B11-1.0 DIURON

B11-1.1 Background Information

IUPAC: 3-(3,4-dichlorophenyl)-1,1-dimethyl-urea

CAS: N'-(3,4-dichlorophenyl)-N, N-dimethylurea

CASRN: 330-54-1

DIURON USAGE:

Diuron can be used to control a wide variety of annual and perennial broadleaf and grassy weeds on both crop and non-crop areas. Diuron can also be used on numerous crop sites such as forage crops, field crops, fruits, vegetables, nuts, and ornamental crops. In non-crop applications, diuron can be used on industrial sites, on rights-of-way, around farm buildings, and on irrigation and drainage ditches (Extoxnet, 1993).

Diuron was the active ingredient of several herbicide products that was applied at the CFB Gagetown. These include, Krovar® which was applied in 1994. Karmex DF® was applied in years 2001 and 2002 in conjunction with herbicide product Arsenal® (Imazapyr). Diurex 80W® was applied in 2004 in conjunction with herbicide product Roundup® Transorb (Glyphosate).

Diuron was used at CFB Gagetown between 1994 and 2004 (JW, 2006).

Table B11-1 Fenoprop Usage at CFB Gagetown[a]

Year	Amount of Diuron Applied (kg)	Total Area Treated (ha)
1994	2566.8	356.5
2000	328	20.5
2001	440	27.5
2002	272.3	17.02
2004	261.2	17.0
Total	**3.9E+03**	**4.4E+02**

[a] Adapted from JW, 2006.

B11-2.0 CHEMICAL AND PHYSICAL PROPERTIES

Formula: $C_9H_{10}Cl_2N_2O$

Activity: Herbicide: Systemic substituted phenyl urea. Diuron functions by inhibiting the Hill reaction in photosynthesis, limiting the production of high energy compounds such as ATP (Moncada, 2004).

Notes: 3,3′,4,4′-tetrachloroazoxybenzene and 3,3′,4,4′-tetrachloroazobenzene was reported as potential contaminants in the Diuron formulation mixtures used at CFB Gagetown (JW, 2006).

Structure:

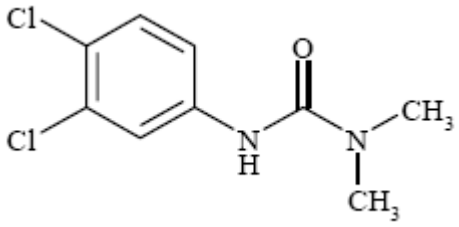

Figure B11-1 Diuron CASRN: 330-54-1 Structure

Table B11-2 Chemical and Physical Properties of Diuron

Chemical/Physical Property	Result	Reference
Colour/Form	White crystal	U.S. EPA, 2003
Henry's Law constant	5.40 x 10^{-10} atm-m^3/mole at 25 °C	JW, 2006
Log K_{ow}	2.68	U.S. EPA, 2003; JW, 2006
Melting Point	158°C	U.S. EPA, 2003
Soil Adsorption Coefficient (K_{oc})	468	JW, 2006
Molecular Weight	233.1	U.S. EPA, 2003; JW, 2006
Odour	None	U.S. EPA, 2003
Vapour Pressure	2 x 10^{-7} mm Hg at 30 °C	U.S. EPA, 2003
	6.90 x 10^{-8} mm Hg at 25 °C	JW, 2006
Water Solubility	42 ppm 25 °C	U.S. EPA, 2003; JW, 2006

B11-3.0 PMRA EVALUATIONS

Diuron was scheduled to be re-evaluated by the PMRA (2004) in a work-plan under Program 1, published on December, 2004.

B11-4.0 TOXICOLOGICAL SUMMARY

B11-4.1 Human Health Effects

Table B11-3 Human Health Effects Resulting from Acute Exposure to Diuron[a,b]

Exposure	Effects	Response
Acute	Ophthalmic	Ocular irritation
	Respiratory	Irritation of the respiratory mucous membranes
	Cardiovascular	CNS depression and hypoxemia may be noted if methemoglobinemia is present.
	Gastrointestinal	Nausea, vomiting, and diarrhea may be noted following ingestion.
	Genitourinary	Some metabolites may cause irritation of the urinary tract.
	Hematological	Sulfhemoglobin has been observed in the blood of human overdose of monolinuron. Methemoglobinemia may result from effects of metabolites of some urea-based herbicides.
	Dermatological	Cyanosis unresponsive to oxygen therapy may be noted in patients with methemoglobinemia due to absorption of excessive amounts of these agents.

