B-10-1.0 GLYPHOSATE

B10-1.1 Background Information

IUPAC name: N-(phosphonomethyl) glycine

CAS name: N-(phosphonomethyl) glycine

CASRN: 1071-83-6; 38641-94-0 [as isopropylamine salt]; 70901-12- [as potassium salt]

GLYPHOSATE USAGE:

Glyphosate is a wide-spectrum, nonselective systemic herbicide used for the control of annual and perennial plants including grasses, sedges, broad-leaved weeds, and woody plants. It can be used on non-cropland as well as on a great variety of crops (EXTOXNET, 1996).

Glyphosate was the active ingredient of several herbicide products that was applied at the CFB Gagetown. These include, Vision® which was applied in 1989. Herbicide product Roundup® was applied in years 1989; 1990; 1991, and 1996. Roundup® Transorb was applied in years 2001 to 2004. Furthermore glyphosate was also an active ingredient in the herbicide product Roundup Weathermax® Transorb 2 which was applied in 2004.

Glyphosate was used at CFB Gagetown between 1989 and 2004 (JW, 2006).

Table B10-1 Glyphosate Usage at CFB Gagetown[a]

Year	Amount of Glyphosate Applied (kg)	Area Treated (ha)
1989	No information	No information
1990	3,133	1,800
1991	4,514	314
1996	867	405
2001	1,323	613
2002	1,184	548
2003	1,277	608
2004	1,061	361
Total	**1.3E+04**	**4.7E+03**

[a] Adapted from JW, 2006.

B-10-2.0 CHEMICAL AND PHYSICAL PROPERTIES

Formula: $C_3H_8NO_5P$

Activity: Glyphosate is an herbicide. It inhibits the shikimic acid pathway in plants and some micro-organisms. This will cause a deficit in aromatic amino acid production. The shikimic pathway is absent from animals and may account for glyphosate's low toxicity in mammals. However, glyphosate causes acute effects in animals at very high doses following intraperitoneal administration. This shows

that at high doses, glyphosate may alter mitochondrial activity and lead to the uncoupling of oxidative phosphorylation (WHO, 1996).

Notes: Glyphosate is inherently an acid, but it is usually used in a salt form, most commonly the isopropylamine salt. The information presented in this toxicological profile refers to the technical grade of the acid form of glyphosate, unless otherwise noted. Glyphosate, present as the mono (isopropylammonium) salt is the active ingredient in the pesticides Roundup®, Roundup® Weathermax With Transorb 2 Technology, Vision, Roundup® Transorb.

Structure:

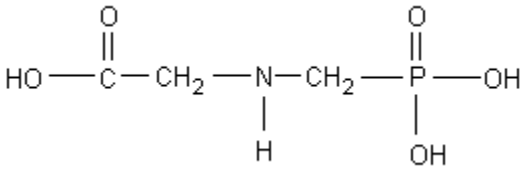

Figure B10-1 Glyphosate CASRN 1071-83-6 Structure

Table B10-2 Chemical and Physical Properties of Glyphosate

Chemical/Physical Property	Result	Reference
Colour/Form	colourless, crystalline solid	Tomlin, 1994
Dissociation Constant (pKa)	5.70	Worthing, 1991
Henry's Law constant (25ºC)	1.41 x 10^{-5}	Montgomery, 1993
	1.82 x 10^{-17}	JW, 2006
Octanol/Water Partition Coefficient, Log K_{ow}	-2.77	JW, 2006
	-1.6 to -3.25	Reinert *et al*., 1987; Worthing, 1991; Montgomery, 1993
Melting Point (ºC)	200 to 230	Worthing, 1991; Tomlin, 1994; Montgomery, 1993; Milne, 1995
Molecular Weight (g/mol)	169.1	Mackay *et al*., 1997
-mono (isopropylammonium) salt	228.18	JW, 2006
Odour	Odourless	Tomlin, 1994.
Vapour Pressure	6.06 10^{-11}mm Hg	JW, 2006
	4.00 x 10^{-5} to 0.001 Pa	Worthing, 1991; Montgomery, 1993
Water Solubility (25ºC) (mg/L)	10,000 to 12,000	Spencer 1973; 1981; Martin and Worthing, 1977; Kenaga, 1980; Worthing 1987; 1991; Montgomery, 1993
	12,000	JW, 2006

B10-3.0 PMRA EVALUATION

Agriculture Canada has granted temporary registration for the preharvest application, by ground equipment, of glyphosate on wheat, barley, soybeans, peas, lentils, canola and flax.

From 1992 to the present time, Health Canada has approved a variety of roundup ® ready crops for agricultural uses in Canada. These include: Glyphosate tolerant Sugarbeet, H7-1; Glyphosate tolerant alfalfa, J101 and J163; Glyphosate tolerant corns GA21, MON 802 and MON832;

Glyphosate tolerant canola GT73 andGT2; Glyphosate tolerant soybeans, GTS 40-3-2 (Health Canada, 2006).

