five of the assessed scenarios have cancer risks greater than 1×10^{-4} at the highest feasible level of mitigation (private farmer/commercial applicator, typical/max rate) and are of concern (See *Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document for Diuron. Renee Sandvig and Christina Jarvis. October 16, 2001*). Twenty-six of the scenarios have cancer risks between 1×10^{-4} and 1×10^{-6} at the highest feasible level of mitigation (private farmer/commercial applicator, typical/max rate).

7.1.2 Postapplication Exposures

EPA has determined that there are potential postapplication exposures to individuals entering treated fields. The current diuron labels have a restricted entry interval (REI) requirement of 12 hours with the following early entry PPE required: coveralls over long sleeved shirt and long pants, waterproof gloves, chemical resistant footwear plus socks, protective eye wear and chemical resistant headgear for overhead exposures.

Many of the applications of diuron are soil directed or pre-plant, since the application of diuron to most of the registered crops would result in plant damage. Only the crops whose foliage can be sprayed without damage were assessed for postapplication exposure to foliage. The crops that can be sprayed without foliage damage are oats, wheat, birdsfoot treefoil, clover, grass grown for seed, alfalfa, asparagus, pineapple, and sugarcane.

Significant exposure to diuron may result from contact with treated soil when planting seedlings, moving irrigation lines, or other soil related activities since diuron is applied directly to the soil. At this time, no transfer coefficients exist for activities resulting in contact with treated soil. There are also no data on the soil residue dissipation of diuron. A worker exposure study and a diuron soil residue dissipation study would be needed to assess this risk. Transfer coefficients do not exist for the mechanical harvesting of alfalfa and asparagus and these activities are considered of special concern according to the Agriculture Transfer Coefficient Exposure SAC policy 3.1. Significant worker exposure is possible from mechanical harvesting of these crops.

Since diuron can be applied as a defoliant soon before harvest, exposure to cotton harvesters is of special concern for this chemical. Data recently submitted to the Agency show that there is exposure during the mechanical harvesting of cotton. Exposure can result from the following occupational job functions: picker operator, module builder, tramper, and raker. A picker operator is the individual that drives the harvesting machine, usually with an enclosed cab. A module builder operator is the individual that operates the controls of the module builder into which the picker loads the cotton. The module builder is used to receive the cotton and then compact it into modules or bales. A tramper is the individual who stands on top of the module builder and helps direct the cotton out of the picker and into the module builder. The tramper than jumps into the module builder and redistributes the cotton within the module builder. A raker is the individual who rakes up the spilled cotton and puts it back into the module builder. The models presently used to assess occupational postapplication exposure cannot be used since the foliage has dropped off of the cotton plants by the time of harvest. There are no standard default transfer coefficients for these activities at this time. Data on these exposure potentials are requested. Diuron labels with the cotton defoliant use should specify that cotton can only be harvested mechanically.

Chemical-specific postapplication exposure and/or environmental fate data have not yet been submitted by the registrant in support of reregistration of diuron. In lieu of these data, a surrogate postapplication assessment was conducted to determine potential human risks incurred from applying diuron to the foliage of the crops that can be sprayed without damage to the leaves. The surrogate assessment in Table 17 is based on both the typical and maximum application rates that a private farmer/grower may reasonably be expected to be exposed to for a short duration (10 days). The surrogate assessment in Table 18 is based on the typical application rates that a commercial applicator may be reasonably expected to be exposed to for a more extended duration (30 days). The maximum application rates are not included in the postapplication assessment for the commercial applicator, as it is unlikely that a commercial applicator would be exposed at the maximum application rate for 30 days a year, i.e. it was assumed that as the frequency of the exposure increased, the probability of being exposed to a maximum application rate would decrease.

7.1.2.1 Noncancer Postapplication Exposure and Risk Estimates

A noncancer postapplication risk assessment was not conducted, since no systemic toxicity by the dermal route is expected for the short- or intermediate-term durations.

7.1.2.2 Postapplication Exposure and Risk Estimates for Cancer

In general, the Agency is concerned when postapplication occupational cancer risk estimates exceed 1×10^{-4}. This diuron postapplication cancer assessment assumes that a worker would contact day zero residues (residues on the day of application) for ten or thirty days a year, every year for 35 years. Since it is unlikely that a postapplication worker would contact the highest possible residue value for that length of time, this assessment is considered very conservative.

7.1.2.2.1 Private Growers (10 Days Exposure Per Year)

Postapplication cancer risks for private growers were calculated at both the typical application rate and the maximum application rate for each crop grouping. All cancer risks to private growers were less than 1×10^{-4} on the day of treatment (Table 17).

7.1.2.2.2 Commercial Farm Workers (30 Days Exposure Per Year)

Postapplication cancer risks for commercial farm workers were calculated at the typical application rate for each crop grouping. All potential cancer risks to commercial farm workers were less than 1×10^{-4} on the day of treatment (Table 18).

Historically, setting REIs on cancer endpoints has been difficult because of the need for lifetime use assumptions. To estimate the LADD (Life-time Average Daily Dose), the typical application rate, the number of days worked per year, and the number of years one would be exposed during a working lifetime are needed. Each one of these variables is dependent upon many factors. For example, the number of days worked per year must correspond to the days worked when the pesticide of concern has been applied. Additionally, the residue dissipation over the work interval should be estimated. Without an estimate for residue dissipation one needs to assume (conservatively) that the worker travels from one treated field to another so that the highest residue value is always contacted. In the case of diuron, a screening estimate was developed because lifetime use data are not available.

7.2 Mildewcide in Paints, Solvents, Adhesives, and Coatings

7.2.1 Occupational Handler Exposures/Risks

Diuron is used as a mildewcide in paints, solvents, adhesives, stains, polymer latices, plaster, stuccos, sealants, caulking, fillers, and coatings. For these uses, four labels exist: EPA Reg. Nos. 67071-15, 67071-2, 67071-17, and 5383-101. These products are formulated as a flowable concentrate, a tablet, an emulsifiable concentrate, and a paste form, respectively. Traditionally, OPP’s Antimicrobial Division assesses antimicrobial uses of pesticides. However, in the case of diuron, the antimicrobial uses were assessed by HED. These pesticide products are incorporated into paint at 0.20 to 2.5 % during the initial phase of the manufacturing process. HED has identified and assessed the primary handlers as those individuals who mix and load diuron formulation at the manufacturing facility for use as a mildewcide in adhesives, caulks, sealants, and paints (see discussion of primary vs. secondary handlers in section 4.4.1 Home Uses). The secondary handlers are commercial applicators who apply adhesives, caulks, sealants, and paints.

No handler exposure data have been submitted to determine the extent of these exposures. The Agency assessed the risks to the primary handlers using the dermal and inhalation exposure data for loading liquids and tablet formulations from the proprietary Chemical Manufacturers Association (CMA) antimicrobial exposure study (MRID 42587501). No unit exposure data exist to assess the mixing and loading of the paste formulation into paint. It is assumed that this exposure would be similar to mixing and loading liquids into paint products. Two *primary* handler exposure scenarios have been identified and include: 1) Mixing/Loading liquids and 2) Loading tablets.

In addition to the primary handlers, secondary handlers are assessed using an airless sprayer and a paint brush. Unit exposure data used to assess the exposure resulting from applying paint containing diuron with an airless sprayer and a paintbrush were taken from a previous chlorothalonil assessment (again, see discussion in section 4.4.1 Home Uses). The clothing and PPE scenarios for each type of exposure reflect the clothing and PPE worn in the study from which the unit exposure values were derived. Although there is potential exposure during the application of the other treated materials (e.g., caulks and sealants), they are not included because no data are available to assess the uses. There is also potential for exposure from applying paint with a roller. It is HED's professional judgement that the airless sprayer and paintbrush scenarios represent the high end exposures for diuron antimicrobial secondary uses. Two *secondary* handler exposure scenarios have been identified and include: 3) Applying paints with an airless sprayer, and 4) Applying paints with a paint brush.