[a] Rumack and Hall, 2006.
[b] MEDITEXT®, 2006.

B11-4.2 Health Effects by Route of Exposure

Values below are adapted from the U.S. EPA, 2003 RED document for Diuron and the Australian Pesticide and Veterinary Medicines Authority's diuron technical assessment reports.

B11-4.2.1 Oral Exposure

B11-4.2.1.1 Death

Table B11-4 Mammalian LD_{50} Values Resulting from Oral Exposure to Diuron

Test Organism (Species/Sex)	LD_{50} (mg/kg)	Reference
Acute		
Mice	8590 (M)	APVMA, 2005
	8244 (F)	

M denotes male
F denotes female

B11-4.2.1.2 Systemic Effects

Table B11-5 Mammalian Systemic Effects Resulting from Oral Exposure to Diuron

Test Organism (Species)	Daily Dose (Duration)	Response	Reference
Chronic			
Mice	0, 25, 250 or 2,500 ppm male and female for 2 years	Increased leucocytes, blood ALT and bilirubin, haemosiderin accumulation in the liver, spleen and kidneys, urothelium hyperplasia, neoplasia in ovary and mammary.	Eiben *et al*, 1990
Rats	0, 75, 250 or 500 mg/kg/day for 13 weeks	Haemolytic anaemia: reduced RBC, Hgb and Hct, and increased MCV, blood bilirubin and urea nitrogen.	Wandrag, 1996a
Rats	0.7, 0.8, 1.6, 1.8 mg/kg/day for 6 months	Reduced haemoglobin (females) and increased reticulocyte counts.	Schmidt *et al*., 1986a
Rats	0, 25, 250 or 2,500 ppm for 2 years	Changes in haematology, clinical chemistry, organ weights, and pathology of spleen, bone marrow, urothelium hyperplasia and neoplasia in the urinary bladder.	Schmidt, 1985
Dogs	0, 50 , 300 or 1,800 ppm for 1 year	Haemosiderin accumulation in the spleen and kidneys.	Hoffmann *et al*., 1985
Dogs	0, 25, 125, 250 or 2,500 ppm for 2 years	Haematological changes and blood pigments.	Hodge and Downs, 1964

B11-4.2.1.3 Neurological Effects

No data found.

B11-4.2.1.4 Mammalian Reproductive/Developmental Effects

Table B11-6 Mammalian Reproductive and Developmental Effects Resulting from Oral Exposure to Diuron

Test Organism (Species)	Exposure	Dose (Duration)	Response	Reference
Rats	Gavage	0, 10, 250 or 1,750 ppm for two generations	Lower food consumption and body weight gain and fibroadenoma in the mammary gland. No reproductive toxicity in all dose levels tested. Lower pup weight gain was observed.	Cook, 1990
Rats	Gavage	0, 16, 80 or 400 mg/kg/day gestation days 6-15	Maternal toxicity: lower food consumption and body weight gain and fibroadenoma in the mammary gland. Developmental toxicity: lower pup weight and developmental retardation of skeleton.	Dearlove, 1986a
Rabbits	Gavage	0, 2, 10 or 50 mg/kg/day gestation days 7-19	Maternal toxicity: lower food consumption and body weight gain. No developmental toxicity at all dose levels tested.	Dearlove, 1986b