B10-4.0 TOXICOLOGICAL SUMMARY

B10-4.1 Human Health Effects

Table B10-3 Reported Human Health Effects Associated With Acute Exposure to Glyphosate[a,b]

Exposure	Effects	Response
Acute	**Cardiovascular**	Shock occurs in most severe cases. Dysrhythmias including ventricular dysrhythmias, bradycardia, and cardiac arrest have been reported.
	Respiratory	Life-threatening effects include pulmonary edema and aspiration pneumonitis. Irritation occurs.
	Neurologic	Mental status changes may be seen late in the course of glyphosate poisoning.
	Gastrointestinal	Nausea and vomiting; erythema of mucous membranes; epigastric pain. Hemorrhage; paralytic ileus; prolonged dehydrating diarrhea; necrosis and, hemorrhage of mucous membranes.
	Hepatic	Elevated liver enzymes may be seen following toxic exposures to glyphosate.
	Genitourniary	Oliguria and anuria are primary toxic effects of severe glyphosate poisonings.
	Fluid-Electrolyte	Hyperkalemia may be present following toxic exposures to glyphosate.
	Hematologic	Leukocytosis may be seen following severe glyphosate ingestions.
	Dermatologic	Commercial glyphosate formulations have caused erythema, piloerection, and contact dermatitis. Chemical burns resulting in necrotic epidermis and eroded lesions occurred in one elderly adult.

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

B10-4.2 Health Effects by Route of Exposure

Health effects were derived from animal studies. Most values displayed in this section are adapted from U.S. EPA (1993), Reregistration Eligibility Decision (RED) document, and other values were selected from more recent studies that were not included in the RED document.

B10-4.2.1 Oral Exposure

B10-4.2.1.1 Death

Table B10-4 Mammalian LD_{50} Values Resulting from Oral Exposure to Glyphosate

Test Organism (Species/Sex)	LD_{50} (mg/kg)	Reference
Acute		
Mice	10,000	Monsanto, 1985
Rat	>4,320	Birch, 1970
Rabbit	10,000	Monsanto, 1985
Goats	10,000	Monsanto, 1985

B10-4.2.1.2 Systemic Effects

Table B10-5 Systemic Effects Resulting from Oral Exposure to Glyphosate

Test Organism (Species)	Daily Dose (Duration)	Response	Reference
Sub-chronic			
CD-1 mice	0, 250, 500, or 2,500 mg/kg/day for 90 days	Reduced body weight gains by 24% and 18% in high dose male and females respectively.	Street *et al*., 1980
B6CF1 mice (M/F)	0, 3,125, 12,500, 25,000, 50,000 ppm	Decreased body weight gains at 25,000 ppm and 50,000 ppm. Alteration of parotid salivary glands was noted microscopically at doses above 6,250 ppm dose level.	NTP, 1992
Sprague-Dawley rats (M)	0,63,317,1,267 mg/kg/day for 90 days	Increased serum phosphorus and potassium Increased serum glucose in the mid-dose and high-dose malesIncreased blood urea nitrogen and serum alkaline phosphatase in the high-dose males. Occurrence of pancreatic lesions in the high-dose males.	Stout *et al*., 1987; Lankas *et al*., 1981
Sprague-Dawley rats (F)	0, 54, 404, 1,623 mg/kg/day for 90 days	Increased serum phosphorus and potassium	
F344 rats (M/F)	0, 3,125, 6,250, 12,500, 25,000, 5,0000 ppm for 13 weeks	Mean body weight gains reduced in males at high doses, only marginal effects observed in females. Alterations in the parotid, and submandibular glands were noted.	NTP, 1992
Chronic			
Sprague-Dawley rats (M)	0, 3, 10, 31 mg/kg/day for 26 months	No effects	Lankas *et al*., 1981
Sprague-Dawley rats (F)	0, 3, 11, 34 mg/kg/day for 26 months	No effects	
Sprague-Dawley rats (M)	0, 89,362, 940 mg/kg/day for 2 years	Increased incidence of cataracts and lens abnormalities Decreased urine pH, Increased absolute liver weight and increase liver weight/brain weight ratio	Stout *et al*., 1990
Sprague-Dawley rats (F)	0, 113, 457, 1,183 mg/kg/day for 2 years	Decreased body weight gains.	
Beagle dogs (M/F)	0, 20, 100, 500 mg/kg/day for 1 year	No effects	Reyna, 1985

B10-4.2.1.3 Neurological Effects

No data found.