These four exposure scenarios were used to assess the handler risks to diuron's antimicrobial uses. The noncancer and cancer risk equations and assumptions stated previously in this assessment were also used to calculate exposure from diuron's antimicrobial uses. The industrial and commercial painter exposure scenarios are believed to have a short (one to 30 days) and intermediate-term (one month to 180 days) exposure duration. It is assumed that diuron would only be mixed into paint every other week, five days a week. This type of intermittent exposure frequency is not considered a chronic exposure scenario (greater then 180 days) because diuron is not believed to be used continuously for at least 180 days and the rat metabolism study (MRID 440196-01) indicates that urinary and fecal excretion of diuron is nearly complete within 24 hours in the low-dose groups (10 mg/kg/day) and within 48 hours in high-dose groups (400 mg/kg/day). For the cancer risk assessment, workers handling diuron in the industrial setting (mixing diuron into paints) are assumed to be exposed to diuron in paints 125 days per year (50 weeks worked/year x 0.5 "every other week" x 5 days/week) and commercial painters applying diuron treated paint are assumed to be exposed 50 days per year (only in paints needing mildewcide and not all paint is treated with diuron).

7.2.1.1 Noncancer Risks

The short-term inhalation NOAEL of 10 mg/kg/day and the intermediate-term inhalation NOAEL of 1.0 mg/kg/day were used for all noncancer exposures and have a target MOE of 100. The calculations of short-term inhalation risk indicate that inhalation MOEs are more than <u>100</u> at the assessed level of mitigation for the all the exposure scenarios and therefore, not of concern. The calculations of intermediate-term inhalation risk indicate that inhalation MOEs are more than <u>100</u> at the assessed level of mitigation for the all the exposure scenarios <u>except</u> the following (Table 19):

- Applying paints with an airless sprayer indoors.

7.2.1.1 Cancer Risks

In general, the Agency is concerned when occupational cancer risk estimates exceed 1×10^{-4}. The Agency will seek ways to mitigate the risks, to the extent that it is practical and economically feasible, to lower the risks to 1×10^{-6} or less.

The following scenarios have cancer risks <u>between 1×10^{-4} and 1×10^{-6}</u> at the assessed level of mitigation (Table 20):

- (1) Mixing/loading of liquids into paint products;

- (2) Loading of tablets into paint products;

- (3) Applying paints with an airless sprayer; and

- (4) Applying paints with a paint brush.

All scenarios were assessed at the maximum rate of application. Average application rate for the paint use is unknown and is requested to refine this risk.

7.2.2 Postapplication Exposures to Paint Containing Diuron

Postapplication exposures may occur in industrial settings around open vats used in paint processing. Inhalation and dermal exposures may also occur while maintaining industrial equipment. No postapplication exposure data have been submitted to determine the extent of postapplication exposures in the industrial settings. Nonetheless, inhalation exposures are expected to be minimal because of the low vapor pressure of diuron (2×10^{-7} mmHg at 30 EC) and aerosol formation is not expected. Dermal postapplication exposures are expected to be lower than when handling/loading the formulated product. Therefore, postapplication exposures in the industrial settings are expected to be minimal and not of concern.

7.3 Algaecide in Commercial Fish Production

7.3.1 Handlers

Diuron is also used as an algaecide in the commercial production of ornamental fish, bait fish, and catfish. For these uses, there are two state labels (FL99000200 and AR99000800), a section 18, and several other Griffin labels pending approval. Based on the use patterns of diuron as an algaecide, four occupational exposure scenarios were identified: (1a) Mixing/loading dry flowables for catfish production; (1b) Mixing/loading dry flowables for ornamental fish production; (2a) Mixing/loading wettable powders for catfish production; and (2b) Mixing/loading wettable powders for ornamental fish production. All handler exposures are expected to be short-term in duration. An occupational assessment on the use of diuron in commercial catfish production has already been conducted by the Agency (*ID #99MS0001. Section 18 Exemption for the Use of Diuron 80W in Catfish Ponds in Mississippi. Pam Hurley, Rick Loranger, and Steven Weiss. May 13, 1999*). All assumptions used to calculate exposure are based on this assessment. Since no other data exist at this time, the assumptions used for catfish production in this assessment are assumed to be applicable to ornamental fish production as well. The noncancer and cancer risk equations and assumptions stated previously in this assessment were also used to calculate exposure from commercial fish production. HED assumed an average pond size of 15 acres, 4 feet deep, with 20 ponds per farm (no more than 25% would be expected to be treated per day). The assumptions on pond size and numbers of ponds per farm are based on telephone conversations between HED staff (Pilot Interdisciplinary Risk Assessment Team) and contacts at Auburn and Mississippi State Universities in 1996.

7.3.1.1 Noncancer Exposures/Risks for Pond Uses

The LOC or target MOE for short-term inhalation exposures is 100. The inhalation MOEs from all four of the commercial fish production scenarios were greater than 100 at the baseline level, without mitigation, and are not considered a risk of concern (Table 21).

7.3.1.2 Cancer Exposures/Risks

In general, the Agency is concerned when occupational cancer risk estimates exceed 1×10^{-4}. The Agency will seek ways to mitigate the risks, to the extent that it is practical and economically feasible, to lower the risks to 1×10^{-6} or less. <u>All four exposure scenarios have cancer risks between 1×10^{-4} and 1×10^{-6}</u> at the baseline level of mitigation. When additional PPE was added as a mitigation measure, exposures from mixing/loading dry flowables for catfish ponds and mixing/loading wettable powders resulted in potential cancer risks of <u>less than 1×10^{-6}</u> and not of concern. When additional PPE was added to the mixing/loading dry flowables for ornamental fish ponds scenario, the potential cancer risk was calculated to be <u>between 1×10^{-4} and 1×10^{-6}.</u> All four exposure scenarios have cancer risks of <u>less than 1×10^{-6}</u> with maximum feasible mitigation, including engineering controls (Table 22).

7.3.2 Occupational Postapplication Exposures to Commercial Fish Ponds

Occupational postapplication exposure to diuron in treated fish production ponds is not likely to result in a risk of concern based on the extremely high dilution rate (maximum application rate is 0.00000838 lb ai/gallon of pond water), low frequency of postapplication activities, and a low dermal absorption value (4%).

7.4 Incident Data

The Agency searched several databases for reports of incidents occurring resulting from exposures to diuron. The databases searched were the Incident Data System (IDS), American Association of Poison Control Centers (AAPCC), California Pesticide Illness Surveillance Program, and National Pesticide Telecommunication Network (NPTN). There were incidents reported involving both adults and children. Most were treated on an outpatient basis but a few required hospitalization and one death occurred. A direct connection between exposure to diuron as the cause and the reported death has not been made as of this writing. Some incident reports described symptoms such as eye irritation, rash, dizziness, respiratory irritation and headaches for both agricultural and non-agricultural exposures. Specific details may be found in *Review of Diuron Poisoning Incident Data. Chemical: # 035505. Ruth Allen. October 11, 2001.*

The incident data show that the number of poisoning incidents for diuron alone is relatively small in any one surveillance system. Also, the incidents are scattered in time and location, and many of the incidents involve diuron use in mixtures. Therefore, few conclusions can be drawn. However, the 1995 Louisiana elementary school incident in which diuron was associated with the illnesses of 23 children and 9 adults, remains unexplained. There are no known recreational or school building registered uses of diuron. The Agency has an independent initiative to reduce the use of pesticides in and around schools. If diuron is associated with other illnesses in schools, consideration should be given to label language modifications that would specifically prohibit use in and around schools.

8.0 DATA NEEDS/LABEL REQUIREMENTS

Product Chemistry

1. The product chemistry data base is not complete; new confidential statements of formula (CSFs) are required which reflect preliminary analyses of current products together with discussions of formation of impurities.

2. UV/Visible absorption data/spectra are required (830.7050).

Residue Chemistry

Refer to Table B on page 52 of the *Residue Chemistry Chapter for the Diuron Reregistration Eligibility Decision (RED) Document. John Punzi. July 29, 2001* for more details of the requirements, listed by guideline.

3. Label revisions are required for many crops in order to reflect the parameters of use patterns for which residue data are available. Many of the revisions concern retreatment intervals, Preharvest Intervals (PHI's) and rotational crop restrictions.