B11-4.2.1.5 No Observed Adverse Effect Levels in Mammals

Table B11-7 Mammalian NOELs and LOELs from Oral Exposure to Diuron

Test Organism (Species)	Effect	Value (mg/kg/day)	Endpoint	Reference
Mice	NOEL	51/78 (M/F)	Increased leucocytes, blood ALT and bilirubin, haemosiderin accumulation in the liver, spleen and kidneys, urothelium hyperplasia, neoplasia in ovary and mammary.	Eiben *et al*, 1990
	LOEL	640/876 (M/F)		
Rats	NOEL	Not established	Haemolytic anaemia: reduced RBC, Hgb and Hct, and increased MCV, blood bilirubin and urea nitrogen.	Wandrag, 1996a
	LOEL	75		
Rats	NOEL	0.7/0.8 (M/F)	Reduced haemoglobin (females) and increased reticulocyte counts.	Schmidt *et al.*, 1986a
	LOEL	1.6/1.8 (M/F)		
Rats	NOEL	Not established	Changes in haematology, clinical chemistry, organ weights, and pathology of spleen, bone marrow, urothelium hyperplasia and neoplasia in the urinary bladder.	Schmidt, 1985
	LOEL	1.0/1.7 (M/F)		
Rats	NOEL	25 ppm	Urinary bladder hyperplasia and neoplasms.	Schmidt, 1986b
Rats	LOEL	1	Evidence of haemolytic anemia and compensatory haematopoiesis was observed	U.S. EPA, 2003
Rats	NOEL	1.0	Altered haematological parameters observed at 6 months.	U.S. EPA, 2003
	LOEL	10		

Table B11-7 Mammalian NOELs and LOELs from Oral Exposure to Diuron

Test Organism (Species)	Effect	Value (mg/kg/day)	Endpoint	Reference
Dogs	NOEL	1.25	Haemosiderin accumulation in the spleen and kidneys.	Hoffmann *et al*., 1985
	LOEL	7.5		
Dogs	NOEL	0.6	Haematological changes and blood pigments.	Hodge and Downs, 1964
	LOEL	3.1		

Table B11-8 Diuron Mammalian Reproductive and Developmental NOEL and LOEL Values from Oral Exposure to Diuron

Test Organism (Species)	Effect	Daily Value (mg/kg)	Endpoint	Reference
Rats	NOEL (M/F)	15/16	General Toxicity: Lower food consumption and body weight gain and fibroadenoma in the mammary gland.	Cook, 1990
	LOEL (M/F)	101/116		
	NOEL (M/F)	101/116	No reproduction toxicity in all dose levels tested.	
	LOEL (M/F)	-		
	NOEL (M/F)	15/16	Fetal/pup toxicity: lower pup weight.	
	LOEL (M/F)	101/116		
Rats	NOEL	16	Maternal toxicity: lower food consumption and body weight gain.	Dearlove, 1986a
	LOEL	80		
	NOEL	80	Developmental toxicity: lower pup weight and developmental retardation of skeleton.	
	LOEL	400		
Rabbits	NOEL	10	Maternal: Decreased body weight and food consumption.	Dearlove, 1986b
	LOEL	50		

B11-4.2.2 Dermal Exposure

B11-4.2.2.1 Death

Table B11-9 Mammalian Acute LD_{50} Values Resulting from Dermal Exposure to Diuron

Test Organism (Species/Sex)	LD_{50} (mg/kg)	Reference
Acute		
Unspecified	>2,000	U.S. EPA, 2003

B11-4.2.2.2 Systemic Effects

Table B11-10 Mammalian Systemic Effects Resulting from Dermal Exposure to Diuron

Test Organism (Species)	Dose (mg/kg/day) (Duration)	Response	Reference
Sub-acute			
Rats	0, 250, 500 or 1,000 mg/kg/day for 5 days per week, in a 13 week period	No deaths. Reduction in red blood cell count, haemoglobin and haematocrit, and an increased in MCV and MCH at all dose levels. Increased total serum bilirubin was also observed in all treated groups.	Wandrag, 1996b
Rabbit	0, 50, 500 or 1,200 mg/kg/day for 6h per day, 21 consecutive days	No deaths. Higher incidence of skin irritation observed at highest dose. No systemic effects observed	McKenzie, 1992
Rabbit	0, 50 or 250 mg/kg/day 6h per day for 21 consecutive days	No deaths. Slightly more severe and longer lasting skin reponses with no dose response relationship. No systemic changes observed.	Mihail and Schide, 1984
Sub-chronic			
Rats	1.0 mg/kg/day 6 months – life time[a]	Evidence of hemolytic anemia and compensatory hematopoiesis was observed	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997

[a] Absorption factor of 4% used for conversion from oral to dermal route.