B10-4.2.1.4 Reproductive/Developmental Effects

Table B10-6 Reproductive and Developmental Effects Resulting from Oral Exposure to Glyphosate

Test Organism (Species)	Exposure	Dose (Duration)	Response	Reference
Developmental Effects				
Pregnant Charles River COBS CD rats	Gavage	0,300,1,000, or 3,500 mg/kg/day from gestation days 6 through 19	Maternal effects: Diarrhea; Decreased mean body weight gain; Breathing rattles; Inactivity; Red matter around the nose and mouth, forelimbs, dorsal head; Decreases in total implantations; inviable fetuses; and, Death	Rodwell *et al*., 1980
			Fetal effects: At high doses: Increased number of litters and fetuses with unossified sternebrae; and, Decreased mean fetal body weights.	
Pregnant Dutch Belted rabbits	Gavage	0, 75, 175, 350 mg/kg/day from gestation days 6 through 27	Maternal effects: Diarrhea; Nasal discharge; and, Death.	Rodwell *et al*., 1980
			Fetal effects: no developmental effects were observed.	
Reproductive Effects				
F344 rats (M/F)	Diet	25000, 50000 ppm for 13 weeks	Reduced epididymal sperm concentrations. An increase in estrous cycle length from 4.9 to 5.4 days.	NTP, 1992
Sprague-Dawley rats (M/F)	Diet	0, 3, 10, 30 mg/kg/day for three successive generations	Fetal effects: Increased incidence of focal tubular dilation of the kidney, both unilateral and bilateral combined in the high-dose male F_{3b} pups.	Reyna, 1990
Sprague-Dawley rats (M/F)	Diet	0, 100, 500, 1500 mg/kg/day for two successive generations	Soft stools, very frequent, in the F_0 and F_1 generations; Decreased food consumption and body weight gain of the F_0 and F_1 generations during growth/pre-mating period; Decreased body weight gain of the F_1 and F_2 generations during the second and third weeks of lactation.	Street, 1982

B10-4.2.1.5 No Observable Effect Levels

Table B10-7 NOAELs and LOAELs from Oral Exposure to Glyphosate[a]

Test Organism (Species)	Effect	Value	Endpoint	Reference
Sub-chronic				
CD-1 mice	NOEL	500 mg/kg/day	Systemic effects	Street *et al*., 1980
	LOEL	2,500 mg/kg/day	Systemic effects	
B6CF1 mice (M/F)	NOAEL	2,490 mg/kg/day	Suppression of weight gains	NTP, 1992
Sprague-Dawley rats (M/F)	NOEL	<1,000 ppm[a]	Systemic effects	Stout *et a*l., 1987; Lankas *et al*., 1981
F344 rats (M/F)	NOAEL	209 mg/kg/day	Change in serum enzymes	NTP, 1992
Chronic				
Sprague-Dawley rats (M)	NOEL	31 mg/kg/day	Systemic effects	Lankas *et al*., 1981
Sprague-Dawley rats (F)	NOEL	34 mg/kg/day	Systemic effects	
Sprague-Dawley rats (M)	NOEL	362 mg/kg/day	Systemic effects	Stout *et al*., 1990
	LOEL	940 mg/kg/day	Systemic effects	
Sprague-Dawley rats (F)	NOEL	457 mg/kg/day	Systemic effects	
	LOEL	1183 mg/kg/day	Systemic effects	
Rats	NOAEL	100 mg/kg/day	Systemic effects	WHO, 2004
	LOAEL	300 mg/kg/day		
	NOAEL	1214 mg/kg/day	Carcinogenesis	
Beagle dogs (M/F)	NOEL	≥ 500 mg/kg/day	Systemic effects	Reyna, 1985

[a] Not determined definitively.

Table B10-8 Glyphosate Reproductive and Developmental NOEL and LOEL Values

Test Organism (Species)	Effect	Dose (mg/kg/day)	Endpoint	Reference
Developmental Effects				
Pregnant Charles River COBS CD rats	NOEL Maternal:	1,000	Maternal effects	Rodwell *et al*., 1980a
	NOEL Fetal:	1,000	Developmental effects	
	LOEL Maternal:	3,500	Maternal effects	
	LOEL Fetal:	3,500	Developmental effects	
Pregnant Dutch Belted rabbits	NOEL Maternal:	175	Maternal effects	Rodwell *et al*., 1980b
	NOEL Fetal:	≥175	Developmental effects	
	LOEL Maternal:	350	Maternal effects	

Table B10-8 Glyphosate Reproductive and Developmental NOEL and LOEL Values

Test Organism (Species)	Effect	Dose (mg/kg/day)	Endpoint	Reference
Reproductive Effects				
Sprague-Dawley rats (M/F)	NOEL	≥ 30	Systemic effects	Reyna, 1990
	NOEL	≥ 30	Reproductive effects	
	NOEL	10	Developmental effects	
	LOEL	10	Developmental effects	
Sprague-Dawley rats (M/F)	NOEL	500	Systemic effects	Street, 1982
	LOEL	1,500	Systemic effects	
	NOEL	500	Developmental effects	
	LOEL	1,500	Developmental effects	