4. Though adequate analytical methods exist for data collection and tolerance enforcement in plants, independent laboratory validation of the enforcement method is required for livestock methods prior to Agency validation.

5. Multiresidue methods for diuron and metabolites of toxic concern are required for plants and livestock.

6. Results from animal feeding studies suggest that tolerances are necessary for poultry or egg commodities and for meats and milk. Residue data are not available for several potential feed items. If the maximum dietary burden does not increase when recalculated from all potential feed items after acceptable field trial data are submitted, then the established tolerances for residues in fat, meat, and meat byproducts of cattle, goats, hogs, horses, and sheep can be lowered.

7. The reregistration requirements for magnitude of the residue in plants are not fulfilled for: alfalfa forage; globe artichoke; barley hay; cotton gin byproducts; field corn aspirated grain fractions; field corn forage and stover; filbert; grass forage, hay, seed screenings, and straw; lemon; pear; oat forage, hay; olive; field pea vines and hay; sorghum aspirated grain fractions, stover, and forage; wheat forage and hay. Additional crop field trial data are required for these commodities.

8. The reregistration requirements for processing data are not fulfilled for: field corn and olives.

9. The registrants have indicated that a Section 3 tolerance for diuron in/on catfish is desired. Since the metabolism committee is concerned with a monochlorinated diuron metabolite identified in water, a metabolism study of diuron in fish is required. The registrants are directed to OPPTS 860.1400 for study guidelines and encouraged to submit a study protocol prior to initiating the study.

10. Field rotational crop trials have been conducted on representative crops at less that the maximum application rates, and with 1 year plant back intervals (PBI). Some labels indicate a 2 year PBI. The Agency recommends that the registrants provide additional data to support the higher application rate and believes that the 2-yr PBI is not practical. The registrants should remove the 2-

yr PBI from the registered uses and provide data to support the 3.2 lb ai/A application rate and 1-yr PBI. Until adequate data are supplied, labels should be amended to restrict rotational crops to those crops which currently are registered as primary crops.

Toxicology

11. A 28-day inhalation study is required to address the concern for inhalation exposure potential based on the use pattern. The registrant can follow the 90-day inhalation study protocol but cease exposure at 28 days.

Occupational/Residential Exposures

12. Data are needed to assess the following occupational handler scenarios: mixing/loading/applying wettable powders or dry flowables with a backpack sprayer, and mixing/loading/applying dry flowables with a low-pressure handwand.

13. Average application rate for the paint use is unknown and is requested to refine the cancer risk from paint use.

14. No transfer coefficients exist for activities resulting in contact with treated soil. There are also no data on the soil residue dissipation of diuron. A worker exposure study and a diuron soil residue dissipation study would be needed to assess the risk from postapplication contact with treated soil.

15. Transfer coefficients do not exist for the mechanical harvesting of alfalfa and asparagus and these activities are considered of special concern according to the Agriculture Transfer Coefficient Exposure SAC policy 3.1.

ATTACHMENTS

Carcinogenicity Peer Review of Diuron. Linda Taylor and Esther Rinde. May 8, 1997.

Diuron (PC 035505): Assessment of Mode of Action on Bladder Carcinogenicity. Yung Yang. September 20, 2001.

DIURON: Cancer Classification and Mechanism of Action. Yung Yang. October 10, 2001.

Diuron - Chronic Dietary Exposure Assessment (PC Code 035505); DP Barcode D276683; Case 0046. John Punzi. September 10, 2001.

Diuron. List A Reregistration Case 0046. PC Code 035505. Product Chemistry Chapter for the

Reregistration Eligibility Decision [RED] Document. DP Barcode D274489. Ken Dockter. June 26, 2001.

Diuron Metabolism Committee Briefing Memo. John Punzi. August 27, 2001.

DIURON - Report of the FQPA Safety Factor Committee. Brenda Tarplee. August 7, 2001.

DIURON: 2nd Report of the Hazard Identification Assessment Review Committee. Yung Yang. August 28, 2001.

Diuron. Results of the Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Meeting Held on 03-JULY-2001. John Punzi. August 10, 2001.

Diuron - Revised Q1*, (3/4's Interspecies Scaling Factor), 1985 Wistar Rat 2 Year Dietary Study. PC 035505. Bernice Fisher. September 23, 1998.

Diuron - Toxicology Disciplinary Chapter for the Reregistration Eligibility Decision. Yung Yang. 0ctober 2, 2001.

Drinking Water Assessment for Diuron and its Degradates. Ibrahim Abdel-Saheb. March 11, 2001.

MONURON: Quantitative Risk Assessment (Q_1^*) Based On F344/N Rat Dietary Study With $^3/_4$'s Interspecies Scaling Factor. PC Code 035501. Lori L. Brunsman. July 5, 2001.

Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document for Diuron. Renee Sandvig and Christina Jarvis. December 5, 2001.

Quantitative Usage Analysis for Diuron. Alan Halvorson. March 20, 2001.

Residue Chemistry Chapter for the Diuron Reregistration Eligibility Decision Document. John Punzi. July 29, 2001.

Review of Diuron Poisoning Incident Data. Chemical: #035505. Ruth Allen. October 11, 2001.

Updated QUA. Alan Halvorson. April 27, 2001.

Table 14: Summary of Short-Term Exposure Variables and MOEs for Agricultural and Non-crop Uses

Exposure Scenario (Scenario #)	Crop[a]	Application rates[b]	Area Treated[c]	Inhalation Baseline MOE[d,e]	Inhalation Min PPE MOE[d,f]	Inhalation Max PPE MOE[d,g]	Short-term Inhalation Eng. Control MOE[d,h]
Mixer/Loader							
Mixing/Loading Liquids for Aerial application (1a)	Sugarcane	6 lb ai per acre	350 Acres per day	280	-	-	-
	Alfalfa	3.2 lb ai per acre	1200 Acres per day	150	-	-	-
Mixing/Loading Liquids for Chemigation application (1b)	Sugarcane	6 lb ai per acre	350 Acres per day	280	-	-	-
Mixing/Loading Liquids for Groundboom application (1c)	Grapes	9.6 lb ai per acre	80 Acres per day	760	-	-	-
	Alfalfa	3.2 lb ai per acre	200 Acres per day	910	-	-	-
Mixing/Loading Liquids for Rights-of-Way Sprayer application (1d)	Grapes	0.19 lb ai per gallon	1000 Gallons per day	3,000	-	-	-
	Utility/industrial areas	0.90 lb ai per gallon		650	-	-	-
Mixing/Loading Liquids for High-Pressure Handwand application (1e)	Grapes	0.19 lb ai per gallon	1000 Gallons per day	3,000	-	-	-
	Utility/industrial areas	0.90 lb ai per gallon		650	-	-	-
Mixing/Loading Dry Flowables for Aerial application (2a)	Sugarcane	6.4 lb ai per acre	350 Acres per day	410	-	-	-
	Alfalfa	3.2 lb ai per acre	1200 Acres per day	240	-	-	-
Mixing/Loading Dry Flowables for Chemigation application (2b)	Sugarcane	6.4 lb ai per acre	350 Acres per day	410	-	-	-
Mixing/Loading Dry Flowables for Groundboom application (2c)	Grapes	9.6 lb ai per acre	80 Acres per day	1,200	-	-	-