B11-4.2.2.3 Neurological Effects

No data found.

B11-4.2.2.4 Reproductive/Developmental Effects

No data found.

B11-4.2.2.5 No Observed Adverse Effect Level

Table B11-11 Mammalian NOELs and LOELs for Dermal Exposure to Diuron

Test Organism (Species)	Effect	Value (mg/kg/day)	Endpoint	Reference
Subchronic				
Rats	LOEL	250	Altered haematology	Wandrag, 1996b
Rabbit	NOEL	250	Systemic effects	Mihail and Schide, 1984
Rabbit	NOEL	1,200	Systemic effects	McKenzie, 1992

B11-4.2.3 Inhalation Exposure

B11-4.2.3.1 Death

Table B11-12 Mammalian LC_{50} Value Resulting from Inhalation Exposure to Diuron

Test Organism (Species/Sex)	LC_{50}	Reference
Acute		
Unspecified	7.1 mg/L	U.S. EPA, 2003

B11-4.2.3.2 Systemic Effects

Table B11-13 Mammalian Systemic Effects Resulting from Inhalation Exposure to Diuron

Test Organism (Species)	Daily Dose (Duration)	Response	Reference
Sub-acute			
Rats	6.6, 48 or 311 mg/m^3 diuron aerosol for 6 hours per day, 5 days per week for 3 weeks	Males at 311 mg/m^3 had lower body weight gains. Rats at 48 and 311 mg/m^3 exhibited haemolytic anaemia including slight falls in erythrocyte count, increased in MCV and MCH with simultaneous reticulocytosis, as well as concentration- related Heinz body formation. Rats at 311 mg/m^3 showed slightly reduced plasma protein concentrations and lower T3 and T4 levels, accompanied by increased thyroxine binding capacity. Spleen weights were significantly higher at 311 mg/m^3 and appear to be dark, swollen and congested.	Pauluhn, 1986a
Rats	4.1, 37 or 268 mg/m^3 diuron aerosol for 6 hours per day, 5 days per week for 4 or 8 weeks	Dark and swollen spleen was observed at 37 and 268 mg/m^3, with correlated increase in spleen weight, and iron accumulation in the spleen. Slight haemolytic anaemia, and decreases in AST, ALT, and LDH activities at higher dosages.	Pauluhn, 1986b
Chronic			
Rats	10 mg/kg/day for 1 to 6 months	Altered hematological parameters observed at 6 months.	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997
Rats	1 mg/kg/day 6 month to life time exposure	Evidence of hemolytic anemia and compensatory hematopoiesis was observed	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997

B11-4.2.3.3 Neurological Effects

No data found.

B11-4.2.3.4 Reproductive/Developmental Effects

Table B11-14 Mammalian Reproductive and Developmental Effects Resulting from Inhalation Exposure to Diuron

Test Organism (Species)	Exposure	Dose (Duration)	Response	Reference
Rabbits	Incidental Oral	50 mg/kg/day for 1 to 30 days	Decreased maternal body weight and food consumption	Dearlove, 1986b

B11-4.2.3.5 No Observed Adverse Effect Level

Table B11-15 Mammalian NOELs and LOELs for Inhalation Exposure to Diuron

Test Organism (Species)	Effect	Value (mg/m^3)	Endpoint	Reference
Subchronic				
Rats	NOEL	4.1	Haemolytic anaemia	Pauluhn, 1986b
Rats	NOEL	6.6	Haemolytic anaemia	Pauluhn, 1986a

B11-4.3 Carcinogenicity

Diuron was classified as a "known/likely" human carcinogen by the U.S. EPA in 2003. They based this characterization on a few cases. These include, urinary bladder carcinomas observed in both sexes of the Wistar rats, kidney carcinomas in male rats, and mammary gland carcinomas in the female NMRI mice. U.S. EPA, hence developed a low dose linear extrapolation model with a linear low-dose (Q_1*) of 1.91×10^{-2} $(mg/kg/day)^{-1}$. This linear extrapolation model was based on the urinary bladder carcinomas of the rat, and will be applied to the animal data for the quantification of possible human risks. However, U.S. EPA conceded that there were no diuron uses that could result in chronic residential exposures. Furthermore, U.S. EPA, believed that based on their weight of evidence, diuron cancer risk is not of concern (U.S. EPA, 2003).