B10-4.2.2 Dermal Exposure

B10-4.2.2.1 Death

Table B10-9 Mammalian acute LD_{50} Value Resulting from Dermal Exposure to Glyphosate

Test Organism (Species/Sex)	LD_{50} (mg/kg)	Reference
Acute		
Rabbit	> 2,000	Birch., 1970

B10-4.2.2.2 Systemic Effects

No data found. The U.S. EPA (1993) stated that a dermal penetration study with technical grade glyphosate is not required because there are no toxicological endpoints to indicate the study will be necessary.

B10-4.2.2.3 Neurological Effects

No data found.

B10-4.2.2.4 Reproductive/Developmental Effects

No data found.

B10-4.2.2.5 No Observed Adverse Effect Level

No data found.

B10-4.2.3 Inhalation Exposure

U.S. EPA (1993) waived acute inhalation study due to the fact that glyphosate technical grade is not a volatile solid and adequate inhalation studies were conducted on the end-use product formulations.

B10-4.2.3.1 Death

No data found.

B10-4.2.3.2 Systemic Effects

No data found.

B10-4.2.3.3 Neurological Effects

No data found.

B10-4.2.3.4 Reproductive/Developmental Effects

No data found.

B10-4.2.3.5 No Observed Adverse Effect Level

No data found.

B10-4.3 Carcinogenicity

The weights of evidence for carcinogenic hazard potential are usually expressed by the U.S. EPA using summary rankings from human and animal cancer studies. The summary rankings place the overall evidence in classification groups from A to E, where group A is associated with the greatest risk of human carcinogenicity, and group E is associated with evidence of non-carcinogenicity in humans (Williams *et al.*, 2000). U.S. EPA (1993) classified glyphosate in group E, depicting it as having evidence of a non-carcinogen for humans on June 26, 1991. This classification was based on adequate studies in rats and mice.

In 2000, a peer-reviewed assessment of glyphosate studies by Williams *et al*., 2000 stated that multiple lifetime feeding studies have failed to demonstrate any tumorigenic potential for glyphosate. Hence, they reached a conclusion that glyphosate is noncarcinogenic (Williams *et al.*, 2000).
WHO (2004), reported on pesticide residues in food, stated that long-term studies of toxicity and carcinogenicity in mice and rats conveyed no toxic effects at up to a high dose of 1,000 mg/kg/day. Hence, they concluded there is no evidence of glyphosate causing carcinogenicity (WHO, 2004).

Table B10-10 Animal Carcinogenicity Data for Glyphosate

Test Subjects	Exposure	Dose (mg/kg/day)	Response	Reference
CD-1 mice	Diet	0, 150, 750, 4,500	Increased incidence of hepatocellular hypertrophy, hepatocellular necrosis and interstitial nephritis in males Increased incidence of proximal tubule epithelial basophilia and hypertrophy in females. Slight increase of renal tubular adenomas[a]	McConnel, 1985

Table B10-10 Animal Carcinogenicity Data for Glyphosate

Test Subjects		Exposure	Dose (mg/kg/day)	Response	Reference
Sprague-Dawley rats	M	Diet	0, 3, 10, 31	Increased incidence of interstitial cell (leydig cell) testicular tumors.[a]	Lankas *et al*., 1981
	F	Diet	0, 3, 11, 34	Increased incidence of thyroid C-cell carcinomas[a]	
Sprague-Dawley rats	M	Diet	0, 89, 362, 940	Slight increase in:- the incidence of pancreatic islet cells adenomas[a] - thyroid C-cells adenomas[a]	Stout *et al*., 1990
	F	Diet	0,113,457, 1,183	Slight increase in: - thyroid C-cells adenomas[a]	

[a] U.S. EPA, concluded that these neoplasms were not related to glyphosate treatment, results were not statistically significant.

The U.S. EPA (1993) indicated that glyphosate has been tested for mutagenicity and genotoxicity in bacteria, rats, and mammalian cell cultures with negative results. Gene mutation assays using Ames Test was conducted with glyphosate, both in the presence and without metabolic activation. The strains of Salmonella typhimurium used were TA98, TA100, TA1535 and TA1537. The investigators observed no increases in reverse mutations at any concentration (Kier *et al*., 1978).

Gene mutation assays in mammalian cells was conducted with glyphosate using the Chinese hamster ovary (CHO) cells/hypoxanthine - guanine -phosphoribosyl transferase (HGPRT) assay, in the presence and without metabolic activation. The investigators observed no mutagenic response either with or without metabolic activation up to the limit of cytotoxicity (10 mg/Ml) (Li *et al*., 1983).