Exposure Scenario (Scenario #)	**Crop[a]**	**Application rates[b]**	**Area Treated[c]**	**Inhalation Baseline MOE[d,e]**	**Inhalation Min PPE MOE[d,f]**	**Inhalation Max PPE MOE[d,g]**	**Short-term Inhalation Eng. Control MOE[d,h]**
	Alfalfa	3.2 lb ai per acre	1200 Acres per day	1,400	-	-	-
Mixing/Loading Dry Flowables for Rights-of-Way Sprayer application (2d)	Grapes	0.19 lb ai per gallon	1000 Gallons per day	4,700	-	-	-
	Utility/Industrial Areas	0.96 lb ai per gallon		950	-	-	-
Mixing/Loading Dry Flowables for High-Pressure handwand application (2e)	Grapes	0.19 lb ai per gallon	1000 Gallons per day	4,700	-	-	-
	Utility/Industrial Areas	0.96 lb ai per gallon		950	-	-	-
Mixing/Loading Wettable Powders for Aerial application (3a)	Sugarcane	6.4 lb ai per acre	350 Acres per day	7.3	36	73	1,300
	Alfalfa	3.2 lb ai per acre	1200 Acres per day	4.2	21	42	760
Mixing/Loading Wettable Powders for Chemigation application (3b)	Sugarcane	6.4 lb ai per acre	350 Acres per day	7.3	36	73	1,300
Mixing/Loading Wettable Powders for Groundboom application (3c)	Grapes	9.6 lb ai per acre	80 Acres per day	21	110	-	-
	Alfalfa	3.2 lb ai per acre	200 Acres per day	25	130	-	-
Mixing/Loading Wettable Powders for Rights-of-Way Sprayer application (3d)	Grapes	0.19 lb ai per gallon	1000 Gallons per day	85	420	-	-
	Utility/Industrial Areas	0.96 lb ai per gallon		17	85	170	-
Mixing/Loading Wettable Powders for High-Pressure handwand application (3e)	Grapes	0.19 lb ai per gallon	1000 Gallons per day	85	420	-	-

Exposure Scenario (Scenario #)	Crop[a]	Application rates[b]	Area Treated[c]	Inhalation Baseline MOE[d,e]	Inhalation Min PPE MOE[d,f]	Inhalation Max PPE MOE[d,g]	Short-term Inhalation Eng. Control MOE[d,h]
	Utility/Industrial Areas	0.96 lb ai per gallon		17	85	170	-
Loading Granulars for Tractor-Drawn Spreaders application (4)	Utility/Industrial Areas	87.1 lb ai per acre	80 Acres per day	59	300	-	-
Applicator							
Applying Sprays for Aerial application (5)	Sugarcane	6.4 lb ai per acre	350 Acres per day	see eng. controls	see eng. controls	see eng. controls	4,600
	Alfalfa	3.2 lb ai per acre	1200 Acres per day	see eng. controls	see eng. controls	see eng. controls	2,700
Applying Sprays for Groundboom application (6)	Grapes	9.6 lb ai per acre	80 Acres per day	1200	-	-	-
	Alfalfa	3.2 lb ai per acre	200 Acres per day	1500	-	-	-
Applying Sprays for Rights-of-Way Sprayer application (7)	Grapes	0.19 lb ai per gallon	1000 Gallons per day	930	-	-	NF
	Utility/Industrial Areas	0.96 lb ai per gallon		190	-	-	NF
Applying Sprays for High-Pressure handwand application (8)	Grapes	0.19 lb ai per gallon	1000 Gallons per day	46	230	-	NF
	Utility/Industrial Areas	0.96 lb ai per gallon		9.2	46	**92**	NF
Applying Granulars for Tractor-Drawn Spreaders application (9)	Utility/Industrial Areas	87.1 lb ai per acre	80 Acres per day	84	420	-	460
Applying Granulars with a spoon (10)	Industrial Areas	87.1 lb ai per acre	100 sq ft per day	78,000	-	-	NF
Applying Granulars for Hand application (11)	Industrial Areas	87.1 lb ai per acre	100 sq ft per day	740	-	-	NF
Flagger							

Exposure Scenario (Scenario #)	Crop[a]	Application rates[b]	Area Treated[c]	Inhalation Baseline MOE[d,e]	Inhalation Min PPE MOE[d,f]	Inhalation Max PPE MOE[d,g]	Short-term Inhalation Eng. Control MOE[d,h]
Flagging for Sprays application (12)	Sugarcane	6.4 lb ai per acre	350 Acres per day	890	-	-	-
Mixer/Loader/Applicator							
Mixing/Loading/Applying Liquids for Low Pressure Handwand application (13)	Industrial Areas	0.90 lb ai per gallon	40 Gallons per day	650	-	-	NF
Mixing/Loading/Applying Liquids for Backpack sprayer application (14)	Industrial Areas	0.90 lb ai per gallon	40 Gallons per day	650	-	-	NF
Mixing/Loading/Applying Wettable Powders for Low Pressure Handwand application (15)	Industrial Areas	0.96 lb ai per gallon	40 Gallons per day	17	83	170	NF
Loading/Applying Granulars with a pump feed granular spreader (16)	Industrial Areas	87.1 lb ai per acre	5 Acres per day	380	-	-	NF
Loading/Applying Granulars with a gravity feed granular spreader (17)	Industrial Areas	87.1 lb ai per acre	5 Acres per day	36	180	-	NF
Loading/Applying Granulars for Belly Grinder application (18)	Industrial Areas	87.1 lb ai per acre	1 Acre per day	130	-	-	NF
Loading/Applying Granulars for Push-type spreader (ORETF) application (19)	Industrial Areas	87.1 lb ai per acre	5 Acres per day	210	-	-	NF

Footnotes:

a Crops named are index crops which are chosen to represent all other crops at or near that application rate for that use. See the application rates listing in the use summary section of this document for further information on application rates used in this assessment.
b Application Rates are based on the maximum application rates listed on the diuron labels.
c Amount handled per day are from Science Advisory Council on Exposure's Policy # 9.1.[9]
d Short-term MOE = Short- term NOAEL (mg/kg/day)/ Daily Inhalation Dose (mg/kg/day).
e Baseline: no respirator.
f Minimum PPE: dust mist respirator.
g Maximum PPE: organic vapor respirator.
h Engineering controls: closed mixing/loading, enclosed cab, truck or cockpit.

See the appendix, Tables A, B, C and D for the inputs and dermal and inhalation dose calculations.

- Scenario's calculated MOE exceeds the target MOE at the previous level of mitigation.
(MOE > 100), NF = Not feasible for this scenario (no available engineering controls).
Bolded MOE values show a risk of concern at the highest possible level of mitigation for the corresponding scenario.

Table 15: Summary of Intermediate-Term Exposure Variables and MOEs for Agricultural and Non-crop Uses

Exposure Scenario (Scenario #)	Crop[a]	Application rates[b]	Area Treated[c]	Inhalation Baseline MOE[d,e]	Inhalation Min PPE MOE[d,f]	Inhalation Max PPE MOE[d,g]	Inhalation Eng. Control MOE[d,h]
Mixer/Loader							
Mixing/Loading Liquids for Aerial application (1a)	cotton	2.2 lb ai per acre	350 Acres per day	76	380	-	-
			1200 Acres per day	22	110	-	-
Mixing/Loading Liquids for Chemigation application (1b)	cotton	2.2 lb ai per acre	350 Acres per day	76	380	-	-
Mixing/Loading Liquids for Groundboom application (1c)	cotton	2.2 lb ai per acre	80 Acres per day	330	-	-	-
			200 Acres per day	130	-	-	-
Mixing/Loading Liquids for Rights-Of-Way Sprayer (1d)	utility/industrial areas	0.9 lb ai per gallon	1000 gallons per day	65	320	-	-
Mixing/Loading Dry Flowables for Aerial application (2a)	cotton	2.2 lb ai per acre	350 Acres per day	120	-	-	-
			1200 Acres per day	34	180	-	-
Mixing/Loading Dry Flowables for Chemigation application (2b)	cotton	2.2 lb ai per acre	350 Acres per day	120	-	-	-
Mixing/Loading Dry Flowables for Groundboom application (2c)	cotton	2.2 lb ai per acre	80 Acres per day	520	-	-	-
			1200 Acres per day	210	-	-	-
Mixing/Loading Dry Flowables for Rights-Of-Way Sprayer (2d)	utility/industrial areas	0.96 lb ai per gallon	1000 gallons per day	95	490	-	-
Mixing/Loading Wettable Powders for Aerial application (3a)	cotton	2.2 lb ai per acre	350 Acres per day	2.1	11	21	380
			1200 Acres per day	0.62	3.1	6.2	110
Mixing/Loading Wettable Powders for Chemigation application (3b)	cotton	2.2 lb ai per acre	350 Acres per day	2.1	11	21	380