The APVMA in 2005 expressed a different classification for Diuron. Diuron was considered unlikely to be a genotoxic carcinogen. APVMA stated that the development of the urinary carcinomas in rats was dependent on long term administration of high doses of diuron (a mitogen) and a specific rat diet (Altromin 1321 diet) which will lead to an alkaline urinary pH. Since the two factors have little relevance to human exposure, APVMA concluded that at relevant human exposures to diuron, tumour induction in humans was unlikely.

Table B11-16 Animal Carcinogenicity Data

Test Subjects	Exposure	Dose	Response	Reference
Wistar Rats	Gavage	2,500 ppm for 24 month	Hyperplasia of urothelium. Higher incidence of urinary bladder transitional epithelial carcinomas, and occasional squamous cell carcinomas in both sexes. Pappillomas in male rats	Schmidt, 1985
Rats	Dietary	2,500 ppm for 2, 4, 12 and 26 weeks with recovery	Urothelial alterations. Increased thickness of the bladder wall. Changes were reversed during recovery periods	Schmidt, 1986b
Rats	Diet	600 mg/kg/day[a]	Urinary bladder carcinoma in both sexes of the Wistar rat	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997; Eiben, 1983; Hardesty *et al*., 1994.
Rats and mice	Diet	Not reported	kidney carcinomas in the male rat (a rare tumor), and mammary gland carcinomas in the female NMRI mouse	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997; Eiben, 1983; Hardesty *et al*., 1994.

[a] U.S. EPA's Q_1* of 1.91 x 10^{-2} $(mg/kg/day)^{-1}$ was based on this dose.

Diuron was not mutagenic in bacteria or in mammalian cell cultures. Furthermore, there were no indications of DNA damage in primary rat hepatocytes, or aberrations in bone marrows of Sprague Dawley rats when diuron was assessed (U.S. EPA, 2003). Since diuron is not DNA reactive, and proliferative histological bladder tissue response to diuron only occurs when exposure is continuous. Diuron is classified as a mitogen and adheres to a mitogenic mode of action where tumour reversibility is dependent on its withdrawal. Hence, hyperplasia induced by diuron on the urothelium is caused by a direct mitogenic effect of it or its metabolite in a chronic local stimulation with an alkaline urine environment (APVMA, 2005).

Based on the evaluation of diuron by the U.S. EPA (2003), APVMA (2005) and Health Canada (2004), diuron was considered to be a non-carcinogen for the purposes of this risk assessment. The U.S. EPA (2003) derived an oral slope factor of $1.91x19^{-2}$ $(mg/kg/day)^{-1}$; however, based on their weight of evidence the U.S. EPA stated that diuron cancer risk was not of concern. Similarly, APVMA (2005) determined that at relevant human exposures to diuron tumour induction was unlikely. In addition, Health Canada (2004) does not provide carcinogenic toxicological reference values for diuron. Therefore, diuron will be evaluated as a non-carcinogen for this risk assessment.

B11-4.4 Populations at Special Risk

No data found.

B11-4.5 Toxicokinetics

Diuron is absorbed rapidly from the gastrointestinal and respiratory systems in rats. At low doses, diuron will be metabolized within 24 hours and within 48 hours post-dose period at higher

dose levels. The urine is the major route of excretion. Small amounts of diuron administered orally to rats is also detected in the feces. The highest tissue concentrations of diruon were found in the liver and kidneys 4 days post diuron use in a rat metabolism study. The metabolism of diuron involved N-oxidation, ring hydroxylation, demethylation, dechlorination. Furthermore, diuron will also conjugate to sulfate and glucuronic acid for excretion (U.S. EPA, 2003). In humans, diuron is metabolized rapidly *via* hydroxylation and N-dealkylation, and then excreted *via* urine (Hayes, 1982). The main metabolites of diuron are 3-(3,4-dichlorophenyl)-1methyl urea, 3-(3,4-dichlorophenyl) urea, as well as 3,4-dichloraniline (APVMA, 2005)

Dermal absorption

The U.S. EPA (2002) used a dermal absorption value of 4%, from submitted studies, for risk assessment purposes. This upper-bound estimation of 4% was extrapolated using the maternal LOAEL of 50 mg/kg/day from an oral developmental toxicity study in the rabbit as well as the NOAEL of 1,200 mg/kg/day from a 21 day dermal toxicity study in the rabbit. The ratio of these two values is 4% or 50/1,200 (U.S. EPA, 2002).