Structural Chromosomal Aberration Assays were conducted only using a single dose of glyphosate administered intraperitoneally (i.p.) to male and female Sprague-Dawley rats. The dose used by the investigators was 1 g/kg of body weight. The bone marrow cells were examined for clastogenic (chromosome-damaging) effect. The investigators observed no significant clastogenic effects (Li *et al*., 1983).

Glyphosate was also tested in two assays: the rec-assay using B. subtilis H17 (rec+) and M45 (rec-); and the reverse mutation assays using E. coli WP2 hcr and Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538, in the presence and without metabolic activation. The investigators observed no increases in mutation rates in either study. (Shirasu *et al.*, 1978).

A summary of results from more recent genotoxicity studies of glyphosate, Roundup ®, and other glyphosate formulations can be found in Williams *et al.*, 2000.

B10-4.4 Populations at Special Risk

No data found.

B10-4.5 Toxicokinetics

B10-4.5.1 Absorption

Studies have shown that glyphosate is incompletely absorbed *via* the oral route (Williams *et al*., 2000). From the administration of a single dose of glyphosate at 10 mg/kg, it was found that approximately 30 to 36% (males and females, respectively) of the dose was absorbed (Williams *et al*., 2000). NTP conducted a study in 1992, which showed similar results. NTP investigators found that 30% of the administered 5.6 mg/kg dose of glyphosate was absorbed (NTP, 1992).

Furthermore, absorption showed inverse relation to dose. At relatively high dosage of 1,000 mg/kg, the absorption appeared to be lower (approximately 19 to 23%) based on the percentage of material excreted in urine at 10 and 1,000 mg/kg/day (NTP, 1992). In the 14 day repeated dose study conducted at dietary concentrations up to 100 ppm, it was estimated that 15% of the administered material was absorbed (Williams *et al*., 2000).

Dermal Absorption

The U.S. EPA (1993) stated that glyphosate is poorly absorbed dermally; however, a specific dermal absorption factor was not provided.

The dermal penetration of glyphosate is very low based on the results of studies in rhesus monkeys and *in vitro* studies with human skin samples. When undiluted Roundup herbicide was applied to the skin of monkeys during an *in vivo* dermal absorption study, slow penetration was observed (0.4 and 1.8% absorbed over 24 hour and 7 days, respectively) (Maibach, 1983). In a second study in rhesus monkeys, dermal absorption of diluted glyphosate (1:29) used to simulate a spray solution was found to be 0.8 and 2.2% at the low and high dose (500 or 5,400 mg/cm^2, respectively) (Wester *et al*., 1991). Wester *et al*. (1991) also reported that the *in vitro* perctutaneous absorption of glyphosate through human skin was no more than 2% when applied for up to 16 hour either as concentrated Roundup or as a diluted spray solution. In another *in vitro* study when glyphosate was applied as formulated Roundup, a spray dilution of Roundup, or another concentrated glyphosate formulation, dermal penetration rates ranged from 0.028 to 0.152% for the three materials tested (Franz, 1983).

B10-4.5.2 Distribution

Maximum concentrations in the small intestine and blood were observed 2 hours after oral glyphosate administration, while peak levels in other organs occurred 6.3 hours after dosing (Williams *et al*., 2000). Glyphosate was shown to distribute to small intestine, colon, kidney, and bone *via* radioactive labeling (Williams *et al*., 2000). However, the tissue retention times of glyphosate were relatively short, and the vast majority of the body burden was unmetabolized parent glyphosate (Williams *et al*., 2000).

In an acute feeding study, where glyphosate was fed to Wistar rats in the diet for 14 days, steady-state tissue levels of glyphosate were reached within approximately 6 days of dosing (Colvin *et al*., 1973). The highest glyphosate concentration was found in the kidneys (0.85 mg/kg tissue dry wt at the 100 ppm dosage level) followed in decreasing magnitude by spleen, fat, and liver (Colvin *et al*., 1973). Tissue residues declined markedly after dosing was terminated. Ten days

after dosing was discontinued, tissue levels ranged from only 0.067 to 0.12 mg/kg at the highest dosage tested (Colvin *et al*., 1973).

B10-4.5.3 Metabolism

Orally administered glyphosate is poorly biotransformed in animals. It was shown to be rapidly excreted unchanged in the urine and feces of rats (Williams *et al*., 2000). Metabolite analysis showed that a minor negligible metabolite, aminomethylphosphonic acid (AMPA) was present in the gut content and colon tissue of a few animals (Williams *et al*., 2000).