Exposure Scenario (Scenario #)	Crop[a]	Application rates[b]	Area Treated[c]	Inhalation Baseline MOE[d,e]	Inhalation Min PPE MOE[d,f]	Inhalation Max PPE MOE[d,g]	Inhalation Eng. Control MOE[d,h]
Mixing/Loading Wettable Powders for Groundboom application (3c)	cotton	2.2 lb ai per acre	80 Acres per day	9.2	46	92	1,700
			200 Acres per day	3.7	18	37	660
Mixing/Loading Wettable Powders for Rights-Of-Way Sprayer (3d)	utility/industrial areas	0.96 lb ai per gallon	1000 gallons per day	1.7	8.5	17	300
Applicator							
Applying Sprays for Aerial application (5)	cotton	2.2 lb ai per acre	350 Acres per day	see eng. controls	see eng. controls	see eng. controls	1,300
			1200 Acres per day	see eng. controls	see eng. controls	see eng. controls	390
Applying Sprays for Groundboom application (6)	cotton	2.2 lb ai per acre	80 Acres per day	540	-	-	-
			200 Acres per day	210	-	-	-
Applying Sprays for Rights-Of-Way (7)	utility/industrial areas	0.96 lb ai per gallon	1000 gallons per day	19	93	190	-
Flagger							
Flagging for Sprays application (12)	cotton	2.2 lb ai per acre	350 Acres per Day	260	-	-	-

Footnotes:

a Crops named are index crops which are chosen to represent all other crops at or near that application rate for that use. See the application rates listing in the use summary section of this document for further information on application rates used in this assessment.
b Application Rates are based on the maximum application rates listed on the diuron labels.
c Amount handled per day are from Science Advisory Council on Exposure's Policy # 9.1.[9]
d Short-term MOE = Short- term NOAEL (mg/kg/day)/ Daily Inhalation Dose (mg/kg/day).
e Baseline: no respirator.
f Minimum PPE: dust mist respirator.
g Maximum PPE: organic vapor respirator.
h Engineering controls: Closed mixing/loading, enclosed cab, truck or cockpit.
See the appendix, Tables E, F, G, and H for the inputs and dermal and inhalation dose calculations.
- Scenario's calculated MOE exceeds the target MOE at the previous level of mitigation.
(MOE > 100), NF = Not feasible for this scenario (no available engineering controls).
Bolded MOE values show a risk of concern at the highest possible level of mitigation for the corresponding scenario.

Table 16: Cancer(Q*) Risk Summary for Agricultural and Non-crop Uses

Exposure Scenario (Scenario #)	Baseline[a]			Maximum PPE[b]			Engineering Control[c]		
	Private Farmer/10 days/Maximum Rate Cancer Risk[d]	Private Farmer/10 days/Typical Rate Cancer Risk[e]	Commercial applicator/30 days/Typical Rate Cancer Risk[f]	Private Farmer/10 days/Maximum Rate Cancer Risk[d]	Private Farmer/10 days/Typical Rate Cancer Risk[e]	Commercial applicator/30 days/Typical Rate Cancer Risk[f]	Private Farmer/10 days/Maximum Rate Cancer Risk[d]	Private Farmer/10 days/Typical Rate Cancer Risk[e]	Commercial applicator/30 days/Typical Rate Cancer Risk[f]
Mixer/Loader									
Mixing/Loading Liquids for Aerial application (1a)	9.2 E-4	6.1 E-4	1.8 E-3	6.3 E-6	4.2 E-6	1.3 E-5	3.4 E-6	2.2 E-6	6.7 E-6
	1.7 E-3	1.3 E-3	3.9 E-3	1.2 E-5	9.0 E-6	2.7 E-5	6.1 E-6	4.8 E-6	1.4 E-5
Mixing/Loading Liquids for Chemigation application (1b)	9.2 E-4	6.1 E-4	1.8 E-3	6.3 E-6	4.2 E-6	1.3 E-5	3.4 E-6	2.2 E-6	6.7 E-6
Mixing/Loading Liquids for Groundboom application (1c)	3.4 E-4	1.4 E-4	4.2 E-4	2.3 E-6	9.6 E-7	2.9 E-6	1.2 E-6	5.1 E-7	1.5 E-6
	2.8 E-4	2.2 E-4	6.6 E-4	1.9 E-6	1.5 E-6	4.5 E-6	1.0 E-6	8.0 E-7	2.4 E-6
Mixing/Loading Liquids for Rights-of-Way Sprayer application (1d)	8.4 E-5	2.8 E-5	8.4 E-5	5.7 E-7	1.9 E-7	5.7 E-7	3.1 E-7	1.0 E-7	3.1 E-7
	3.9 E-4	3.9 E-4	1.2 E-3	2.7 E-6	2.7 E-6	8.1 E-6	1.4 E-6	1.4 E-6	4.3 E-6
Mixing/Loading Liquids for High-Pressure handwand application (1e)	8.4 E-5	2.8 E-5	8.4 E-5	5.7 E-7	1.9 E-7	5.7 E-7	3.1 E-7	1.0 E-7	3.1 E-7
	3.9 E-4	3.9 E-4	1.2 E-3	2.7 E-6	2.7 E-6	8.1 E-6	1.4 E-6	1.4 E-6	4.3 E-6
Mixing/Loading Dry Flowables for Aerial application (2a)	2.9 E-5	1.8 E-5	5.4 E-5	1.6 E-5	1.0 E-5	3.1 E-5	5.6 E-7	3.5 E-7	1.1 E-6
	4.9 E-5	3.8 E-5	1.2 E-4	2.8 E-5	2.2 E-5	6.6 E-5	9.6 E-7	7.5 E-7	2.3 E-6
Mixing/Loading Dry Flowables for Chemigation application (2b)	2.9 E-5	1.8 E-5	5.4 E-5	1.6 E-5	1.0 E-5	3.1 E-5	5.6 E-7	3.5 E-7	1.1 E-6
Mixing/Loading Dry Flowables for Groundboom application (2c)	9.8 E-6	4.1 E-6	1.2 E-5	5.6 E-6	2.3 E-6	7.0 E-6	1.3 E-7	8.0 E-8	2.4 E-7
	8.2 E-6	6.4 E-6	1.9 E-5	4.7 E-6	3.7 E-6	1.1 E-5	1.9 E-7	1.3 E-7	3.8 E-7

Exposure Scenario (Scenario #)	Baseline[a]			Maximum PPE[b]			Engineering Control[c]		
	Private Farmer/10 days/Maximum Rate Cancer Risk[d]	Private Farmer/10 days/Typical Rate Cancer Risk[e]	Commercial applicator/30 days/Typical Rate Cancer Risk[f]	Private Farmer/10 days/Maximum Rate Cancer Risk[d]	Private Farmer/10 days/Typical Rate Cancer Risk[e]	Commercial applicator/30 days/Typical Rate Cancer Risk[f]	Private Farmer/10 days/Maximum Rate Cancer Risk[d]	Private Farmer/10 days/Typical Rate Cancer Risk[e]	Commercial applicator/30 days/Typical Rate Cancer Risk[f]
Mixing/Loading Dry Flowables for Rights-of-Way Sprayer application (2d)	2.5 E-6	8.2 E-7	2.5 E-6	1.4 E-6	4.7 E-7	1.4 E-6	4.8 E-8	1.6 E-8	4.8 E-8
	1.2 E-5	1.2 E-5	3.7 E-5	7.0 E-6	7.0 E-6	2.1 E-5	2.4 E-7	2.4 E-7	7.2 E-7
Mixing/Loading Dry Flowables for High-Pressure handwand application (2e)	2.5 E-6	8.2 E-7	2.5 E-6	1.4 E-6	4.7 E-7	1.4 E-6	4.8 E-8	1.6 E-8	4.8 E-8
	1.2 E-5	1.2 E-5	3.7 E-5	7.0 E-6	7.0 E-6	2.1 E-5	2.4 E-7	2.4 E-7	7.2 E-7
Mixing/Loading Wettable Powders for Aerial application (3a)	1.6 E-3	10.0 E-4	3.0 E-3	8.0 E-5	5.0 E-5	1.5 E-4	5.3 E-6	3.3 E-6	9.9 E-6
	2.7 E-3	2.1 E-3	6.4 E-3	1.4 E-4	1.1 E-4	3.2 E-4	9.1 E-6	7.1 E-6	2.1 E-5
Mixing/Loading Wettable Powders for Chemigation application (3b)	1.6 E-3	10.0 E-4	3.0 E-3	8.0 E-5	5.0 E-5	1.5 E-4	5.3 E-6	3.3 E-6	9.9 E-6
Mixing/Loading Wettable Powders for Groundboom application (3c)	5.5 E-4	2.3 E-4	6.9 E-4	2.7 E-5	1.1 E-5	3.4 E-5	1.8 E-6	7.6 E-7	2.3 E-6
	4.6 E-4	3.6 E-4	1.1 E-3	2.3 E-5	1.8 E-5	5.3 E-5	1.5 E-6	1.2 E-6	3.5 E-6
Mixing/Loading Wettable Powders for Rights-of-Way Sprayer application (3d)	1.4 E-4	4.6 E-5	1.4 E-4	6.8 E-6	2.3 E-6	6.8 E-6	4.5 E-7	1.5 E-7	4.5 E-7
	6.9 E-4	6.9 E-4	2.1 E-3	3.4 E-5	3.4 E-5	1.0 E-4	2.3 E-6	2.3 E-6	6.8 E-6
Mixing/Loading Wettable Powders for High-Pressure handwand application (3e)	1.4 E-4	4.6 E-5	1.4 E-4	6.8 E-6	2.3 E-6	6.8 E-6	4.5 E-7	1.5 E-7	4.5 E-7
	6.9 E-4	6.9 E-4	2.1 E-3	3.4 E-5	3.4 E-5	1.0 E-4	2.3 E-6	2.3 E-6	6.8 E-6
Loading Granulars for Tractor-Drawn Spreaders application (4)	5.3 E-5	5.3 E-5	1.6 E-4	8.0 E-6	8.0 E-6	2.4 E-5	1.1 E-6	1.1 E-6	3.2 E-6
Applicator									