B11-4-6 Diuron Exposure Limits

Table B11-17 Existing RfD Values for Diuron Exposures

Reference Dose (mg/kg/day)	Route of Exposure	Reference	Endpoint	Study	Reference	NOAEL (mg/kg/day)	Uncertainty Factor
Acute/Short-term							
0.007	Oral	APVMA, 2005	Haemolysis: Reduced haemoglobin (females) and increased reticulocyte counts	6-month rat dietary study	Schmidt *et al*., 1986a	0.7	100
0.16	Oral	U.S. EPA, 1999	Decreased body weight and food consumption	Developmental Dietary study in the rat	--	16.0	100
Not Established	Oral	U.S. EPA, 2003	No adverse effects attributed to a single exposure to diuron were identified in any available studies. Therefore, no acute dietary risk assessment was warranted.	Oral studies unspecified	--	--	--
Intermediate-term							
No Information Found							
Chronic							
0.002	Oral	U.S. EPA, 1988	Abnormal pigments in blood	2 Year Dog Feeding Study	E.I. du Pont de Nemours and Company, 1964	0.625	300
0.003	Oral	U.S. EPA, 1999	Decreased erythrocyte count (F); increased hemosiderin in the spleen, spleen weight, bone marrow activation and hematopoietic marrow (M); decreased fat marrow (M); thickened urinary bladder wall (M)	2 year chronic feeding / carcinogenicity study in the rat	--	1.02[a]	300

Table B11-17 Existing RfD Values for Diuron Exposures

Reference Dose (mg/kg/day)	Route of Exposure	Reference	Endpoint	Study	Reference	NOAEL (mg/kg/day)	Uncertainty Factor
0.003	Oral	U.S EPA, 2003	Evidence of hemolytic anemia and compensatory hematopoiesis was observed	Combined chronic toxicity/carcinogenicity study in rats	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997	1.0 [a]	Interspecies: 10x Intraspecies: 10x FQPA: 1x Use of LOAEL instead of a NOAEL: 3x
0.006	Oral	APMVA, 2005	Haemological changes and blood pigments	2 year dog dietary study	Hodge and Downs, 1964	0.6	100
0.0156	Oral	Health Canada, 1987; 2004	Decreased body weight; increased liver weight; erythroid hyperplasia; decreased haematological values	2 year dog study	Hodge *et al*., 1967	3.125	200

[a] Chronic RfD based on a LOAEL.
(F) Effects observed in females only.
(M) Effects observed in males only.

Table B11-18 Summary of the Toxicological Dose and Endpoints for Diuron used in Human Risk Assessment by the U.S. EPA (2003)

Exposure Scenario	Reference Dose	Endpoint	Study	NOEL (mg/kg/day)	LOEL (mg/kg/day)	LOC for MOE	Reference
Oral Short-term incidental (1-30 days)	0.1	Decreased body weight and food consumption	Developmental toxicity study in rabbits	10	50	100	Dearglove, 1986b
Oral Intermediate-term incidental (1-6 months)	0.01	Altered hematological parameters observed at 6 months	Chronic/toxicity carcinogenicity in rats	1.0	10	100	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997

Table B11-18 Summary of the Toxicological Dose and Endpoints for Diuron used in Human Risk Assessment by the U.S. EPA (2003)