B10-4.5.4 Elimination and Excretion

In the NTP study, body elimination kinetics was evaluated for rats given the single dose of 10 or 1,000 mg/kg/ body weight (NTP, 1992). Elimination kinetics was found to be biphasic. Furthermore, feces were found to be the major route of glyphosate elimination at all dose levels tested; approximately 62 to 69% of the administered dose was excreted in the feces (NTP, 1992). Less than 0.3% of an administered dose was recovered as CO_2 in expired air. In rats given glyphosate at 10 or 1,000 mg/kg, the vast majority (97.5%) of the administered dose was excreted as unchanged parent material. In the first multiple dosage study (1 to 100 mg/kg body wt/day for 14 days), urinary excretion accounted for less than 10% of the dosage, while 80 to 90% of the administered material was excreted in feces (NTP, 1992). The excreted material was shown to be unmetabolized glyphosate. Upon glyphosate withdrawal, the amount of glyphosate in excreta decreased substantially, but reached a plateau temporarily after 4 days. This plateau may be attributed to redistribution of mobilized tissue residues.

B10-4-6 Exposure Limits

Table B10-11 Existing RfD Values for Glyphosate Exposures

Reference Dose (mg/kg/day)	Route of Exposure	Reference	Endpoint	Study	Reference	NOEL (mg/kg/day)	Uncertainty Factor
Acute/Short-term (1-7 days)							
Not required (Acute RfD)	Oral	U.S. EPA, 1993	Acute oral toxicity data for the technical material are in Toxicity Category III	--	--	--	--
Not required	Dermal	U.S. EPA, 1993	No toxicological endpoints to indicate the necessity of dermal studies	--	--	--	--
Not required	Inhalation	U.S. EPA, 1993	Glyphosate is non-volatile	--	--	--	--
0.2[d]	Oral	PSD, 2007	--	--	E.U. Annex I	--	--
Not required (Acute RfD)	Oral	PSD, 2007	--	--	E.U. Annex I, JMPR Endorsed	--	--
Intermediate-term (7 days- Several months)							
Not required	Dermal	U.S. EPA, 1993	No toxicological endpoints to indicate the necessity of dermal studies	--	--	--	--
Not required	Inhalation	U.S. EPA, 1993	Glyphosate is non-volatile	--	--	--	--
Long-term (6 months to lifetime)							
Not required	Dermal	U.S. EPA, 1993	No toxicological endpoints to indicate the necessity of dermal studies	--	--	--	--
Not required	Inhalation	U.S. EPA, 1993	Glyphosate is non-volatile	--	--	--	--
0.03[c]	Oral	Health Canada, 1987, 2004	Reduced body weight gain	2 years rat feeding/oncogenicity study	Lankas, 1981	3.0	100
0.1	Oral	U.S. EPA, 1990	Increased incidence of renal tubular dilation in F3 offspring	3 generation rat reproduction study	Monsanto Company, 1981	10	100
0.3[a]	Oral	WHO, 1986	Maternal mortality	26 months feeding study in the rat	WHO, 2004	31	100
1.0[a,b]	Oral	WHO, 2004	Salivary gland alterations	2 years study of toxicity and carcinogenicity in rats	WHO, 2004	100	100

Table B10-11 Existing RfD Values for Glyphosate Exposures

Reference Dose (mg/kg/day)	Route of Exposure	Reference	Endpoint	Study	Reference	NOEL (mg/kg/day)	Uncertainty Factor
2.0	Oral	U.S. EPA, 1993	Diarrhea, nasal discharge and death	Rabbit developmental toxicity study	Rodwell *et al*., 1980b	175	100

[a] Acceptable Daily Intake (ADI) - The amount of a chemical a person can be exposed to on a daily basis over an extended period of time (usually a lifetime) without suffering deleterious effects.

[b] Value derived for glyphosate with its metabolite AMPA taken into account.

[c] Neglible daily intake (NDI).

[d] Acceptable Operator Exposure limit (AOEL).

A chronic TRV of 1.0 mg/kg/day (WHO, 2004) was used for the risk assessment purposes of this report. This TRV was derived using a NOAEL of 100 mg/kg bw/day and adjusted by a uncertainty factor of 100 (10 for interspecies variation and ×10 for intraspecies variation). An acute oral RfD of 0.2 mg/kg/day, based on an acceptable operator exposure limit, was selected for risk assessment purposes of this report.

Glyphoste is absorbed poorly through the dermal exposure pathways (U.S. EPA, 1993). The U.S. EPA stated that a dermal penetration study (Guideline 85-2) with technical grade glyphosate was not being required because there were no toxicological endpoints to indicate this study was necessary (U.S. EPA, 1993).

The acute oral and dermal toxicity data for the technical glyphosate has been grouped in Toxicity Category III and IV by the U.S. EPA. Furthermore, the U.S. EPA (1993) has waived the acute inhalation toxicity studies for technical glyphosate because it was non-volatile. There were also adequate inhalation studies with end-use glyphosate products showing low toxicity (U.S. EPA, 1993).