Exposure Scenario (Scenario #)	**Baseline[a]**			**Maximum PPE[b]**			**Engineering Control[c]**		
	Private Farmer/10 days/Maximum Rate Cancer Risk[d]	**Private Farmer/10 days/Typical Rate Cancer Risk[e]**	**Commercial applicator/30 days/Typical Rate Cancer Risk[f]**	**Private Farmer/10 days/Maximum Rate Cancer Risk[d]**	**Private Farmer/10 days/Typical Rate Cancer Risk[e]**	**Commercial applicator/30 days/Typical Rate Cancer Risk[f]**	**Private Farmer/10 days/Maximum Rate Cancer Risk[d]**	**Private Farmer/10 days/Typical Rate Cancer Risk[e]**	**Commercial applicator/30 days/Typical Rate Cancer Risk[f]**
Applying Sprays for Aerial application (5)	See eng controls	See eng controls	See eng controls	See eng controls	See eng controls	See eng controls	2.2 E-6	1.4 E-6	4.2 E-6
	See eng controls	See eng controls	See eng controls	See eng controls	See eng controls	See eng controls	3.9 E-6	3.0 E-6	9.0 E-6
Applying Sprays for Groundboom application (6)	3.7 E-6	1.6 E-6	4.7 E-6	1.5 E-6	6.2 E-7	1.8 E-6	7.0 E-7	2.9 E-7	8.7 E-7
	3.1 E-6	2.4 E-6	7.3 E-6	1.2 E-6	9.6 E-7	2.9 E-6	5.8 E-7	4.5 E-7	1.4 E-6
Applying Sprays for Rights-of-Way Sprayer application (7)	4.0 E-5	1.3 E-5	4.0 E-5	8.6 E-6	2.9 E-6	8.6 E-6	NF	NF	NF
	2.0 E-4	2.0 E-4	6.0 E-4	4.3 E-5	4.3 E-5	**1.3 E-4**	NF	NF	NF
Applying Sprays for High-Pressure handwand application (8)	1.1 E-4	3.6 E-5	1.1 E-4	1.6 E-5	5.3 E-6	1.6 E-5	NF	NF	NF
	5.2 E-4	5.4 E-4	1.6 E-3	8.0 E-5	8.0 E-5	**2.4 E-4**	NF	NF	NF
Applying Granulars for Tractor-Drawn Spreaders application (9)	4.2 E-5	4.2 E-5	1.3 E-4	7.5 E-6	7.5 E-6	2.3 E-5	7.9 E-6	7.9 E-6	2.4 E-5
Applying Granulars with a Spoon (10)	9.3 E-8	9.3 E-8	2.8 E-7	6.6 E-8	6.6 E-8	2.0 E-7	NF	NF	NF
Applying Granulars for Hand application (11)	2.5 E-5	2.5 E-5	7.4 E-5	1.2 E-5	1.2 E-5	3.7 E-5	NF	NF	NF
Flagger									
Flagging for Spray application (12)	6.6 E-6	4.1 E-6	1.2 E-5	3.6 E-6	2.3 E-6	6.8 E-6	1.3 E-7	8.3 E-8	2.5 E-7
Mixer/Loader/App									
Mixing/Loading/Applying Liquids for Low Pressure Handwand application (13)	5.4 E-4	5.4 E-4	1.6 E-3	2.4 E-6	2.4 E-6	7.2 E-6	NF	NF	NF

Exposure Scenario (Scenario #)	Baseline[a]			Maximum PPE[b]			Engineering Control[c]		
	Private Farmer/10 days/Maximum Rate Cancer Risk[d]	**Private Farmer/10 days/Typical Rate Cancer Risk[e]**	**Commercial applicator/30 days/Typical Rate Cancer Risk[f]**	**Private Farmer/10 days/Maximum Rate Cancer Risk[d]**	**Private Farmer/10 days/Typical Rate Cancer Risk[e]**	**Commercial applicator/30 days/Typical Rate Cancer Risk[f]**	**Private Farmer/10 days/Maximum Rate Cancer Risk[d]**	**Private Farmer/10 days/Typical Rate Cancer Risk[e]**	**Commercial applicator/30 days/Typical Rate Cancer Risk[f]**
Mixing/Loading/Applying Liquids for Backpack sprayer application (14)	1.8 E-5	1.8 E-5	5.3 E-5	9.0 E-6	9.0 E-6	2.7 E-5	NF	NF	NF
Mixing/Loading/Applying Wettable Powders for Low Pressure Handwand application (15)	2.1 E-4	2.1 E-4	6.2 E-4	5.1 E-5	5.1 E-5	**1.5 E-4**	NF	NF	NF
Loading/Applying Granulars with a Pump Feed Backpack Spreader (16)	1.4 E-5	1.4 E-5	4.0 E-5	7.8 E-6	7.8 E-6	2.4 E-5			
Loading/Applying Granulars with a Gravity Feed Backpack Spreader (17)	1.1 E-4	1.1 E-4	3.3 E-4	5.4 E-5	5.4 E-5	**1.6 E-4**			
Loading/Applying Granulars for Belly Grinder application (18)	1.5 E-4	1.5 E-4	4.5 E-4	7.6 E-5	7.6 E-5	**3.1 E-4**	NF	NF	NF
Loading/Applying Granulars for Push-type spreader (ORETF) application (19)	3.5 E-5	3.5 E-5	1.1 E-4	5.5 E-6	5.5 E-6	1.7 E-5	NF	NF	NF

Footnotes:

a Baseline represents long pants, long sleeved shirt, no gloves (except scenarios 10, 11, 14, 15, 16 and 17 which represent gloves), open mixing/loading, open cab/tractor, and no respirator.

b Maximum PPE represents long sleeves, long pants, coveralls, chemical resistant gloves, open mixing/loading, open cab tractor and an organic vapor respirator, except for scenarios 10, 16 and 17, which represent single layer of clothing, gloves and a dust-mist respirator (minimum PPE) which is the clothing scenarios from the proprietary studies (EPA MRIDs 451672-01 and 452507-02).

c Engineering controls: closed mixing/loading, enclosed cab, truck or cockpit. Baseline level clothing. Chemical resistant gloves for the mixing/loading of liquids.

d Cancer risk assessed using the maximum label application rates and 10 days of exposure per year assumed for a private farmer.

e Cancer risk assessed using the typical application rates given to EPA by Griffin, sources quoted are Doanes, NCFAP, USDA, and Griffin Information. Maximum application rates were used for the non-crop/industrial areas, because no information of the typical rates of these uses is available. 10 days of exposure per year assumed for a private farmer.

f Cancer risk assessed using the typical application rates given to EPA by Griffin, sources quoted are Doanes, NCFAP, USDA, and Griffin Information. Maximum application rates were used for the non-crop/industrial areas, because no information of the typical rates of these uses is available. 30 days of exposure per year assumed for a commercial applicator.