Exposure Scenario	Reference Dose	Endpoint	Study	NOEL (mg/kg/day)	LOEL (mg/kg/day)	LOC for MOE	Reference
Dermal Short- and Intermediate term (1-d to 6 months)	Not required	No systemic toxicity following repeated dermal dosing at 1,200 mg/kg/day was seen in the dermal toxicity study. Also, there is no developmental concern. No hazard was identified and no quantitative assessment is required.					
Dermal Long-term (>6 months)	0.003	Evidence of hemolytic anemia and compensatory hematopoiesis was observed	Combined chronic toxicity and carcinogenicity study in rats	-- (Dermal absorption rate = 4%)	1.0	300	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997
Inhalation Short-term (1-30 days)	0.03	Decreased body weight and food consumption	Developmental toxicity study in rabbits	10 (inhalation absorption rate = 100%)	50	300	Dearglove, 1986b
Inhalation Intermediate-term (1-6 months)	0.01	Altered hematological parameters observed at 6 months	Chronic/toxicity Carcinogenicity in rats	1.0 (inhalation absorption rate = 100%)	10	100	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997
Inhalation Long-term (>6 months)	0.003	Evidence of hemolytic anemia and compensatory hematopoiesis was observed	Combined chronic toxicity and carcinogenicity study in rats	-- (inhalation absorption rate = 100%)	1.0	300	Schmidt, 1985; Rossberg and Wirnitzer, 1995; Rossberg, 1995; Malek, 1997

Based on the general population (Table B11-17) and occupational (Table B11-18) reference doses, as well as available slope factors (Section B11-4.3), the following exposure limits were selected for the risk assessment purposes of this report (Table B11-19).

Table B11-19 Summary of Selected TRVs for Diuron

COC	TRV Type	Route	TRV value (mg/kg/day)	Major Health Effects	Route of Exposure in Primary Study	Reference
Diuron	Acute/Short-term RfD (1- 30 days)	Oral	0.1	Decreased body weight and food consumption	Oral	U.S. EPA, 2003
		Dermal	Not required	No systemic toxicity following repeated dermal dosing at 1,200 mg/kg/day was seen in the dermal toxicity study. Also, there is no developmental concern. No hazard was identified and no quantitative assessment is required.		U.S. EPA, 2003
		Inhalation	0.1	Decreased body weights and food consumption	Oral	U.S. EPA, 2002
	Intermediate-term RfD (1- 6 months)	Oral	0.01	Altered hematological parameters observed at six months.	Oral	U.S. EPA, 2003
		Dermal	Not required	No systemic toxicity following repeated dermal dosing at 1,200 mg/kg/day was seen in the dermal toxicity study. Also, there is no developmental concern. No hazard was identified and no quantitative assessment is required.		U.S. EPA, 2003
	Long-term RfD (>6 months)	Inhalation	0.01	Altered hematological parameters observed at 6 months.	Oral	U.S. EPA, 2003
		Oral	0.003	Evidence of hemolytic anemia and compensatory hematopoiesis was observed	Oral	U.S. EPA, 2003
		Dermal	0.003	Evidence of hemolytic anemia and compensatory hematopoiesis was observed	Oral	U.S. EPA, 2003
		Inhalation				

B11-5.0 ENVIRONMENTAL FATE AND EXPOSURE

B11-5.1 Air

Diuron is relatively non volatile. This is indicated by its low vapor pressure of 6.90 $x10^{-8}$ mm Hg (JW, 2006) Diuron also has a low Henry's Lawconstant of 5.10 x 10^{-10} atm m^3/mol (JW, 2006). This indicates that it have little tendency to escape from an aqueous solution. Hence, diuron is not expected to be found in air, except in potential spray drift.

Table B11-20 Half-life of Diuron in Air

Conditions	Half-life	Reference
Mean half-life	1	Mackay *et al*., 1997
Range half-life	10-30 hours	Mackay *et al*., 1997

B11-5.2 Water

Diuron's has a low soil adsorption coefficient which indicates that it will have relatively low tendency to adsorb to sediments, in water. Diuron's hydrolysis and aqueous photolysis half-lives are long. As a result, diuron tends to be both mobile and persistent, and will therefore be prone to off-site movement in surface runoff, and migration to groundwater. In aquatic environments, microorganisms serve as the primary means for the degradation of diuron (Moncada, 2004).