B10-5.0 ENVIRONMENTAL FATE AND EXPOSURE

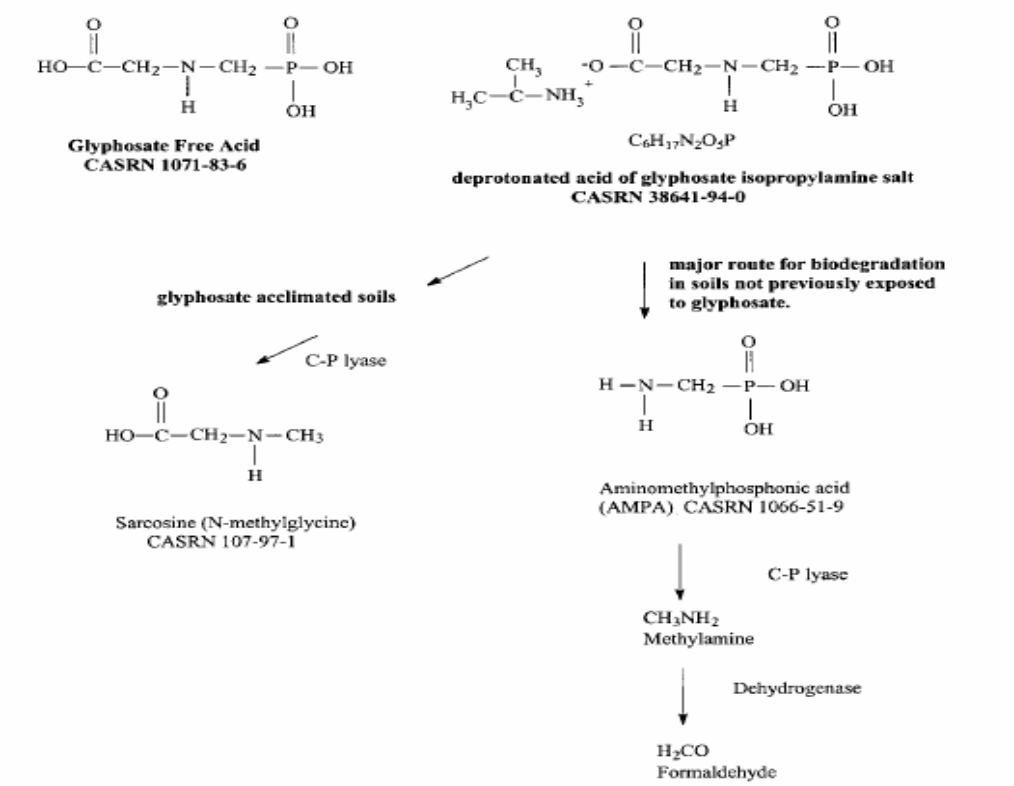

Figure B10-2 Simplified Pathway for Degradation of Glyphosate in the Terrestrial Environment, Adapted from Williams *et al*., 2000

B10-5.1 Air

B10-5.1.1 Transport and Partitioning

Glyphosate is usually released into the atmosphere as an aerosol during aerial spraying and it will be removed by gravitational settling (HSDB, 2003).

B10-5.1.2 Transformation and Degradation

Due to its ionic state in water, glyphosate would not be expected to volatilize from water or soil. However, as an aerosol sprayed aerially, in the atmosphere glyphosate may degrade by photolysis. (HSDB, 2003)

Table B10-12 Half-life of Glyphosate in Air

Conditions	Half-life	Reference
Mean half-life	1 week	Mackay *et al.*, 1997
Range half-lives	100-300 hours	Mackay *et al.*, 1997

B10-5.2 Water

B10-5.2.1 Transport and Partitioning

When glyphosate enters water as runoff, it adsorbs strongly to sediment and particulate matter in the water column. Sediments adsorb glyphosate from flowing water; once adsorbed, it is not readily eluted. However, suspended sediment is not a major mechanism for glyphosate transport in rivers (Feng *et al*., 1990). Glyphosate may also form insoluble complexes with metal ions and precipitate. Evidence from microcosm studies suggests that sediment adsorption and/or biodegradation will lead to glyphosate dissipation in aquatic systems (Goldsborough *et al*., 1989). Hence, glyphosate levels in sediment will rise at first and then fall to very low or undetectable levels (Goldsborough *et al*., 1989).

Gyphosate has been detected in ground water at very low levels (HSDB, 2003). In a survey of farm wells in Ontario, Canada performed between 1986 and 1987, glyphosate was not detected in any wells (Frank, 1990). However, glyphosate was only used in 28 farms between 1986 and 1987 (Frank, 1990).

B10-5.2.2 Transformation and Degradation

Glyphosate is stable to hydrolysis reactions at pH 3, 6 and 9 at either 5 or 35ºC (Brightwell *et al*., 1978). Glyphosate is stable to photodegradation at pH 5, 7, and 9 buffered solutions under natural sunlight (Castle *et al*., 1990).