Cancer risk = LADD (mg/kg/day) * Q1 (1.91 E-2 $mg/kg/day^{1}$). See appendix Tables I , J , and K for the inputs and calculations of total daily dose, LADD and cancer risk.

NF = Not feasible for this scenario (no available engineering controls).

Bolded cancer risks values have risks less than 1.0 E-4 at the highest possible level of mitigation.

Table 17: Cancer Postapplication for Private Growers (Shorter-Term Duration/10 Days Exposure Per Year)

Transfer Coefficient Crop Grouping[a]	Diuron Specific Crops [b]	Highest Crop Group Application Rate (lbs ai/acre)[c]	Transfer Coefficient[d] (cm^2/hr)	Activity[e]	DAT[f]	DFR[g] (Fg/cm^2)	LADD[h]	Cancer Risk[i]
Field/row crops, low/medium	Oats, Wheat, Birdsfoot Trefoil, Clover, Grass Grown For Seed, and Alfalfa.	2.5 (typical)	100 (low)	Irrigation, scouting, thinning	0	5.61	3.5e-5	6.7e-7
			1500 (medium)	Irrigation, scouting	0	5.61	5.3e-4	1.0e-5
		3.25 (maximum)	100 (low)	Irrigation, scouting, thinning	0	7.29	4.6e-5	8.7e-7
			1500 (medium)	Irrigation, scouting	0	7.29	6.8e-4	1.3e-5
Sugarcane	Sugarcane	2.4 (typical)	1000 (medium)	Scouting immature plants	0	5.39	3.4e-4	6.4e-6
		6.4 (maximum)	1000 (medium)	Scouting immature plants	0	14.36	9.0e-4	1.7e-5
Vegetable, Stem./ Stalk	Asparagus and Pineapple.	4 (typical)	300 (low)	Irrigation, scouting, thinning	0	8.98	1.7e-4	3.2e-6
			500 (medium)	Irrigation and scouting mature plants	0	8.98	2.8e-4	5.4e-6
			1000 (high)	hand harvesting and pruning	0	8.98	5.6e-4	1.1e-5
		6.4 (maximum)	300 (low)	Irrigation, scouting, thinning	0	14.36	2.7e-4	5.2e-6
			500 (medium)	Irrigation and scouting mature plants	0	14.36	4.5e-4	8.6e-6
			1000 (high)	hand harvesting and pruning	0	14.36	9.0e-4	1.7e-5

Footnotes:

a Crops were grouped according to the transfer coefficient crop groups listed in Science Advisory Council on Exposure Policy 3.1.[14]
b Crops within the transfer coefficient group that are registered for diuron.
c Highest application rate for all of the diuron specific crops within the transfer coefficient crop group.
d Transfer Coefficients from Science Advisory Council on Exposure Policy 3.1.[14]
e Activities from Science Advisory Council on Exposure Policy 3.1.[14] Every activity listed may not occur for every crop in the group.
f DAT is "days after treatment" (0 days = 12 hours after application).
g DFR (Fg/cm^2) = application rate * correction factor * fraction of ai retained on foliage (20%) * (1-dissipation rate (10%))$^{\text{time(hours)}}$.

h Lifetime average daily dose (LADD) (mg/kg/day) = Average Daily Dose (mg/kg/day) * (10 days of exposure per year / 365 days/year) * (35 years exposed / 70 years in a lifetime).

i Cancer risk = LADD (mg/kg/day) * Q1 (1.91 E-2 $mg/kg/day^{1}$).

Table 18: Cancer Postapplication for Commercial Farm Workers (Longer-Term Duration/30 Days Exposure Per Year)

Transfer Coefficient Crop Grouping[a]	Diuron Specific Crops [b]	Highest Crop Group Application Rate (lbs ai/acre)[c]	Transfer Coefficient[d] (cm^2/hr)	Activity[e]	DAT[f]	DFR[g] (Fg/cm^2)	LADD[h]	Cancer Risk[i]
Field/row crops, low/medium	Oats, Wheat, Birdsfoot Trefoil, Clover, Grass Grown For Seed, and Alfalfa.	2.5 (typical)	100 (low)	Irrigation, scouting, thinning, weeding immature/low foliage plants	0	5.61	1.1e-4	2.0e-6
			1500 (medium)	Irrigation, scouting, weeding mature/high foliage plants	0	5.61	1.6e-3	3.0e-5
Sugarcane	Sugarcane	2.4 (typical)	1000 (medium)	Scouting immature plants	0	5.39	1.0e-3	1.9e-5
Vegetable, Stem./ Stalk	Asparagus and Pineapple.	4 (typical)	300 (low)	Irrigation, scouting, thinning, weeding immature plants	0	8.98	5.1e-4	9.7e-6
			500 (medium)	Irrigation and scouting mature plants	0	8.98	8.4e-4	1.6e-5
			1000 (high)	hand harvesting and pruning	0	8.98	1.7e-3	3.2e-5

Footnotes:

a Crops were grouped according to the transfer coefficient crop groups listed in Science Advisory Council on Exposure Policy 3.1.[14].
b Crops within the transfer coefficient group that are registered for diuron.
c Highest application rate for all of the diuron specific crops within the transfer coefficient crop group.
d Transfer Coefficients from Science Advisory Council on Exposure Policy 3.1.[14]
e Activities from Science Advisory Council on Exposure Policy 3.1.[14] Every activity listed may not occur for every crop in the group.
f DAT is "days after treatment" (0 days = 12 hours after application).
g DFR (Fg/cm^2) = application rate * correction factor * fraction of ai retained on foliage (20%) * (1-dissipation rate (10%)) $^{time(hours)}$.
h Lifetime average daily dose (LADD) (mg/kg/day) = Average Daily Dose (mg/kg/day) * (30 days of exposure per year / 365 days/year) * (35 years exposed / 70 years in a lifetime).
i Cancer risk = LADD (mg/kg/day) * Q1 (1.91 E-2 mg/kg/day^1).

Table 19: Short- and Intermediate-term Antimicrobial Uses of Diuron and MOEs

Exposure Scenario (Scenario #)		Clothing Attire	Dermal Unit Exposure (mg/lb ai)[a]	Inhalation Unit Exposure (Fg/lb ai)[b]	Max Appl. Rate[c] (lb ai/gal)	Amount Treated[d]	Dermal Dose (mg/kg/day)[e]	Inhalation Dose (mg/kg/day)[f]	Short-term Inhalation MOE[g]	Int.-term Inhalation MOE[g]
Primary Handlers										
Mixing/loading of Liquids into Paint Products (1)		Open pour, long pants, long-sleeved shirt, chemical resistant gloves, and a 5-fold PF dust/mist type respirator	0.184	1.7	0.0532	100 gal	0.014	0.00013	77,000	7,700
						1,000 gal	0.14	0.0013	7,700	770
Loading of Tablets into Paint Products (2)			0.412	11.8	0.0532	100 gallons	0.031	0.00090	11,000	1,100
						1,000 gal	0.31	0.0090	1,100	110
Secondary Handlers										
Applying Paints with an Airless Sprayer (3)	Indoor	Long pants, long sleeved shirt, and a 5-fold PF dust/mist type respirator	36.22	470	0.0532	50 gallons	1.4	0.018	560	**56**
		Long pants, long sleeved shirt, gloves, and a 5-fold PF dust/mist type respirator	12	470			0.46	0.018	560	**56**
	Outdoor	Long pants, long sleeved shirt, and a 5-fold PF dust/mist type respirator	33.33	86.6	0.0532	50 gallons	1.3	0.0033	3,000	300
		Long pants, long sleeved shirt, gloves, and a 5-fold PF dust/mist type respirator	8.87	86.6			0.34	0.0033	3,000	300
Applying Paints with a Paint Brush (4)		Long pants, long sleeved shirt, and a 5-fold PF dust/mist type respirator	290	101	0.0532	5 gallons	1.1	0.00038	26,000	2,600