Table B11-21 Half-life of Diuron in Water

Conditions	Half-life	Reference
Photolysis	43 days	JW, 2006
Mean half-life	3 weeks	Mackay *et al*., 1997
Range half-life	300-1,000 hours	Mackay *et al*., 1997

B11-5.3 Sediment and Soil

Diuron can be moderate to highly persistent as indicated by its half lives in various soil types. Microbial degradation serves as its primary mean of dissipation from soil. Small amounts of diuron can also undergo photodegradation. Diuron is mobile in soils, as it has a low adsorption coefficient. Its sorption ability is highly correlated with the organic matter. Hence, leaching of diuron will be greatest in soils with low organic matter, and soils with high water permeability. Course soils are especially prone of leaching diuron. As a result of diuron's long half lives and mobility, there is a high possibility that it would be detected in groundwater supplies.

Under aerobic soil conditions, diuron will degrade *via* N-demethylation. Some of these degradation metabolites include N-(3,4-dichlorophenyl)-N-methylurea; 3,4-dichlorophenylurea; and dichloroaniline. Under anaerobic soil conditions, diuron will degrade to N-(3-chlorophenyl)-N-methylurea through dechlorination (Moncada, 2004).

Table B11-22 Half-life of Diuron in Soil

Conditions	Half-life	Reference
Photolysis	172 days	JW, 2005
--	1-12 months	JW, 2005
Aerobic soil studies	372 days	JW, 2005
Anaerobic soil studies	1000 days	JW, 2005
Sand	73 days	U.S. EPA, 2003
Silt loam	139 days	U.S. EPA, 2003
Silty clay loam	133 days	U.S. EPA, 2003
Mean half-life	2 months	Mackay *et al*., 1997
Range half-life	1,000-,3000 hours	Mackay *et al*., 1997

B11-5.4 Other Environmental Media

The maximum acceptable concentration (MAC) for diuron in drinking water established by Health Canada is 150 µg/L (Health Canada, 1987).

B11-5.5 Plant Residues and Metabolism

Once Diuron is applied, it can be easily taken up from the soil by the root system of plants. Once diuron has crossed the root into the xylem, it will rapidly translocate into stems and leaves by the transpiration system. Diuron was found to bind to the Q-enzyme B binding pocket on D1 protein of the photosystem II complex in chloroplast thylakoid membranes (Hess and Warren, 2002) . This means that diuron will block electron transport from Q-enzyme A to Q-enzyme B, preventing CO_2 fixation and the production of ATP and other high enevergy compounds. The inability to reoxidize Q-enzyme A will promote formation of the triplet state of chlorophyll, which will interact with O_2 to form reactive oxygen species (ROS). ROS will then react with hydrogen from unsaturated lipids, producing lipid radicals (Hess and Warren, 2002). The lipid radicals formed will initiate a chain reaction of lipid peroxidation reactions. Most of lipids and proteins in the plant are attacked and oxidized, resulting in a net loss of chrlorophyll and caroteniods. This will compromise photosynthesis. Furthermore, lipid peroxidation chain reactions will also cause leaky membranes which will induce organelles to dry and disintegrate rapidly (Hess and Warren, 2002).

B11-6.0 SUMMARY

Diuron can be used to control a wide variety of annual and perennial broadleaf weeds on both agricultural and non-agricultural lands (EXTOXNET, 1993). While diuron is a systemic substituted phenyl-urea class of herbicide, it functions by inhibiting the Hill reactions of photosynthesis, thereby limiting the production of high-energy compounds such as the ATP (Moncada, 2004). Between 1994 and 2004 approximately 3,900 kg of diuron was applied over an area of 440 ha at CFB Gagetown (JW, 2006).

Diuron has low acute toxicity. Chronic studies in rodents have shown increased incidences of urinary bladder carcinomas in both sexes, kidney carcinomas in males, and mammary gland carcinomas in the females. The U.S. EPA (2003), classified diuron as a known/likely human carcinogen, and developed a Q_1* value of 1.91×10^{-2} $(mg/kg/day)^{-1}$. Furthermore, the U.S. EPA (2003) estimated that the cancer risks from diuron-contaminated drinking water exceeded that of

the dietary cancer risk. However, the U.S. EPA conceded that no uses could possibly result in chronic residential diuron exposures. Hence, the U.S. EPA (2003) stated that the cancer risks of diuron were not of concern (U.S. EPA, 2003).

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