Table B10-13 Half-life of Glyphosate in Water

Conditions	Half-life	Reference
Mean half-life	2 month	Mackay *et al.*, 1997
Range half-lives	1,000-3,000 hours	Mackay *et al.*, 1997
Degradation *via* microbes	12 days – 10 weeks	JW, 2005
Hydrolysis	35 days	JW, 2005

B10-5.3 Sediment and Soil

B10-5.3.1 Transport and Partitioning

The mobility of glyphosate in soil applied aerially to forests, fields, and other land, is limited and is affected by pH and phosphate levels, as well as by soil type (Spankle *et al*., 1975). Glyphosate will adsorb strongly to organic matter and clay in soil, and it could also form insoluble complexes with metal ions in the soil. Its soil adsorption coefficient (K_{oc}) range from 884 to 60,000 (JW, 2006). Glyphosate is strongly adsorbent to the upper layers of soil and will have a low propensity for leaching (Feng *et al*., 1990). Glyphosate residues dissipated with a half-life of 45 to 60 days. After 360 days, residues levels will be 6 to 18% of initial levels (Feng *et al*., 1990). Hence, glyphosate is moderately persistent in soil, high water solubility, but low movement due to adsorption to organic matter (JW, 2005).

B10-5.3.2 Transformation and Degradation

Glyphosate is predominantly degraded in the soil by microorganisms (Figure. 1). Glyphosate will break down to harmless natural substances such as carbon dioxide and phosphonic acid (Williams *et al*., 2000). Furthermore, glyphosate also have a photolysis rate of 101 days in soil (JW, 2006).

Table B10-14 Half-life of Glyphosate in Soil

Conditions	Half-life	Reference
Mean half-life	2 month	Mackay *et al.*, 1997
Range half-lives	1,000-3,000 hours	Mackay *et al.*, 1997
--	1-174 days	JW, 2005

B10-5.4 Other Environmental Media

B10-5.4.1 Transport and Partitioning

Glyphosate is not expected to bioconcentrate in aquatic organisms due to its solubility in water (Lyman *et al.*, 1982). It has a bioconcentration factor of 0.04 to 0.05 (JW, 2006).

B10-5.4.2 Transformation and Degradation

Refer to Section B10-4.5 Toxicokinetics.

B10-5.5 Plant Residues and Metabolism

Glyphosate enters plants through their foliage and moves throughout the plant and into the root systems (CPCR, 1992; WASSA, 1989). Therefore, all parts of the plants treated with glyphosate may contain the herbicide (CPCR, 1992). However glyphosate is applied to crops before their emergence as otherwise crop destruction would result (CPDR, 1992; WASSA, 1989). H ence, the uptake through the root system is precluded by soil inactivation (WASSA, 1989). Therefore, crops should not contain glyphosate.

However, with the emergence of Roundup® ready crops, methods of application for glyphosate containing herbicides have been broadened. Farmers no longer need to spray on pre-emergent crops to prevent crop damage. They may choose to spray on crops once they have emerged, and once more prior to harvest to eliminate all unwanted weeds. Since Roundup® ready crops will not metabolize glyphosate into metabolites, there could be a possibility that these plants may contain traces of glyphosate. Williams *et al.* (2000), reported that glyphosate-tolerant soybeans treated with maximum levels of allowed glyphosate applications contained highest level of glyphosate residues compared to other type of plants.

B10-6.0 SUMMARY

Glyphosate is a broad-spectrum, nonselective systemic herbicide used for the control of annual and perennial plants (EXTOXNET, 1996). Being inherently an acid, glyphosate is usually used in a salt form (most commonly the isopropylamine salt). Once glyphosate is absorbed by plants, it will carry out the inhibition of shikimic acid pathways and hence stalling the production of aromatic amino acids (WHO, 1996). The shikimic acid pathway is absent from animals and may account for the low toxicity of glyphosate in mammals (WHO, 1996). However, mortality in animals due to very high glyphosate administrations will still occur. This occurs since glyphosate may alter mitochondrial activity and lead to the uncoupling of oxidative phosphorylation in mammals (WHO, 1996). Between 1989 and 2004 approximately 13,000 kg of glyphosate was applied over an area of 4,700 ha at CFB Gagetown (JW, 2006).

Glyphosate has low inherent toxicity, as most of the toxicity studies showed minimal effects even at the highest doses tested. There is some evidence of chronic systemic effects and some signs of developmental impairment when animals were exposed to glyphosate. Maternal toxicity, based on reduced body weight gains and systemic effects, was also observed. In 1993, U.S. EPA classified glyphosate as a non-carcinogen in humans (Group E) (U.S. EPA, 1993).

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