Footnotes:

a,b Dermal and inhalation unit exposures are from CMA and Chlorothalonil studies.[11,12]

c Application rates are based on diuron paint labels

d Amount treated is based on assumptions from EPA's Antimicrobial Division and HED Expo SAC Policy # 9.1.[9]

e Dermal dose (mg/kg/day) = [(unit exposure (mg/lb ai) * Appl. rate (lb ai/gallon) * gallons handled)/ Body weight (70 kg).

f Inhalation dose (mg/kg/day) = [unit exposure (Fg/lb ai) * 0.001 mg/Fg unit conversion * max appl rate (lb ai/gal) * gallons handled] / Body weight (70 kg).

g MOE = NOAEL (mg/kg/day) / Daily Dose [Intermediate-term inhalation NOAEL = 1.0 mg/kg/day]. Target MOE is 100 for occupational/commercial.

Table 20: Diuron Cancer Assessment for Antimicrobial Uses

Exposure Scenario (Scenario #)		Clothing Attire	Dermal Unit Exposure (mg/lb ai)[a]	Inhalation Unit Exposure (µg/lb ai)[b]	Maximum Application Rate[c] (lb ai/gal)	Amount Treated[d]	Total Absorbed Dose (mg/kg/day)[e]	LADD (mg/kg/day)[f]	Risk[g]
Primary Handlers (125 day/year)									
Mixing/loading of Liquids into Paint Products (1)		Open pour, long pants, long-sleeved shirt, chemical resistant gloves, and a 5-fold PF dust/mist type respirator	0.184	1.7	0.0532	100 gal	6.9 E-4	1.2 E-4	2.3 E-6
						1,000 gal	6.9 E-3	1.2 E-3	2.3 E-5
Loading of Tablets into Paint Products (2)			0.412	11.8	0.0532	100 gallons	2.1 E-3	3.7 E-4	7.0 E-6
						1,000 gallons	2.1 E-2	3.7 E-3	7.0 E-5
Secondary Handlers (50 day/year)									
Applying Paints with an Airless Sprayer (3)	Indoor	Long pants, long sleeved shirt, and a 5-fold PF dust/mist type respirator	36.22	470	0.0532	50 gallons	7.3 E-2	5.0 E-3	9.5 E-5
		Long pants, long sleeved shirt, gloves, and a 5-fold PF dust/mist type respirator	12	470			3.6 E-2	2.5 E-3	4.7 E-5
	Outdoor	Long pants, long sleeved shirt, and a 5-fold PF dust/mist type respirator	33.33	86.6	0.0532	50 gallons	5.4 E-2	3.7 E-3	7.1 E-5
		Long pants, long sleeved shirt, gloves, and a 5-fold PF dust/mist type respirator	8.87	86.6			1.7 E-2	1.1 E-3	2.2 E-5
Applying Paints with a Paint Brush (4)		Long pants, long sleeved shirt, and a 5-fold PF dust/mist type respirator	290	101	0.0532	5 gallons	4.4 E-2	3.0 E-3	5.8 E-5

Footnotes:

a,b Dermal and inhalation unit exposures are from CMA and Chlorothalonil studies.[11,12]

c Application rates are based on diuron paint labels

d Amount treated is based on assumptions from EPA's Antimicrobial Division and HED Expo SAC Policy # 9.1.[9]

e Total daily absorbed dose (mg/kg/day) = [(dermal dose (mg/lb ai) * dermal absorption (4%)+ inhalation dose (mg/lb ai)]. See Table 6 for the corresponding dermal dose and inhalation dose.

f LADD (Lifetime average daily dose) mg/kg/day = Total daily absorbed dose (mg/kg/day) * (days worked per year/365 days per year) * (35 years worked/70 year lifetime). Days worked per year are estimates.

g Risk = LADD (mg/kg/day) * Q_1^* = 1.91e-2 $(mg/kg/day)^{-1}$.

Table 21: Short-Term Baseline Table for Algaecide Use in Commercial Fish Production

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)[a]	Inhalation Unit Exposure (Fg/lb ai)[b]	Use	Application Rate [c]	Dermal Dose (mg/kg/day)[d]	Inhalation Dose (mg/kg/day)[e]	Inhalation MOE [f]
Mixer/Loader							
Mixing/Loading Dry Flowables (1a)	0.066	0.77	Catfish Production	7.5 lb ai per day	0.0071	0.000083	120,000
Mixing/Loading Dry Flowables (1b)	0.066	0.77	Ornamental Fish Production	819 lb ai per day	0.77	0.0090	1,100
Mixing/Loading Wettable Powders (2a)	3.7	43	Catfish Production	7.5 lb ai per day	0.40	0.0046	2,200
Mixing/Loading Wettable Powders (2b)	3.7	43	Ornamental Fish Production	15.0 lb ai per day	0.79	0.0092	1,100

Footnotes:
a Baseline dermal exposure represents long sleeves and long pants.
b Baseline inhalation unit exposure represents no respirator.
c Application Rates are based on the diuron commercial fish production labels and EPA estimates.
d Daily Dermal Dose (mg/kg/day) = (Dermal Unit Exposure (mg/lb ai) x Application Rates (lb ai/A and lb ai/sq. ft.) x Area Treated per day (acres and square feet))/ body weight (70 kg).
e Daily Inhalation dose (mg/kg/day) = (Inhalation Unit Exposure (Fg/lb ai) x (1mg/1000 Fg) Conversion Factor x Application Rate (lb ai/gallon) x Amount Treated per day (gallons/day))/ body weight (70 kg).
f Short-term Inhalation MOE = Inhalation NOAEL (10 mg/kg/day) / Daily Inhalation Dose (mg/kg/day).

Table 22: Cancer(Q*) Risk Table for Algaecide Use in Commercial Fish Production

Exposure Scenario (Scenario #)	Use	Application Rate[a]	Exposures Per Year[a]	Baseline Total Daily Dose[b]	Baseline Daily LADD[c]	Baseline Risk[d]	Max PPE Total Daily Dose[b]	Max PPE LADD[c]	Max PPE Risk[d]	Eng Cont Total Daily Dose[b]	Eng Cont LADD[c]	Eng Cont Risk[d]
Mixer/Loader												
Mixing/Loading Dry Flowables (1a)	Catfish Production	7.5 lb ai per day	9	0.00037	4.50E-6	8.60E-8	0.00021	2.59E-6	4.94E-8	0.0000072	8.85E-8	1.70E-9
Mixing/Loading Dry Flowables (1b)	Ornamental Fish Production	819 lb ai per day	3	0.040	1.64E-4	3.13E-6	0.023	9.41E-5	1.80E-6	0.00078	9.66E-6	1.85E-7
Mixing/Loading Wettable Powders (2a)	Catfish Production	7.5 lb ai per day	9	0.020	2.52E-4	4.82E-6	0.0010	1.25E-5	2.40E-7	0.000068	8.35E-7	1.59E-8
Mixing/Loading Wettable Powders (2b)	Ornamental Fish Production	15.0 lb ai per day	9	0.041	5.05E-4	9.64E-6	0.0020	2.51E-5	4.79E-7	0.00014	1.67E-6	3.19E-8

Footnotes:

a Based on diuron commercial fish production labels and EPA estimates.

b Total Daily Dose (mg/kg/day) = Daily Dermal Dose (mg/kg/day) + Daily Inhalation Dose (mg/kg/day). See Table 8 for daily dermal and inhalation doses.

c Lifetime average daily dose (LADD) (mg/kg/day) = Average Daily Dose (mg/kg/day) * (number of days of exposure per year / 365 days/year) * (35 years exposed / 70 years in a lifetime).

d Cancer risk = LADD (mg/kg/day) * Q1 (1.91E-2 $mg/kg/day^{1}$).